Innova Results - Preview
November 10th 2020
Lateral flow antigen test evaluation: PHE Porton Down & Oxford collaboration - status @ 31.10.20

**Phase 1**
- Scanning & selection
- 52 products identified so far by DHSC for Phase 2 evaluation at PHE Porton Down
- 11 products in process of being ordered/shipped to PHE Porton Down

**Phase 2**
- “Futility Test” at PHE Porton Down
- 41 products delivered to PHE Porton Down
- 39 futility tests performed
- 2 futility tests to be carried out w.c. 2 November
- 10/39 products tested so far have passed and progressed to Phase 3A

**Phase 3**
- 3A: lab testing at PHE Porton Down
- 5 products passed and progressed to Phase 3B Field Testing
- 2 products failed Phase 3A
- 3 products to start Phase 3A on receipt of kits from supplier
- 3A Sensitivity x200 true positives Specificity x1,000 true negatives
- 3B Sensitivity 300 positives Specificity 500 negatives
- 4 products have been evaluated, 1 now being piloted in Schools and Universities (3 others to follow)
- 1 product is currently being evaluated

- Positive cases identified through Lighthouse RTS sites
- Negative cases from staff volunteers at PHE Porton Down & staff and patients at Oxford – completed for 4 products

DHSC Ministerial commission received
15 August, first Phase 2 testing started at PHE Porton Down within 48 hrs
Approximately 17K individual samples processed in the lab so far
Examples of Innova Results: Numbers Refer to Viral Load CT values
### Number of evaluations performed. Kit failure rate and PCR results

<table>
<thead>
<tr>
<th>Innova LFD evaluation phase</th>
<th>LFD failures</th>
<th></th>
<th>LFD successes</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>fail//total</td>
<td>%</td>
<td>PCR+</td>
<td>PCR-</td>
<td>PCR-void</td>
<td>PCR-not done</td>
<td>TOTAL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 2 negatives</td>
<td>0/72</td>
<td>0.00%</td>
<td>0</td>
<td>72</td>
<td>0</td>
<td>0</td>
<td>72</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 2 positive dilution series</td>
<td>0/215</td>
<td>0.00%</td>
<td>215</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>215</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 3a positives</td>
<td>12/212</td>
<td>5.67%</td>
<td>199</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>200</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 3a negatives</td>
<td>50/1040</td>
<td>4.84%</td>
<td>0</td>
<td>990</td>
<td>0</td>
<td>0</td>
<td>990</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 3b FALCON (Dry swabs- field)</td>
<td>28/296</td>
<td>9.56%</td>
<td>252</td>
<td>15</td>
<td>1</td>
<td>0</td>
<td>268</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 3b FALCON (Dry swabs- lab)</td>
<td>9/221</td>
<td>4.06%</td>
<td>204</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>212</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 3b FALCON (VTM swabs)</td>
<td>9/166</td>
<td>5.50%</td>
<td>142</td>
<td>14</td>
<td>1</td>
<td>0</td>
<td>157</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 4 hospital staff</td>
<td>17/375</td>
<td>4.55%</td>
<td>2</td>
<td>346</td>
<td>10</td>
<td>0</td>
<td>358</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 4 armed forces</td>
<td>6/163</td>
<td>3.71%</td>
<td>46</td>
<td>111</td>
<td>0</td>
<td>0</td>
<td>157</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 4 PHE staff</td>
<td>19/231</td>
<td>8.28%</td>
<td>0</td>
<td>212</td>
<td>0</td>
<td>0</td>
<td>212</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 4 school 1</td>
<td>311/2166</td>
<td>14.42%</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1855</td>
<td>1855</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 4 school 2 + 3 + 4</td>
<td>14/2146</td>
<td>0.65%</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2132</td>
<td>2132</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 4 COVID-19 testing centre</td>
<td>27/1973</td>
<td>1.37%</td>
<td>139</td>
<td>1789</td>
<td>18</td>
<td>0</td>
<td>1946</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>502/9276</td>
<td>5.40%</td>
<td>1199</td>
<td>3557</td>
<td>31</td>
<td>3987</td>
<td>8774</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Kit failure rates ranged from 0.65% to 16.8% (P<0.00001; chi(2)=530)
This suggests that there might be differences between batches.
### Specificity (against conventional PCR)

<table>
<thead>
<tr>
<th>Evaluation Phase</th>
<th>Test Center</th>
<th>False positives/total</th>
<th>False positives 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 2 evaluation</td>
<td>Porton</td>
<td>0/72</td>
<td>0.00% (0.00-5.07)</td>
</tr>
<tr>
<td>Phase 3a evaluation- negative samples</td>
<td>Porton</td>
<td>0/940</td>
<td>0.00% (0.00-0.41)</td>
</tr>
<tr>
<td>Phase 4 evaluation- armed forces</td>
<td>Porton</td>
<td>0/105</td>
<td>0.00% (0.00-3.53)</td>
</tr>
<tr>
<td>Phase 4 evaluation- PHE staff</td>
<td>Porton</td>
<td>0/209</td>
<td>0.00% (0.00-1.80)</td>
</tr>
<tr>
<td>Phase 4 evaluation- hospital staff</td>
<td>Oxford</td>
<td>1/329*</td>
<td>0.30% (0.05-1.70)</td>
</tr>
<tr>
<td><strong>Subtotal (Experienced laboratory workers)</strong></td>
<td></td>
<td>1/1655</td>
<td>0.06% (0.02-0.3)</td>
</tr>
<tr>
<td>Phase 4 evaluation- school 1</td>
<td>Local</td>
<td>9/1855**</td>
<td>0.49% (0.26-0.92)</td>
</tr>
<tr>
<td>Phase 4 evaluation- school 2 + 3 + 4</td>
<td>Local</td>
<td>7/2130**</td>
<td>0.33% (0.16-0.68)</td>
</tr>
<tr>
<td>Phase 4 evaluation- COVID-19 testing centre</td>
<td>Local</td>
<td>5/1327***</td>
<td>0.38% (0.16-0.88)</td>
</tr>
<tr>
<td><strong>Subtotal (Locally trained)</strong></td>
<td></td>
<td>21/5312</td>
<td>0.39% (0.24-0.60)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td>22/6967</td>
<td>0.32% (0.21-0.47)</td>
</tr>
</tbody>
</table>

Laboratory-based testing testing (0.06%) compared to Field Testing 0.39% P=0.041. Many false positives had ‘weak’ bands and were negative with retesting with LFD.
**Limit of Detection**
saliva spiked with virions (plaque forming units*)

<table>
<thead>
<tr>
<th>PFU/ml</th>
<th>Ct equivalent</th>
<th>Positive LFD /total LFD tests</th>
<th>% positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>100000</td>
<td>16</td>
<td>20/20</td>
<td>100.0</td>
</tr>
<tr>
<td>10000</td>
<td>19</td>
<td>25/25</td>
<td>100.0</td>
</tr>
<tr>
<td>1000</td>
<td>23.7</td>
<td>65/65</td>
<td>100.0</td>
</tr>
<tr>
<td>390</td>
<td>25.2</td>
<td>5/5</td>
<td>100.0</td>
</tr>
<tr>
<td>100</td>
<td>25.5</td>
<td>63/65</td>
<td>95.5</td>
</tr>
<tr>
<td>40</td>
<td>28.5</td>
<td>3/5</td>
<td>60.0</td>
</tr>
<tr>
<td>20</td>
<td>29.3</td>
<td>0/5</td>
<td>0.0</td>
</tr>
<tr>
<td>10</td>
<td>30.2</td>
<td>0/5</td>
<td>0.0</td>
</tr>
<tr>
<td>5</td>
<td>31</td>
<td>0/5</td>
<td>0.0</td>
</tr>
<tr>
<td>2.5</td>
<td>31.7</td>
<td>0/5</td>
<td>0.0</td>
</tr>
<tr>
<td>1.2</td>
<td>32.5</td>
<td>0/5</td>
<td>0.0</td>
</tr>
</tbody>
</table>

*1 plaque forming unit is approximately 1000 RNA copies.
Viral Antigen Detection in VTM from virus obtained from clinical Samples

• Patients with Covid19 had swabs taken and placed in viral transport medium and transported to Porton for PCR and LFD testing
• 200 samples from freezer in Oxford collected from March/April 2020
• Samples collected from individuals tested positive in RTS and recalled for (2-4 days later).
  • 1 swab taken and transported in viral transport medium for qPCR and LFD testing in Porton
  • Second swab with no viral transport medium (‘dry’ swab)
Antigen Detection by Viral Load
(Sample placed in Viral Transport Medium)
Relationship between Antigen Detection with Viral Load

Model: Logistic Regression
Dry Swab Results

• Swabs are used according to manufacture’s instructions. PCR could not be reliably measured from these swabs

• Trained Health Care Professionals
  • 197 swabs were transported to Porton at 4degC for LFD testing
    • PHE Porton Laboratory Scientists
  • 126 swabs were tested local at RTS with LFD
    • Fully Trained Health Care Professionals (Clinical Trial Researchers)

Combined Results are shown.

Interim analysis 4th Novembt
Proportion Individuals Ag Positive by their Viral Load

Individuals swabbed 2-4 days after first positive test: LFD used by trained health-care professional
Conclusions on Relationship between LFD

• ‘Dry Swabs’ perform better than swabs placed in viral transport medium

• LFD detects >95% of individuals with viral loads > median viral load (CT=26 (Porton Cobas result)).

• LFD Detects, overall, 76.7% of all PCR+ cases
Field Trial Repeated

- Consecutive Individuals arriving at RTS with high Covid19 prevalence were invited to participate
  - Overall Prevalence of Ag positivity 14%
- LFD performed locally by self-trained non-health care professionals.
- Parallel swab sent to Lighthouse for PCR.
- 1365 complete results available (372 PCR Positive)
- Proportion of PCR+ Positive individuals with detectable antigen compared to the previous study.
Effect of Training on Proportion Ag Detected
All PCR positive individuals

chi²(2) = 30.1 Pr < 0.000001

Training Level of LFD Operative
Self-Trained (214/372)
Fully-trained HCW (92/126)
Lab Scientist (156/197)
Overall (462/695)
Antigen detection in Asymptomatic Individuals

- Symptoms are available from 170 individuals swabbed at the RTS,
  - tested by a fully-trained HCW
- Asymptomatic: 77% Ag positive (33/43)
- Symptomatics: 79% Ag positive (100/127)
  [Odd Ratio 1.12 (0.44 – 2.71) P=0.78]
Summary

- Overall results:
  - Kit Failures – 5%
  - Specificity – 99.65-99.9%
    - Early results suggest that false positives are often ‘faint bands’ and test negative with a repeat LFD.
    - Sensitivity (against PCR) is 77% when used by competent individuals
      - >95% sensitivity against high viral loads (CT<26) (representing about half the individuals)
- There is good evidence that performance varies according to center.
- There is no evidence that the presence or absence of symptoms affects the ability to detect antigen
- Simple modelling suggests that it is possible that quarantining individuals with positive LFD will reduce the force of transmission by c90%
Current control methods for Covid19

• Decrease rate of transmission from all infectious individuals (background)
  • Universal social distancing
  • Use Face marks / hand washing
  • Avoidance of skin-to-skin contact (outside households)

• Quarantine of individuals at ‘high risk’ of being infectious
  (‘guilty by association’ – unpopular and expensive)
    • Lock down of regions with high disease incidence 1000
    • Quarantine of contacts of known positives 70

• Individual assessments
  • Quarantine of individuals with symptoms suggestive of covid19 70
  • Quarantine of known PCR+ individuals (regardless of viral load) 20
  • Quarantine PCR+ at the time of onset of covid symptom 5

• Positive Lateral flow antigen <5
Challenges for Lateral Flow Antigen Tests

- Direct data on infectiousness with different viral loads
- Many different kits and swabs may cause confusion
- Need for resilience to minor divergences from the protocol
- Reliable training modules and assurance of competence of users
- Reliable recording of results (? aided by photoimaging software)
- Early feedback suggests that uptake will depend on
  - Lifting of some restrictions following negative tests.
  - Self (or at least very local) testing
- Generous supply of testing kits.