ERJ open research
THE BEST IN OPEN ACCESS BASIC, TRANSLATIONAL & CLINICAL RESPIRATORY RESEARCH

Early View

Research letter

Assessing usability of QIAreach QuantiFERON® platform in a high Tuberculosis prevalence low-resource setting

Conceptor Kaaba, Maria Ruperez, Barry Kosloff, Nduku Ndunda, Kwame Shanaube, Helen Ayles

Please cite this article as: Kaaba C, Ruperez M, Kosloff B, *et al*. Assessing usability of QIAreach QuantiFERON® platform in a high Tuberculosis prevalence low-resource setting. *ERJ Open Res* 2021; in press (https://doi.org/10.1183/23120541.00511-2021).

Assessing usability of QIAreach QuantiFERON® platform in a high Tuberculosis prevalence low-resource setting

Conceptor Kaaba[1], Maria Ruperez[2], Barry Kosloff[1,2], Nduku Ndunda[3], Kwame Shanaube[1], Helen Ayles[1,2] on behalf of the TREATS Study Team

Affiliations: [1] Zambart, Lusaka, Zambia; [2] London School of Hygiene and Tropical Medicine, London, UK; [3] Cepheid Middle East, a Danaher company FZ LLC, Dubai, UAE

Correspondence: Conceptor Kaaba, Zambart, Lusaka, Zambia.
Email: Conceptor@zambart.org.zm

Key words:

Tuberculosis,

TB infection,

QIAreachTM QuantiFERON-TB,

Tuberculosis diagnosis

ABSTRACT

Background

We aimed to assess the usability of QIAreach QuantiFERON® platform in a high Tuberculosis prevalence low-resource setting. Assay usability was assessed across 6 laboratories in Zambia.

Methods

Usability of QIAreach QuantiFERON and training needs for assay implementation were assessed across three domains: effectiveness, efficiency, and user satisfaction. Nine laboratory workers participated in the study. For each task, metrics on success (pass, fail, pass with hints), total task time, and ease of use rating (five-point Likert scale) were collected.

Results

Overall tasks completion rate was from 89-100%. 1/9 participants, could not understand software instructions. Average time from set up to results ranged from 22 to 40 minutes. Users with experience performing the QFT-plus assay completed the test faster than users without experience, 26 minutes versus 35 minutes. Two participants had difficulty loading the sample on QIAreach eStick. Two participants could not adjust the pipette to the required volume of 150µL. Two participants did not mix the test sample properly. One participant transferred the sample buffer twice and added insufficient plasma to the sample processing tube. Two participants added the test sample to eStick sample port many times. One participant added wrong information in the software. User satisfaction ranged from 2 to 5.

Conclusion

The QIAreach QFT assay is suitable to be implemented in remote areas with limited infrastructure. Further studies are needed to establish assay's performances as well as the feasibility of introducing this new assay at larger scale to improve TB control in regions with limited infrastructure.

INTRODUCTION

The World Health Organization (WHO) estimates that 1.8 billion people—close to one quarter of the world's population are infected with Mycobacterium tuberculosis (*Mtb)* [1]. Despite substantial declines in TB incidence over the last decade, Zambia still has the seventh highest TB incidence in sub-Saharan Africa and remains one of the 30 WHO high TB burden priority countries [2]. In 2019, there were approximately 59 000 new individuals with active TB disease in Zambia (incidence rate of 333 per 100 000 per year), which resulted in 15 400 TB-related deaths, of which 62% were among PLHIV [2].

Management of TB infection represents a neglected component of national tuberculosis (TB) programmes [3]. A reliable diagnosis followed by successful TB preventive therapy is crucial to reach the End TB strategy goals and to eliminate TB [4, 5]. Tuberculin Skin Test (TST) and Interferon Gamma Release Assays (IGRAs) are the main diagnostic tools for TB infection diagnosis, however, both present strengths and limitations [6]. The TST requires two visits, is not easy to administer and is influenced by conditions, including BCG vaccination, that can reduce the skin reactivity [7–9]. IGRA demonstrated to overcome the drawbacks of TST [10]. To date, two IGRA tests are recommended by the World Health Organization (WHO): T-SPOT®.TB (Oxford Immunotec, Abingdon, UK) and QuantiFERON®-TB Gold Plus (QFT-Plus, QIAGEN, Hilden, Germany) [11].

The QFT-Plus is a new generation IGRA that uses innovative antigens that elicit both CD8 and CD4 T cell responses, enabling a more comprehensive assessment of cell-mediated immune response to TB infection [12, 13]. Need for established laboratory infrastructure and trained personnel represent one of the main barriers for the implementation of QFT plus in low resource settings [14]. QIAGEN has recently developed a new lateral flow immunoassay for the diagnosis of TB infection, the QIAreach QuantiFERON-TB (QIAreach™ QFT) assay. The QIAreach™ QFT is a semi-automated assay that uses the same TB2 tube of QFT-Plus to detect IFN-y in plasma released from both CD4 and CD8 T cells. After incubation, without the need to perform enzyme-linked immunosorbent assay (ELISA), the sample is analyzed on a portable platform, eHubs, performing up to eight tests in 20 minutes time, providing a final qualitative result (positive, negative, error) [15, 16].

In this paper we aimed to assess the usability of QIAreach QuantiFERON® platform in a high tuberculosis prevalence low-resource setting. We report the results of the QIAreach QFT assay usability study conducted across 6 laboratories in Zambia using whole blood collected from participants enrolled in the Tuberculosis Reduction through Expanded Antiretroviral Treatment and Screening (TREATS) infection cohort study.

METHODS

The study was conducted across six laboratories situated in four provinces of Zambia. The six laboratories were the Zambart Central Laboratory located in Lusaka (Lusaka province) and five regional laboratories located in Livingstone (Southern province), Choma (Southern province), Kabwe (Central province), Ndola (Copperbelt province) and Kitwe (Copperbelt province). The selected laboratories were purposively and conveniently chosen due to their involvement with the TREATS Infection cohort study in Zambia. Usability of the QIAreach QFT and training needs for the assay implementation were assessed across three domains: effectiveness, efficiency, and user satisfaction.

To achieve a valid preliminary data on usability, nine laboratory workers (two laboratory assistants, three laboratory scientists and four laboratory technicians) were purposively selected based on their job title and laboratory experience [17]. Operators were provided with the following: the QIAreach QFT eHub, a laptop computer with pre-installed QIAreach QFT software (optional; for connectivity with laboratory reporting systems only), QIAreach QFT test kits and diluent buffer, QIAreach QFT package insert, an adjustable standard laboratory pipette capable of dispensing 150µl and disposable pipette tips, and TB2 tube with harvested plasma. During the usability testing, operators were asked to read the instruction outlined in the package insert, and complete four tasks using both the eHubs and software. The operators did not receive any initial aid from the observer. If participants struggled with a task, the observer provided hints to help users through the process.

For each task, metrics on success (pass, fail, pass with hints), total task time, and ease of use rating (five-point Likert scale) were collected. Total task time is an indicator of user efficiency. Shorter task times on subsequent identical tasks are indicative of learnability. Common errors were collected after assay completion and categorized in those issues that prevent user from completing the assay and those that increase the risk of human error during the task.

Written consent was obtained from eligible participants, who agreed to take part in the TREATS infection cohort at enrolment and there was no additional consent obtained for this study.
Ethics approval for the Infection cohort was obtained from the Biomedical Research Ethics Committees of the University of Zambia, Lusaka, Zambia and the London School of Hygiene & Tropical Medicine, London, UK.

RESULTS

Overall tasks completion rate was from 89-100%. Table 1 provides a visual representation of pass and fail rates of each tasks. One participant out of nine, could not understand the software instructions in the QIAreach QFT package insert. However, the participant was able to complete the assay manually. Two participants had difficulty loading the sample on the QIAreach eStick. The average time from set up to results ranged from 22 to 40 minutes. Users with experience performing the QFT-plus assay completed the test faster than users without experience, 26 minutes versus 35 minutes. Two participants were unable to adjust the pipette to the required volume of 150µL. Two participants tried to mix the test sample up and down without the disposable tip on the pipette. One participant transferred the sample buffer twice and added insufficient plasma to the sample processing tube. Two participants added the test sample to the eStick sample port many times. One participant added wrong information in the software.

On average, participants had seven years of laboratory experience. When asked about previous experience with IGRA technology, six operators reported experience using the QuantiFERON Gold-In-Tube/Plus.

DISCUSSION

The QIAreach QFT test provides a significant contribution to global TB infection diagnostics. The usability assessment of the QIAreach QFT represents an important aspect that affect user acceptance and the introduction of a new test into the TB care cascade. In our study, we found that all participants obtained valid results and could use the platform without any problems or with little difficulties. Operators with prior experience with QFT-plus completed the tasks faster than users without prior experience. Only one operator did not use the software due to his limited computer skill. The study also showed that seven operators out of nine correctly used laboratory pipette without any difficulty. The key issue categorized as being at the risk of human error when performing the assay was a lack

of practice using the standard laboratory pipette. However, considering that the skills for using laboratory pipette in low-resource settings is very limited, a disposable pipette and video training is recommended to reduce errors.

The primary driver of failed task was due to lack of expertise in computer. High inconsistencies with the features of the device and those described in the instructions were found. Regardless of these challenges, ease of use rating was assigned, with a majority of participants reporting ratings of 4 or 5 on a Likert scale assay usability. When asked about satisfaction, the participants commented on the platform being user-friendly, the content being enough and instructions being easy to understand and follow. Time taken for each user to perform the assay from the first to the last sample decreased as the user's experience and familiarity with the assay increased.

This study demonstrated that QIAreach QFT has a number of operational advantages compared to the more complex current IGRA's assay. The QIAreach QFT is an innovative digital lateral flow, battery operated system that replaces the laboratory-based ELISA workflow. The system also uses an optimized single tube workflow requiring 1 mL compared with the 4 mL needed for QFT-plus and T-SPOT. The QIAreach QFT assay requires a time to results of 20 minutes compared to the 150 minutes needed for the ELISA-based detection assay. In addition, the QIAreach QFT allows running eight samples independently eliminating the need to batch samples and provide timely TB infection diagnosis.

CONCLUSION

The QIAreach QFT assay is suitable to be implemented in the remote area where limited infrastructure has hampered the accessibility of IGRA technologies to those in needs. Further studies are needed to establish assay's performances as well as the feasibility of introducing this new assay at larger scale to improve TB control in regions with limited infrastructure.

	P1	P2	P3	P4	P5	P6	P7	P8	P9	Effectiveness -Pass rate
Task 1	P	P	P	P	P	P	P	P	P	9/9 (100%)
Task 2	PH	PH	P	P	P	P	P	P	P	9/9 (100%)
Task 3	PH	PH	P	P	P	P	P	P	P	9/9 (100%)
Tasks 4	F	PH	P	P	P	P	P	P	P	8/9 (89%)
Efficiency - Time from set up to results (minutes)§	40	36	30	30	26	23	29	26	22	
User satisfaction*	2	4	4	4	5	5	4	5	4	

Table 1: Summary of tasks success rate, time from setup to results and user satisfaction by participant

Each column represents a participant and each row is a task
Task 1 -Setup: Place blood tube on eHub, place eStick in eHub, add processing tube on eHub
Task 2 – Load sample: Add buffer to processing tube, Remove plasma from blood tube, Add plasma to processing tube, Mix plasma and buffer in processing tube
Task 3 – Run test: Add test sample to eStick port
Task 4- Process results: Enter and track data on Software
P= Pass; F= Fail; PH= Pass with hint; § = Mean * = Likert scale 1- Very unsatisfied, 2 – Unsatisfied. 3 - Neutral, 4- Satisfied, 5- Very satisfied

Authors contribution

M.R, N.N and H.A conceived and designed the study. C.K made substantial contribution in acquisition of data. C.K, B.K and N.N helped with analysis and interpretation of data. K.S and C.K took the lead in writing the paper with input from all authors. K.S, H.A and C.K revised the paper critically for intellectual content. All authors were involved in the final approval of the version to be submitted.

Conflict of interest

Some of the authors declare receiving a grant from EDCTP for TREATS and one author (Nduku Ndunda) is a former employee of QIAGEN. QIAGEN (Hilden, Germany) provided the QIAreachTM QuantiFERON-TB test kits free of charge.

Competing interest

The authors declare no competing interests.

Author agreement

All authors have seen and approved the final version of the manuscript being submitted. The article is the authors' original work, has not received prior publication, and is not under consideration for publication elsewhere.

Acknowledgement
Authors would like to express their sincere appreciation and gratitude to all members of the TREATS infection cohort study team in Zambia, and to the study participants and their communities, and to the Zambart and non-Zambart laboratory staff, for their contributions to the research. The content herein is solely the responsibility of the authors. QIAGEN (Hilden, Germany) provided the QIAreachTM QuantiFERON-TB test kits free of charge. QIAGEN has no role in study design, collection, analysis and interpretation of data. This project is part of the EDCTP2 programme supported by the European Union (grant number RIA2016S-1632-TREATS).

REFERENCES

1. WHO. Global Pandemic/TB Alliance 2020 [Internet].World Health Organ.Available from: https://www.tballiance.orhttps://www.tballiance.org/why-new-tb-drugs/global-pandemic

2. WHO. Global Tuberculosis Report 2020 [Internet]. World Health. Organ.Available from: https://www.who.int/publications/i/item/9789240013131

3. Harries A, Kumar A, Satyanarayana S, Takarinda K, Timire C, Dlodlo R. Treatment for latent tuberculosis infection in low- and middle-income countries: progress and challenges with implementation and scale-up. *Expert Rev. Respir. Med.* [Internet] Expert Rev Respir Med; 2020 [cited 2021 Jul 11]; 14: 195–208Available from: https://pubmed.ncbi.nlm.nih.gov/31760848/.

4. Chakaya JM, Harries AD, Marks GB. Ending tuberculosis by 2030—Pipe dream or reality? *Int. J. Infect. Dis.* Elsevier; 2020; 92: S51–S54.

5. Matteelli A, Rendon A, Tiberi S, Al-Abri S, Voniatis C, Carvalho ACC, Centis R, D'Ambrosio L, Visca D, Spanevello A, Migliori GB. Tuberculosis elimination: where are we now? *Eur. Respir. Rev.* [Internet] European Respiratory Society; 2018 [cited 2021 Aug 10]; 27Available from: https://err.ersjournals.com/content/27/148/180035.

6. Zhou G, Luo Q, Luo S, Teng Z, Ji Z, Yang J, Wang F, Wen S, Ding Z, Li L, Chen T, Abi M-E, Jian M, Luo L, Liu A, Bao F. Interferon-γ release assays or tuberculin skin test for detection and management of latent tuberculosis infection: a systematic review and meta-analysis. *Lancet Infect. Dis.* [Internet] Elsevier; 2020 [cited 2021 Jul 11]; 20: 1457–1469Available from: http://www.thelancet.com/article/S1473309920302760/fulltext.

7. Zellweger J, Sotgiu G, Corradi M, Durando P. The diagnosis of latent tuberculosis infection (LTBI): currently available tests, future developments, and perspectives to eliminate tuberculosis (TB). *Med. Lav.* [Internet] Med Lav; 2020 [cited 2021 Jul 11]; 111: 170–183Available from: https://pubmed.ncbi.nlm.nih.gov/32624559/.

8. Pai M, Denkinger C, Kik S, Rangaka M, Zwerling A, Oxlade O, Metcalfe J, Cattamanchi A, Dowdy D, Dheda K, Banaei N. Gamma interferon release assays for detection of Mycobacterium tuberculosis infection. *Clin. Microbiol. Rev.* [Internet] Clin Microbiol Rev; 2014 [cited 2021 Jul 11]; 27: 3–20Available from: https://pubmed.ncbi.nlm.nih.gov/24396134/.

9. Farhat M, Greenaway C, Pai M, Menzies D. False-positive tuberculin skin tests: What is the absolute effect of BCG and non-tuberculous mycobacteria? [Internet]. Int. J. Tuberc. Lung Dis. 2006 [cited 2021 Jul 11]. p. 1192–1204Available from: https://www.ingentaconnect.com/content/iuatld/ijtld/2006/00000010/00000011/art00003;jsessionid=1je33ra04q9ea.x-ic-live-01.

10. Lalvani A. Diagnosing tuberculosis infection in the 21st century: New tools to tackle an old enemy. *Chest* [Internet] Chest; 2007 [cited 2021 Jul 11]; 131: 1898–1906Available from: https://pubmed.ncbi.nlm.nih.gov/17565023/.

11. World Health Organization. WHO guidelines on tuberculosis infection prevention and control, 2019 update [Internet]. 2019.Available from: https://www.who.int/publications/i/item/9789241550512.

12. Barcellini L, Borroni E, Brown J, Brunetti E, Campisi D, Castellotti PF, Codecasa LR, Cugnata F, Di Serio C, Ferrarese M, Goletti D, Lipman M, Rancoita PMV, Russo G, Tadolini M, Vanino E, Cirillo DM. First evaluation of QuantiFERON-TB gold plus performance in contact screening. *Eur. Respir. J.* 2016; .

13. Petruccioli E, Vanini V, Chiacchio T, Cuzzi G, Cirillo DM, Palmieri F, Ippolito G, Goletti D. Analytical evaluation of QuantiFERON- Plus and QuantiFERON- Gold In-tube assays in subjects with or without tuberculosis. *Tuberculosis* 2017; .

14. Faust L, Ruhwald M, Schumacher S, Pai M. How are high burden countries implementing policies and tools for latent tuberculosis infection? A survey of current practices and barriers. *Heal. Sci. Reports* [Internet] John Wiley & Sons, Ltd; 2020 [cited 2021 Jul 11]; 3: e158Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/hsr2.158.

15. Fukushima K, Akagi K, Akira K, Toru K, Noriho S, Hiroshi M. First clinical evaluation of the QIAreachTM QuantiFERON-TB for tuberculosis infection and active pulmonary disease. *Pulmonology*.

16. Francis S, Jenny H, Davide M, Jeffrey B, Nduku N, Joanna L, Mei Y, Andrew S, Robin U, Sean P, Chris M, Harmony D, Zoe M, Tim L, Vladyslav N. Evaluation of a Novel Lateral Flow Nanoparticle Fluorescence Assay for TB infection diagnosis. .

17. Molich R. A critique of how to specify the participant group size for usability studies: a practitioner's guide by Macefield. *undefined* 2010.