Innovative solutions for TB infection screening in decentralised settings

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Diagnostic are essential for universal health coverage

Of people around the world still don’t have access to basic diagnostics

47%
Current TB infection care cascade gaps

• Steps in the cascade associated with greater losses included completion of testing

• Among the reasons associated with losses for completing screening and testing:
  • Health systems issues (lack of human resources, hard to access clinic, health insurance etc.)
  • Social issues (wrong perception of the disease, stigma, mistrust etc.)

Implementation of TB infection Test & Treat is essential for TB elimination.

**TODAY**

1. Care site → TEST
2. Care site → TREAT
3. Patients empirically treated

**TOMORROW**

1. Care site → TEST
2. Care site → TREAT

Acceptability
Test accessibility
We want to bring the potential of QFT-plus performances in low- and middle-income countries and make it accessible to those in need.

QIAreach QuantiFERON-TB
Evolution of QFT Technology

First generation
QuantiFERON-TB

2001: FDA approved

• Measured cell-mediated immunity to tuberculin purified protein derivative (PPD)
• Breakthrough: TST becomes a blood test

Second generation
QuantiFERON-TB Gold

2004: FDA approved

• Liquid antigen version
• Antigens specific for M.tb with 99% specificity
• Clinical benchmark: No cross reactivity with BCG

Third generation
QuantiFERON-TB Gold In-Tube

2007: FDA approved

• Logistical advantage – remote incubation
• Lab benchmark: Scalable
• >1500 peer reviewed publications
• >30 million tests sold

Fourth generation
QuantiFERON-TB Gold Plus (QFT-Plus)

2014: CE-IVD
2017: FDA approved

• Addition of patented CD8 antigens – potential biomarker of intracellular TB burden
• New flexible blood draw options

QIAreach
QuantiFERON-TB*

Expected in Q3 2021

• Using QFT-Plus technology to increase access to IGRA testing in high burden / Low resource settings

* Currently under development
QIAreach Solution to address testing needs in low resource settings

No maintenance required
- No maintenance or calibration of the eHub
- Dust protection guard provided and easy to clean ports

Scalable solution
- Scalable from 1 to 8 samples, up to 24 samples/h

Up to 8 h battery backup
Allow uninterrupted operation when the power goes out or an external power source is not available

Digital and connected
- Optional software for results traceability
- Ability to send the results to LIMS

No cold chain
- No cold chain required for any test components

Portable
- eHub < 1 kg and portable
**BLOOD COLLECTION**

Convenient options

**SEND TO LAB / STIMULATION**

Simple & fast T cell incubation
Stimulation with undiluted whole blood
37°C 16-24h

Transportation
Up to 3 days at 4-27°C

**IGRA TEST**

4th generation T cell stimulation technology

TB infection testing made easy

Plasma
Up to 28 days at 2-8°C or -20°C

Centrifugation
15 min at 2000 to 3000 RCF (g)

**RESULTS & INTERPRETATION**

High quality results

ELISA

QuantiFERON®-TB with QIAreach software

Optional centrifugation

QIAreach QuantiFERON®-TB

Transportation
Up to 3 days at 4-27°C

Simple & fast T cell incubation
Stimulation with undiluted whole blood
37°C 16-24h

Centrifugation
15 min at 2000 to 3000 RCF (g)

Optional centrifugation
QIAreach QuantiFERON-TB is an accurate solution for diagnosing TB infection

Clinical performances (Japan)

**Objective**
- To compare the QIAreach QuantiFERON-TB (QIAreach QFT) vs. QuantiFERON-TB Gold Plus assay (QFT-Plus) to detect tuberculosis (TB) infection;
- To evaluate diagnostic sensitivity of QIAreach QFT using active TB as surrogate for TB infection;
- To preliminarily evaluate QIAreach QFT in immunocompromised individuals

<table>
<thead>
<tr>
<th>Healthy controls</th>
<th>Active TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>QFT-Plus positive</td>
<td>0</td>
</tr>
<tr>
<td>QFT-Plus negative</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
</tr>
</tbody>
</table>

**Results**
- This study demonstrates that QIAreach QFT test has high clinical performance: 100% sensitivity, 97.6% specificity, and **98.8% overall concordance using QFT-Plus as the reference standard**
- There is a statistically significant relationship between levels of IFN-γ in plasma of active TB patients and TTR suggesting that TTR could be used as a surrogate marker of IFN-γ concentration in plasma when using QIAreach QFT assay
- Seven cases in the active TB group who were immunocompromised (CD4 <200/μL) returned positive results on QIAreach QFT

**Conclusion**

Agreement between QuantiFERON-TB Gold Plus and QIAreach QuantiFERON-TB: Performance of QIAreach QuantiFERON-TB (QIAreach QFT) was compared to QuantiFERON-TB Gold Plus (QFT-Plus) in a population with a mix of risk factors for TB infection. Specimens were collected from a total of 4 sites. All QFT-Plus ELISA testing and QIAreach QFT testing was performed at a single site. A total of 225 samples were included in the final performance comparison.

<table>
<thead>
<tr>
<th>Counts</th>
<th>Frequency</th>
<th>Agreement</th>
<th>Upper 95% CI</th>
<th>Lower 95% CI</th>
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</thead>
<tbody>
<tr>
<td>OPA*</td>
<td>219/225</td>
<td>97.3%</td>
<td>99.0%</td>
<td>94.3%</td>
</tr>
<tr>
<td>PPA</td>
<td>71/75</td>
<td>94.7%</td>
<td>98.5%</td>
<td>86.9%</td>
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<tr>
<td>NPA</td>
<td>148/150</td>
<td>98.7%</td>
<td>99.8%</td>
<td>95.3%</td>
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</tbody>
</table>

OPA: Overall percent agreement; PPA: Positive percent agreement; NPA: Negative percent agreement.

* When factoring in 15 QFT-Plus indeterminate results, the OPA between QFT-Plus and QIAreach QFT is 91.3% (95% CI: 86.9 – 94.5%).

Conclusion

- In a preliminary performance evaluation versus QFT-Plus (n = 225), QIAreach QFT showed an OPA of 97.3% (95% CI: 99.0 – 94.3%), with a PPA of 94.7% (95% CI: 98.5 – 86.9%) and an NPA of 98.7% (95% CI: 99.8 – 95.3%).
- Significant correlation was observed between the QIAreach QFT time to result and IU/ml responses of QFT-Plus-positive samples.
- QIAreach QFT shows a high level of agreement with QFT-Plus and has the potential to overcome key hurdles for TB screening in high-burden, low-resource settings.
Usability study (Zambia)

Objective

Assess usability the QIAreach QFT and training needs for the assay implementation were assessed across three domains: (1) effectiveness, (2) efficiency, and (3) user satisfaction

Preliminary performance assessment

Effectiveness
Pass rate of 4 tasks

Efficiency
Completion of all tasks in less than 1 hour

Satisfaction
Likert scale 1-5

Conclusion

The characteristics of the platform together with our usability finding make the QIAreach-QFT assay suitable to be implemented in the remote area where limited infrastructure has hampered the accessibility of IGRA technologies to those in needs.
QFT-Plus demonstrated comparative cost-effectiveness with skin-based tests; high potential for QIAreach to exceed

**Cost-effectiveness of newer technologies for the diagnosis of Mycobacterium tuberculosis infection in Brazilian people living with HIV**

Ricardo E. Steffen, Marcia Pinto, Afranio Kritski & Anete Trajman

*Scientific Reports* 10, Article number: 21823 (2020)  Cite this article

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost</th>
<th>Incremental cost</th>
<th>QALY</th>
<th>Incremental QALY</th>
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</thead>
<tbody>
<tr>
<td>Diaskintest</td>
<td>884.70</td>
<td></td>
<td>8.386</td>
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<tr>
<td>EC skin test</td>
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<td>1.90</td>
<td>8.386</td>
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<td>QFT-Plus</td>
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<td>17.40</td>
<td>8.385</td>
<td>– 0.00055</td>
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<tr>
<td>TST PPD RT 23</td>
<td>925.50</td>
<td>40.80</td>
<td>8.356</td>
<td>– 0.02967</td>
</tr>
</tbody>
</table>

- Some operational aspects can have great impact on final test costs and, consequently, its cost-effectiveness
- No societal costs were included (indirect costs, loss of productivity or cost of death)
- No cost-effectiveness of opportunity cost were included
QIAreach – QFT: Hierarchy of effectiveness

1. **Social Impact**
   - Innovative technologies that work for poorer population who would otherwise be disadvantaged by the workings of the «inverse care law»

2. **Cost-effectiveness**
   - Price is what you pay, value is what you get.
   - QIAreach-QFT has the potential to exceed cost-effectiveness of skin-based test

3. **Operational aspects**
   - Ease to use, scalable and accessible to the lower level of health system

4. **Clinical performance**
   - Better performance in term of sensitivity and specificity compared to Skin-based tests