

# FOREWORD

## Global health diagnostics

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Access to appropriate diagnostic tools is an essential component in the evaluation and improvement of global health. Diagnostics are crucial for identifying the presence and cause of disease at both the individual and population levels, correctly assessing the nature of disease, designating an appropriate course of treatment, monitoring the effects of interventions (whether preventive or therapeutic), and determining drug resistance and/or the recurrence of existing disease. However, despite the key role of diagnostics, they tend to receive less attention than research efforts focused on novel therapeutics or preventive strategies.

Current diagnostic tools are largely inadequate for meeting health needs in developing countries. These shortcomings include inability to distinguish the state of the immune response or vaccination, to distinguish between diseases that present with similar symptoms, to determine the presence of latent infectious agents, and to provide practical low-cost monitoring for treatment efficacy, disease recurrence and emergence of drug resistance.

Commercial partners have shown limited willingness to engage in the development of new diagnostics for the developing world. As a result, most existing tools, as well as those under development, are targeted for use in industrialized countries and, as such, are inappropriately complex and expensive when considered for application to global health problems. For example, many current diagnostics must be performed in central facilities that are not available in large parts of the developing world. In addition, inadequate clinical rigor in the evaluation of new diagnostics in relevant settings<sup>1,2</sup>, ineffective training of end users, insufficient advocacy to influence adoption rates<sup>3</sup> and lack of quality assurance<sup>4,5</sup> have all limited the access to appropriate tests for those that need them most.

An increasing number of reports in the literature call for better and more accessible diagnostic tools for a variety of infectious diseases afflicting individuals living in the developing world<sup>1,6</sup>. In a Delphi-based approach to assess biotechnologies for developing world health conditions, accurate, rapid and affordable molecular-based diagnostic tests for infectious diseases were ranked as the most promising biotechnology for improving health in developing countries during the next 5–10 years<sup>7</sup>. However, the potential health impact of such diagnostics in developing

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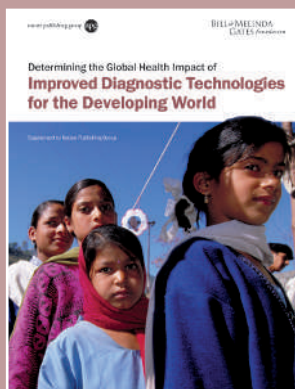
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Although the content of this 'supplement' was not vetted editorially by *Nature* staff, the broad diagnostics agenda being analysed and advocated here is one that I and colleagues endorse. Accordingly, *Nature* is simultaneously and independently publishing a Commentary by some of these authors (*Nature* 7 December 2006), spelling out key elements of the diagnostics challenge for the developing world.

countries has not been quantified, and the required characteristics of these tools are unknown. Mabey and colleagues<sup>8</sup> questioned the accuracy requirements of rapid tests for sexually transmitted diseases, and suggested that mathematical modelling could be useful in predicting their health impact and cost-effectiveness, as well as in determining the performance characteristics needed in specific settings. The authors argued that this information is crucial for engaging technology developers in creating solutions to address diagnostic problems, and for aiding the introduction and adoption of these tools into disease-control programmes.

An initial step in developing a rational strategy for creating diagnostic technologies for global health is to determine the need for, and the health impact of, potential new tests. It is crucial to establish the effect that any specific diagnostic tool might have on reduction of the disease burden, as measured in lives saved, disability-adjusted life years (DALYs) and other appropriate health outcome measures, and to identify the format and performance that a test must have to realize such a reduction.

In pursuit of these goals, the Bill & Melinda Gates Foundation convened the Global Health Diagnostics Forum, which was a partnership with the RAND Corporation, experts in relevant diseases, representatives from the diagnostics industry and technology development arena, and experts in the modelling of disease impact and the introduction and adoption of diagnostic technologies. From September 2004 to May 2006, the forum developed and employed analytic methods to determine the potential impact of disease-specific diagnostic tools for use at the individual level, and to identify the required performance characteristics and infrastructure requirements (for example, electricity or running water) of these diagnostics in order to attain the anticipated health impacts.

To accomplish these goals, six working groups were formed, each focusing on one of the diseases or syndromes that cause the highest health tolls in the developing world — namely, acute lower respiratory infections (ALRIs), human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), diarrhoeal diseases, malaria, tuberculosis and sexually transmitted infections (STIs)<sup>9</sup>. Using an iterative process, which continued throughout the 2-year term of the project, and employing relevant literature and expert opinion as a guide, each working group selected one or two points along the path of disease progression where a diagnostic could potentially have the greatest impact on health outcomes. The working

groups then used static decision-tree models to determine both the potential impact and the required format of an effective diagnostic (Box 1).

In addition to the disease-specific working groups, a technology working group determined the probable health-care infrastructure where diagnostics would be used, and explored the technology platforms required to support the development of diagnostic tools that could substantially improve health in developing countries. The forum also qualitatively explored the potential for diagnostics that can address multiple diseases with common presentation (for example, a child presenting with fever that could be caused by malaria or pneumonia). The results reported in this supplement are also available in a series of RAND reports ([http://www.rand.org/health/feature/research/0612\\_global.html](http://www.rand.org/health/feature/research/0612_global.html)).

Over 2 years, and through a series of meetings with experts across the globe, the forum helped raise awareness about the need for diagnostics to improve the health status of individuals. Although environmental factors and population-based diagnostics play key roles in public health, their consideration was beyond the scope of this project. The analyses reported in this supplement have been conducted using static decision trees and, hence, provide a snapshot in time of the potential benefits of new diagnostics for the developing world. However, although the focus has been on developing diagnostics to improve the health status of individuals, the data provided can also serve as a foundation on which to build links to programmatic and economic models for implementation within health systems.

This series of papers aims to further the dissemination of current knowledge on global health diagnostic needs for the conditions that most severely affect the developing world. The findings clearly articulate the acute need for new diagnostic tools, the potential impact of new diagnostics for people in developing countries and the specific performance requirements of these tools. We hope this information will encourage technology developers in the public and private sectors to do more to accelerate the development and delivery of new diagnostic solutions.

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### Box 1 | Diagnostic intervention nodes analysed

- Acute lower respiratory infections (ALRIs)**  
A test for bacterial ALRI among children aged <5 years presenting with acute respiratory symptoms and a test for severe ALRI among children aged <5 years to identify those requiring hospitalization.
- Human immunodeficiency virus (HIV)**  
A test for HIV infection in infants aged <12 months.
- Diarrhoea**  
A test capable of detecting the enteric pathogens *Cryptosporidium parvum*, enteroaggregative *Escherichia coli* and *Giardia lamblia* to reduce diarrhoea-related stunting in children.
- Malaria**  
A test for malaria among febrile children aged <5 years.
- Tuberculosis (TB)**  
A test for case detection of active TB in symptomatic HIV-positive and HIV-negative individuals.
- Sexually transmitted infections**  
A syphilis screening test for antenatal women and a gonorrhoea and chlamydia diagnostic for female commercial sex workers.