GeneXpert, thematic discussion and Journal Club

03-15 October '11

http://moodle.itg.be/scartcommunity

### SUMMARY REPORT by Shishir Dahal

---

INTRODUCTION

SCART and eSCART alumni were invited to participate in a two-week virtual thematic discussion and journal club on GeneXpert use in Resource limited-settings (RLSs), from October 3rd till October 15th, on the (e)SCART Moodle CoP discussion forum, http://moodle.itg.be/scartcommunity/

This online event was intended to explore the operational considerations for the use of GeneXpert in RLSs, particularly:

1. the operational considerations for the use of geneXpert (burden of cases, human resources, supply chain management, etc); 2/ how to integrate geneXpert into current TB diagnostic protocols, in resource-limited settings (i.e., for smear-negative and extra pulmonary TB); 3/ GeneXpert implementation an scaling up in countries with high HIV/TB burden.
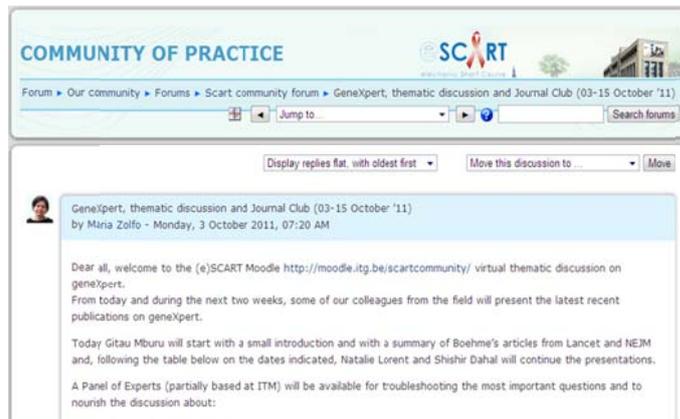
Figure 1. (e)SCART Community of Practice (CoP) Moodle Discussion Forum (available at: http://moodle.itg.be/scartcommunity/mod/forum/discuss.php?d=181)

METHODOLOGY

In order to promote the virtual discussion, announcements were sent to the list server of SCART/eSCART alumni and the Telemedicine (http://telemedicine.itg.be) members.

The thematic discussion took place on the CoP Moodle Discussion Forum (see Figure 1). Eight recent publications on GeneXpert were presented to the participants by 3 facilitators in the time frame of the two weeks; each group of articles introduced a different subtopic for discussion; the facilitators had the task to summarize the articles and present them to the

Moodle CoP, asking the CoP members to commented the presented manuscript (see Table 1).

A panel of experts has been available all along the two weeks to give feedback on the discussion, to high light the important issues and to further nourish the discussion between CoP members.

Table 1. Articles presented for discussion

Date	Articles	Facilitators
3/10/11	Rapid Molecular Detection of Tuberculosis and Rifampin Resistance. Boehme CC, NEJM 2010 Feasibility, diagnostic accuracy, and eff ectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicenter implementation study. Boehme CC, Lancet 2011	Gitau Mburu
6/10/11	GeneXpert MTB/RIF Assay for Mycobacterium tuberculosis Detection and Rifampin Resistance Identification in Patients with Substantial Clinical Indications of Tuberculosis and Smear-Negative Microscopy Results. J Clin Microbiol. 2011 Aug;49(8):3068-70. Epub 2011 Jun 15. Rapid molecular detection of extrapulmonary tuberculosis by the automated GeneXpert MTB/RIF system. J Clin Microbiol. 2011 Apr;49(4):1202-5. Epub 2011 Jan 26.	Natalie Lorent

	Rapid detection of Mycobacterium tuberculosis complex and rifampin resistance in smear-negative clinical samples by use of an integrated real-time PCR method. J Clin Microbiol. 2011 Mar;49(3):1137-9. Epub 2010 Dec 29. PubMed	
11/10/11	Comparison of Xpert MTB/RIF with Other Nucleic Acid Technologies for Diagnosing Pulmonary Tuberculosis in a High HIV Prevalence Setting: A Prospective Study. Scott LE, PLoS Med. 2011 Jul;8(7):e1001061. Epub 2011 Jul 26. Screening for HIV-Associated Tuberculosis and Rifampicin Resistance before Antiretroviral Therapy Using the Xpert MTB/RIF Assay: A Prospective Study Stephen D. Lawn, PLoS Med. 2011 Jul;8(7):e1001067. Epub 2011 Jul 26. Is Scale-Up Worth It? Challenges in Economic Analysis of Diagnostic Tests for Tuberculosis David W. Dowdy, PLoS Med. 2011 Jul;8(7):e1001063. Epub 2011 Jul 26 GeneXpert-A Game-Changer for Tuberculosis Control? Evans CA. PLoS Med. 2011	Shishir Dahal

MODERATOR, ADMINISTRATOR FACILITATORS AND EXPERT ROLES AND TASKS

The Community of Practice (CoP) moderator[1] sent an announcement about the thematic discussion and journal club and the modalities of the discussion to the Moodle CoP and Telemed members two weeks before the official start of the virtual discussion and introduced the 3 facilitators in a welcome message; worked with the facilitators to introduce the articles prior to journal club discussion; took care of the survey (see Annex 1) and of the editing of the report.

The Moodle administrator[2] looked after all the technical issues that rose during the event and also took care of the web site Google analytics.

The three facilitators[3] introduced different scientific papers with brief summary and initiate the discussion by asking participants to comment on the articles. One of the facilitators (SD) compiled the virtual thematic discussion report.

---

[1] M. Zolfo (ITM)
[2] C. Kiyan (ITM)
[3] Gitau Mburu (International HIV/AIDS Alliance, Kenya), Natalie Lorent (ITM, Cambodia), Shishir Dahal (Rolpa District, Nepal)

Experts[4] played their role as the troubleshooter and also gave the important expert opinion on field experience of GeneXpert use, nourishing the discussion.

RESULTS

Over the course of the GeneXpert thematic discussion and journal club, the forum (http://moodle.itg.be/scartcommunity/mod/forum/discuss.php?d=181) received a total of 48 interactions, from different part of the world.
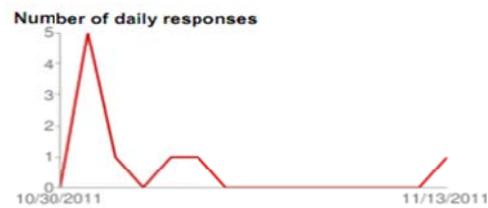
Figure 2. Dashboard online log in (from announcement to end discussion)

Fourteen participants representing 11 countries (see Annex 2) joined actively the online discussion,

---

[4] Lut Lynen (ITM), Elisa Ardizzoni (ITM), Gabriela Torrea (ITM)

6

posting comments and replies, with a total of 48 interactions in the two weeks period.

Contribution to the discussions came from CoP members based in: Belgium, Swaziland, Mozambique, Nepal, United Republic of Tanzania, Yemen, Argentina, Ghana, Cambodia, Nigeria and Kenya.

Participants included individuals working for international NGOs, universities and public/private sector.

THE DISCUSSION

Boehme et all in their research[5] found that the GeneXpert carries a sensitivity detection of M. tuberculosis bacilli of 98.2% among the smear positive patients and 72.5% in smear negative patients. It has a specificity of 99.2%. It can currently identify Rifampincin sensitive bacteria in 97.6% patients and Rifampicin negative bacteria in 98.1% of patients.

Additional studies (see references) also showed very promising results for GeneXpert and for this reason WHO strongly recommended the use of Xpert MTB/RIF as the initial diagnostic test in individuals suspected of MDR-TB or HIV-associated TB. It conditionally recommends Xpert MTB/RIF as a follow-on test to microscopy in settings where MDR-TB or HIV is of lesser concern, especially in further testing of smear-negative specimens. These recommendations also apply to children, based on the

---

[5] Rapid Molecular Detection of Tuberculosis and Rifampin Resistance. Boehme CC, NEJM 2010
http://www.ncbi.nlm.nih.gov/pubmed/20825313

generalization of data from adults and acknowledging the limitations of microbiological diagnosis of TB (including MDR-TB) in children. An important consideration has been that although the algorithms for diagnosing smear-negative TB in high HIV prevalent settings are not ideal, they allow treating TB in a very early stage, based on smear/HIV test and clinical or X-ray findings.

Advantages of the Xpert MTB/RIF–GeneXpert system:

- Simple to perform with minimal training
- Minimal risk of cross-contamination
- Requires minimal biosafety facilities (similar to microscopy)
- Rapid turnaround time, including results for rifampicin drug-resistance testing
- Relatively high sensitivity in smear-negative cases (particularly relevant in HIV-infected patients)
- GeneXpert on the contrary of most of NAAT (Hain for example) provides also quantitative results, that could be helpful in defining sputum mycobacterial load

Disadvantages include the following:

- Cost
- Tests for RIF resistance only
- RIF resistance to be confirmed in low MDR settings (according to WHO <10%)

- Requires stable, uninterrupted electrical power
- Requires secure environment to ensure against damage or theft
- Requires annual calibration by a trained technician using specialized calibration equipment (the module to be sent to Toulouse)
- Most effective means of implementation as yet unknown
- Detect also dead bacilli: not for monitoring of therapy
- Cartridges to be stored between 2-28°C
- Operating T <30°C
- Cartridge requires a lot of space for storage

Possible constraints:

- Temperature > 35°C?
- Dust
- Vibrations: close to centrifuge? (Vietnam experience)
- Disposal of cartridges: incinerator, pits, possibility of chemical pollution?
- Data from extra-pulmonary specimens still limited
- More evaluation needed in countries with extreme climate conditions and irregular power supply (UPS required!)

Online discussion touched all points mentioned above and additionally explored some practical issues like the number of samples to process per day, depending on the number of modules.

Upon completion of the discussion, participants were asked to complete a short online Google survey at http://tinyurl.com/genexperts (see Annex 1) to give a general appreciation on the event. Nine participants completed the evaluation format.

About 4 participants (44%) rated discussion as "extremely/very" relevant to his/her work, 33% felt that the CoP discussion forum was "very relevant" and 22% felt it was" somewhat relevant".

Out of nine two survey respondents (22%) use Moodle web site to read the interaction while 4 (44%) primarily used email, whereas 33% used a combination of both email and Moodle website.

Out of nine only five (56%) posted comments on GeneXpert forum.

100% respondents like to follow other thematic discussion in future.

Seven respondents (78%) downloaded or read the original journal presented at the beginning and eight of them (89%) like to receive more original articles relevant to the discussion.

Few topics suggested for discussion in future are: 1. the problem of shortage of drugs and the new rationing problem; 2. quality of CD4 counts in low resource settings; 3. Kaposi sarcoma treatment; 4. monitoring and evaluation of HIV/AIDS project/program; 5. antibiotic use in HIV patients.

The majority of respondents, 56%, belonged to NGOs, 33% to university/academic or research institution and 11% to government, being mostly clinicians (56%).

Some of the replies to the question: **"What suggestions do you have to improve future discussions?"**

"*Ask participants to give an opinion on certain statements?*"

"*Divide (e)SCARTies in different groups, voluntarily. Give specific task (summarizing, researching on specific topic of different journal) to each group. Rival groups will ask questions. Moderators and expert will intervene to foster mature discussion. Best group/individual should be recognized (by giving certificate/award).*"

REFERENCES

1. Rapid Molecular Detection of Tuberculosis and Rifampin Resistance. Boehme CC, NEJM 2010 http://www.ncbi.nlm.nih.gov/pubmed/20825313

2. Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicenter implementation study. Boehme CC, Lancet 2011 http://www.ncbi.nlm.nih.gov/pubmed/21507477

3. GeneXpert MTB/RIF Assay for Mycobacterium tuberculosis Detection and Rifampin Resistance Identification in Patients with Substantial Clinical Indications of Tuberculosis and Smear-Negative Microscopy Results. J Clin

11

Microbiol. 2011 Aug;49(8):3068-70. Epub 2011 Jun 15.
http://www.ncbi.nlm.nih.gov/pubmed/21677069

4. Rapid molecular detection of extrapulmonary tuberculosis by the automated GeneXpert MTB/RIF system. J Clin Microbiol. 2011 Apr;49(4):1202-5. Epub 2011 Jan 26. http://www.ncbi.nlm.nih.gov/pubmed/21270230

5. Rapid detection of Mycobacterium tuberculosis complex and rifampin resistance in smear-negative clinical samples by use of an integrated real-time PCR method. J Clin Microbiol. 2011 Mar;49(3):1137-9. Epub 2010 Dec 29. http://www.ncbi.nlm.nih.gov/pubmed/21191053

6. Comparison of Xpert MTB/RIF with Other Nucleic Acid Technologies for Diagnosing Pulmonary Tuberculosis in a High HIV Prevalence Setting: A Prospective Study. Scott LE, PLoS Med. 2011 Jul;8(7):e1001061. Epub 2011 Jul 26. http://www.ncbi.nlm.nih.gov/pubmed/21814495

7. Screening for HIV-Associated Tuberculosis and Rifampicin Resistance before Antiretroviral Therapy Using the Xpert MTB/RIF Assay: A Prospective Study Stephen D. Lawn, PLoS Med. 2011 Jul;8(7):e1001067. Epub 2011 Jul 26. http://www.ncbi.nlm.nih.gov/pubmed/21818180

8. Is Scale-Up Worth It? Challenges in Economic Analysis of Diagnostic Tests for Tuberculosis David W. Dowdy, PLoS Med. 2011 Jul;8(7):e1001063. Epub 2011 Jul 26 http://www.ncbi.nlm.nih.gov/pubmed/21814496

9. GeneXpert-A Game-Changer for Tuberculosis Control? Evans CA. PLoS Med. 2011 Jul;8(7):e1001064. Epub 2011 Jul 26. PubMed PMID: 21814497; PubMed Central PMCID: PMC3144196. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3144196/?tool=pubmed

10. Rapid Implementation of the Xpert MTB/RIF diagnostic test Technical and Operational 'How-to' Practical considerations, WHO 2011

11. Accuracy of the Xpert MTB/RIF test for the diagnosis of pulmonary tuberculosis in children admitted to hospital in Cape Town, South Africa: a descriptive study. Mark P Nicol, Lesley Workman, Washiefa Isaacs, Jacinta Munro, Faye Black, Brian Eley et all. Lancet Infect Dis. 2011 Nov;11(11):819-24. http://www.ncbi.nlm.nih.gov/pubmed/21764384

ANNEX 1. SURVEY

1. Do you find the content of the virtual discussion GeneXpert to be relevant to your work?

- Extremely relevant
- Very relevant
- Somewhat relevant
- Low relevance
- No relevance

2. Which tool did you use to read the interactions?

13

- The Moodle website
- The email box
- Moodle website and email box

3. Did you post any comment on the GeneXpert forum? if "not", select "Other" and write down why?

- Yes
- Other

4. Would you like in the future to follow other thematic discussion? *if "not", select "Other" and write down why?

- Yes
- Other

5. Did you download or read the original journal presented at beginning of each session?

- Yes
- Other

6. Would you like to receive more original articles, relevant to the discussion?

- Yes
- Other

7. What suggestions do you have to improve the future discussions?

8. Which topic you would like to discuss in the future?

9. Which of the following best describes your work?

- Public health / Health systems professional
- Clinician
- Academic / Research
- Other

10. Which of the following best describes your organization or institution?

- University / academic / research institution
- Hospital / health care facility
- Government
- Non-government organization
- WHO / UN agency

15

1. Gitau Mburu -Monday, 3rd October 2011, 09:25AM, Kenya

2. Oluwatosin Kuti - Monday, 3rd October 2011, 10:16 AM, Nigeria

3. Elisa Ardizzoni - Monday, 3 October 2011, 07:46 PM Belgium

4. Natalie Lorent - Tuesday, 4 October 2011, 04:53 AM, Cambodia

5. Gabriela Torrea - Tuesday, 4 October 2011, 09:47 AM, Belgium

6. Kwasi Torpey - Tuesday, 4 October 2011, 09:48 AM, Ghana

7. Natalia Tamayo - Tuesday, 4 October 2011, 04:54 PM, Argentina

8. Maria Zolfo - Tuesday, 4 October 2011, 11:13 PM, Belgium

9. Wafa Dahbali - Thursday, 6 October 2011, 08:26 PM Yemen

10. Deborah Kalunga-Carpenter - Saturday, 8 October 2011, 08:56 AM ,
United Republic Of Tanzania

11. Shishir Dahal - Tuesday, 11 October 2011, 04:57 AM, Nepal

12. Tom Decroo - Friday, 14 October 2011, 08:40 AM, Mozambique

13. Lucia Gonzalez - Friday, 14 October 2011, 10:38 AM, Swaziland

14. Lut Lynen - Saturday, 15 October 2011, 08:20 AM, Belgium