ICF commentary

New York TAG core group
• Systems
  – Lab resources – how available are culture facilities?
  – Human resources – how many staff are needed?
• Contamination and “sub-clinical TB” – are all +ve cultures due to tuberculosis?
• Predictive values not sensitivity and specificity
• What is the objective?
  – Morbidity
  – Mortality
  – Transmission
• We do not live in a Platonic world!
How many samples can the lab handle? Do we need to screen?
To exclude TB we need high NPV and we want as many as possible to benefit from IPT.
Sensitivity and specificity of algorithms, stratified by CD4 count (courtesy of Cain CROI 2008)

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>CD4 &lt; 250</th>
<th></th>
<th></th>
<th></th>
<th>CD4 &gt;250</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sens</td>
<td>Spec</td>
<td>NPV</td>
<td>Benefit</td>
<td>Sens</td>
<td>Spec</td>
<td>NPV</td>
<td>Benefit</td>
</tr>
<tr>
<td>Day</td>
<td>97</td>
<td>31</td>
<td>98.9%</td>
<td>28.2</td>
<td>70</td>
<td>39</td>
<td>97.7%</td>
<td>38.7</td>
</tr>
<tr>
<td>Mohammed</td>
<td>92</td>
<td>51</td>
<td>98.3%</td>
<td>46.7</td>
<td>48</td>
<td>67</td>
<td>97.7%</td>
<td>66.6</td>
</tr>
<tr>
<td>Kimerling</td>
<td>92</td>
<td>35</td>
<td>97.5%</td>
<td>32.3</td>
<td>67</td>
<td>54</td>
<td>98.1%</td>
<td>53.4</td>
</tr>
<tr>
<td>Demissie</td>
<td>95</td>
<td>37</td>
<td>98.5%</td>
<td>33.8</td>
<td>81</td>
<td>47</td>
<td>98.8%</td>
<td>46.2</td>
</tr>
<tr>
<td>Pre-IPT</td>
<td>92</td>
<td>51</td>
<td>98.3%</td>
<td>46.7</td>
<td>52</td>
<td>64</td>
<td>97.7%</td>
<td>63.5</td>
</tr>
<tr>
<td>Cough/fever/wt. loss</td>
<td>97</td>
<td>27</td>
<td>98.8%</td>
<td>24.6</td>
<td>81</td>
<td>37</td>
<td>98.4%</td>
<td>36.5</td>
</tr>
</tbody>
</table>
Possible recommendations

• Context is vital, and it may be hard to make one recommendation
• For IPT screening, the main issue is NPV, which must be reported
• For ICF, there is a trade-off between lab workload and PPV, which determines how many samples need to be sent to find one case
Possible recommendations

- In late HIV disease (ARV clinics; home base care settings, CD4<250), the prevalence of culture positivity is 7-10% - we don’t need to screen – everyone needs a culture.

- In earlier HIV (VCT centres; PMTCT; STI clinics; community based screening) prevalence is lower; absence of any cough has a high NPV and allows most people to benefit from IPT; adding other symptoms to the screen improves the NPV a little (but not much), but reduces the number who benefit from IPT substantially.

- Culturing everyone with a cough will overload fragile systems; adding additional symptoms or using cough for >2-3/52 reduces the lab workload but inevitably misses some cases.

- People with symptoms clearly need appropriate referral….
IPT for people infected with HIV

• Early HIV infection

• Late HIV infection
IPT for people infected with HIV

- Early HIV infection
  - No symptoms
  - Short Cough
  - Longer cough +/- others
  - Give IPT
  - Follow up
  - Sputum sample
  - Benefit from IPT
  - TB
  - No symptoms
  - Ongoing care
  - TB found
  - H monotherapy

- Late HIV infection
  - No symptoms
  - Short cough
  - Longer cough +/- others
  - Follow up
  - Sputum sample
  - Ongoing care
  - TB found