Expert Review of Molecular Diagnostics

ISSN: 1473-7159 (Print) 1744-8352 (Online) Journal homepage: informahealthcare.com/journals/iero20

Comprehensive new resource for evidence-based TB diagnosis

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To cite this article: Madhukar Pai, Andrew Ramsay & Richard O'Brien (2009) Comprehensive new resource for evidence-based TB diagnosis, Expert Review of Molecular Diagnostics, 9:7, 637-639, DOI: 10.1586/erm.09.48

To link to this article: https://doi.org/10.1586/erm.09.48

Published online: 09 Jan 2014.

Comprehensive new resource for evidence-based TB diagnosis

Expert Rev. Mol. Diagn. 9(7), 637–639 (2009)

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"According to one estimate, the world spends US$1 billion each year on diagnostics for TB. Such expenditure must be justified by strong evidence."

There is palpable excitement in the TB scientific community over the introduction of new tools (diagnostics, drugs and vaccines) into TB control activities. The development and evaluation of new tools is an important component of the 'Global Plan to Stop TB', the WHO's new global 'Stop TB Strategy', and the Stop TB Partnership's (STP's) Research Movement [1,2].

While innovation and new tool development are critical for clinical medicine and public health, limited resources and the movement toward evidence-based practice guidelines require careful validation of new tools and approaches prior to their widespread routine use. According to one estimate, the world spends US$1 billion each year on diagnostics for TB [3]. Such expenditure must be justified by strong evidence. Ideally, clinical and policy decisions must be guided by the totality of evidence on a given test or intervention. This is highly relevant for TB, where concerns have been raised about the lack of emphasis on evidence of effectiveness in some of the existing TB guidelines and policies [4].

High-quality evidence on TB diagnostics is critical for the development of evidence-based policies on TB diagnosis and, ultimately, for effective control of the global TB epidemic [5,6]. While primary diagnostic trials are needed to generate data on test accuracy (e.g., sensitivity and specificity) and performance and impact in field conditions, systematic reviews provide the best synthesis of current evidence on any given diagnostic test [7]. However, systematic reviews of test accuracy, while necessary, are not sufficient for policy and guideline development. Test accuracy data must be considered along with impact of the test on patient-important outcomes, and other factors including quality of the evidence, the uncertainty about values and preferences associated with the tests and presumed patient-important outcomes, and cost and feasibility, especially in resource-limited settings [8].

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Although a large number of trials on TB diagnostics have been published, surprisingly no systematic reviews were published until recently. In the past few years, more than 35 systematic reviews of diagnostic test accuracy have been published on various TB tests. As reviewed recently, these reviews provide valuable insights into the accuracy of various tests [6]. In addition to informing evidence-based TB diagnosis, systematic reviews have been helpful in informing policies and guidelines, and in development of research agendas. In fact, the new WHO process for policy-making requires compilation and review of evidence syntheses [9,101], in tune with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to guideline development [8]. Unfortunately, since almost all existing primary trials of TB diagnostics are focused on accuracy, there are few data available on patient-important outcomes, cost–effectiveness and impact. Thus, the available systematic reviews are almost exclusively focused on meta-analyses of

 10.1586/ERM.09.48 ISSN 1473-7159

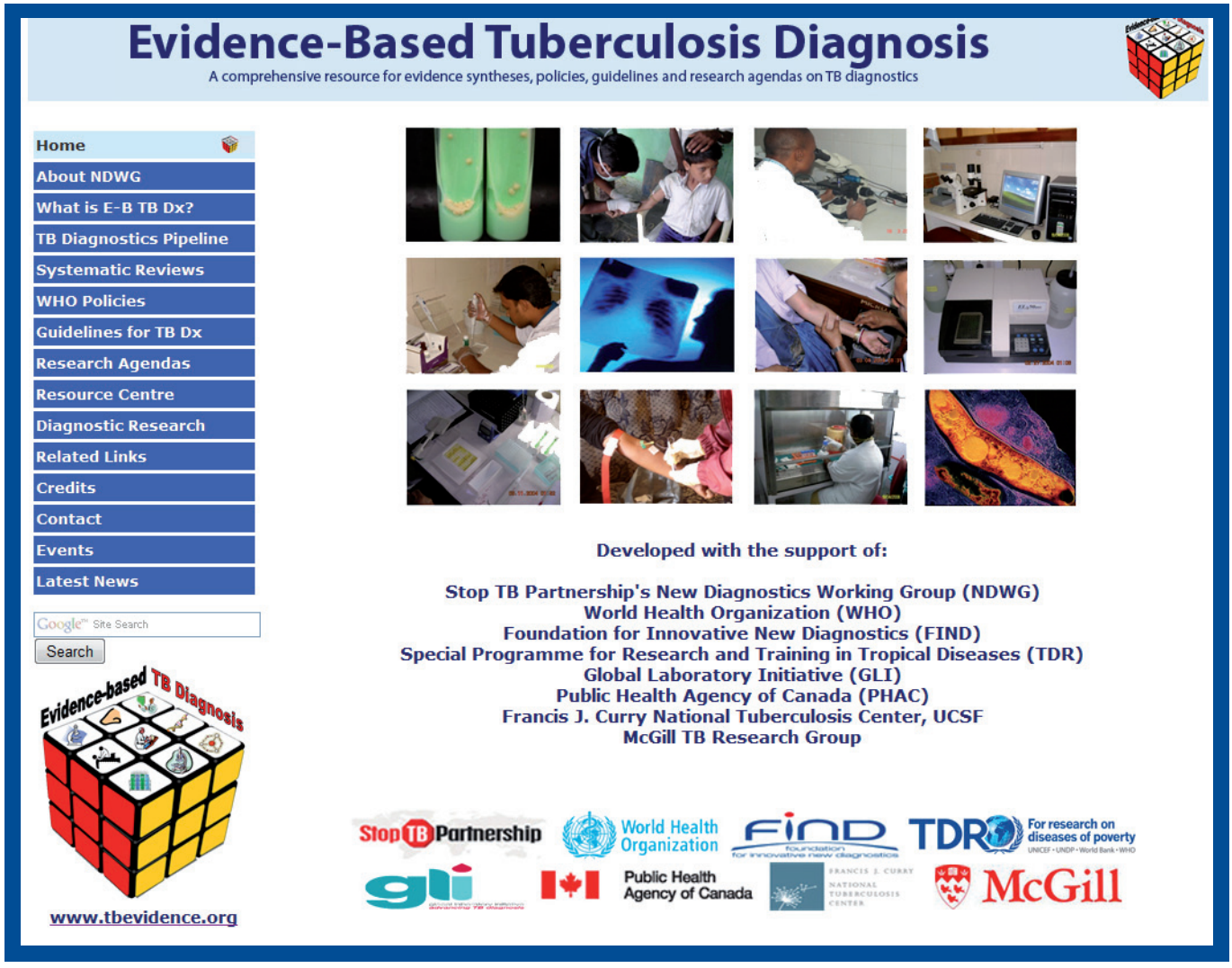

Figure 1. Homepage of the website 'Evidence-based Tuberculosis Diagnosis' [104].

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The STP was established in 1998, to work towards the goal of eliminating TB as a public health problem [102]. It comprises a network of international organizations, countries, donors from the public and private sectors, governmental and nongovernmental organizations, and individuals who have expressed an interest in working together to achieve this goal. The STP has three working groups focused on new tools – for drugs, vaccines and diagnostics. The STP's New Diagnostics Working Group (NDWG) was established in 2001 as one of the core working groups within the Partnership [103].

The NDWG contributes in a major way by coordinating and facilitating the development, evaluation and implementation of new and improved TB diagnostics in a scientifically acceptable, evidence-based and timely manner by linking all stakeholders involved in the diagnostics development and evaluation pathway. The mission of the NDWG is to advocate and implement research and/or operational activities in pursuit of the development and implementation of TB diagnostic tools, and to collaborate with other elements of the Partnership so as to create synergy and add value to actions taken in pursuit of the aims of the Partnership.

Recognizing the growing importance of evidence-based TB diagnosis and policy-making, the NDWG is supporting the production of systematic reviews, facilitating the development and dissemination of evidence summaries on new diagnostics, and actively promoting their use in guideline and policy development processes, along the lines of the GRADE approach [8,9].

Recently, the NDWG launched a new website resource called 'Evidence-based Tuberculosis Diagnosis' (Figure 1) [104]. Although initial funding was provided by the NDWG, several agencies and

groups have contributed to the development and expansion of this comprehensive resource. These include the Foundation for Innovative New Diagnostics (FIND) [105], the Global Laboratory Initiative (GLI) [106], the Special Programme for Research and Training in Tropical Diseases (TDR) [107], Public Health Agency of Canada (PHAC) [108], Francis J Curry National Tuberculosis Center (CNTC) [109] and the WHO [110].

The aim of the Evidence-Based Tuberculosis Diagnosis website is to provide the most comprehensive single source of evidence syntheses, policies, guidelines and research agendas on TB diagnosis. It provides access to all published systematic reviews on TB diagnostics (grouped by various test types or platforms), all the relevant policies, guidelines and research agendas on TB diagnosis, and several reports, monographs and training modules, and slide presentations on TB diagnostics.

The website also provides detailed guidance on how to conduct and report diagnostic research on TB, guidance on how to perform systematic reviews on diagnostics, tools on guideline development, including GRADE, and documents on improvement of laboratory quality and practice. Up-to-date information on the current TB diagnostics pipeline is also provided, along with access to a scientific blueprint for TB diagnostics development. All information is provided as open access, with no registration or fee requirements.

In conclusion, this new website resource addresses a long-standing need for a single portal that compiles all critical evidence on TB diagnosis, along with relevant policies and guidelines for clinicians and public health professionals. We hope similar efforts will be made to compile the available evidence and guidance on all aspects of TB care and control.

Acknowledgements

The views expressed in this paper are the views of the authors and do not necessarily reflect the views or policies of the agencies they are affiliated with. The authors are grateful to several individuals for their help and support in creating the www.tbevidence.org website, including Augustine Kwok, Jessica Minion, Hojoon Sohn and Karen Steingart.

Financial & competing interests disclosure

Madhukar Pai, Andrew Ramsay and Richard O'Brien are editors of the website www.tbevidence.org. They are also members of the New Diagnostics Working Group (NDWG). Madhukar Pai is the Co-Chair of the NDWG, and Andrew Ramsay has served as the secretary of the NDWG. Madhukar Pai and Richard O'Brien are Co-Chairs of the NDWG's subgroup on Evidence Synthesis for TB Diagnostics. Richard O'Brien works for the Foundation for Innovative New Diagnostics (FIND) and Madhukar Pai serves as a consultant for FIND. FIND is a nonprofit agency that collaborates with several industry partners for the development of new diagnostics for neglected infectious diseases. The www.tbevidence.org website was inspired by a paper entitled 'Evidence-based tuberculosis diagnosis' published in PLoS Medicine in 2008. Funding to develop the website was provided by the Stop TB Partnership's NDWG and Public Health Agency of Canada (PHAC), and additional support was provided several other partners and groups. Madhukar Pai is a recipient of a New Investigator Career Award from the Canadian Institutes of Health Research (CIHR).

The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

References

1 Stop TB Partnership and WHO. *The Global Plan to Stop TB 2006–2015*. WHO, Geneva, Switzerland (2006).

2 Raviglione MC, Uplekar MW. WHO's new stop TB strategy. *Lancet* 367(9514), 952–955 (2006).

3 WHO/TDR/FIND. *Diagnostics for Tuberculosis. Global Demand and Market Potential*. WHO, Geneva, Switzerland, 1–203 (2006).

4 Oxman AD, Lavis JN, Fretheim A. Use of evidence in WHO recommendations. *Lancet* 369(9576), 1883–1889 (2007).

5 Pai M, O'Brien R. Tuberculosis diagnostics trials: do they lack methodological rigor? *Expert Rev. Mol. Diagn.* 6(4), 509–514 (2006).

6 Pai M, Ramsay A, O'Brien R. Evidence-based tuberculosis diagnosis. *PLoS Med.* 5(7), E156 (2008).

7 Pai M, McCulloch M, Enanoria W, Colford JM Jr. Systematic reviews of diagnostic test evaluations: what's behind the scenes? *ACP J. Club* 141(1), A11–A13 (2004).

8 Schunemann HJ, Oxman AD, Brozek J *et al.* Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. *BMJ* 336(7653), 1106–1110 (2008).

9 WHO. *World Health Organization Handbook for Guideline Development*. WHO, Geneva, Switzerland (2008).

Websites

101 WHO. Moving research findings into new WHO policies. www.who.int/tb/dots/laboratory/policy/en/index4.html

102 Stop TB Partnership www.stoptb.org

103 Stop TB Partnership's New Diagnostics Working Group (NDWG) www.stoptb.org/wg/new_diagnostics

104 Evidence-based tuberculosis diagnosis website www.tbevidence.org

105 Foundation for Innovative New Diagnostics (FIND) www.finddiagnostics.org

106 Global Laboratory Initiative (GLI) www.who.int/tb/dots/laboratory/gli/en/index.html

107 Special Programme for Research and Training in Tropical Diseases (TDR) http://apps.who.int/tdr

108 Public Health Agency of Canada (PHAC) www.phac-aspc.gc.ca/tbpc-latb/index-eng.php

109 Francis J. Curry National Tuberculosis Center (CNTC) www.nationaltbcenter.edu

110 WHO. Stop TB Department www.who.int/tb/en