

The right tools can save lives

Effective diagnosis, paired with treatment, for developing-world diseases can have far-reaching impacts, says the Global Health Diagnostics Forum.

Millions of people in developing countries die each year from diseases that are treatable or preventable, and just three diseases — AIDS, tuberculosis (TB) and malaria — kill more than 5 million people annually¹. Effective treatment for these and other conditions is limited by the failure to accurately diagnose disease in resource-limited settings. For example, the standard diagnostic test for TB, which is latently carried by one-third of the human population and kills roughly 2 million people each year, misses half of all cases².

Diagnostic technologies are needed not just for identifying disease, but also for designating the appropriate treatment, monitoring the effects of interventions (preventive or therapeutic) and for determining drug resistance. Effective diagnostics, paired with access to treatment, can have a huge impact on health.

Most diagnostic tools were developed for use in industrialized countries, and thus are too complex and expensive for developing-world conditions. All too often such tools are not evaluated in relevant settings³, and suffer from undertrained end users, insufficient advocacy and inadequate quality assurance⁴.

Forum formed

Despite the severe shortage of effective developing-world diagnostics, little has been done to address the problem. This is due to a scarcity of information on the potential health impact and performance of essential diagnostics, and to the low return on investment in diagnostics perceived by the private sector.

To provide information on specific diagnostic needs and characteristics, the Bill & Melinda Gates Foundation, in partnership with the RAND Corporation, convened the Global Health Diagnostics Forum with representatives from the diagnostics industry, technology developers and experts in relevant diseases and public health. Between 2004 and 2006 the Forum focused on six disease groups that have the highest health tolls in the developing world: acute lower respiratory infections (ALRIs), HIV/AIDS, diarrhoeal diseases, malaria, TB and sexually transmitted infections.

For each disease, the Forum identified one or two points along the path of disease progression where a diagnostic test could have the most impact, and then used models to determine the health impact and the required diagnostic characteristics. A key factor was

the eventual healthcare setting: these ranged from severely deficient infrastructure common in home settings (for example, no water, electricity or staff expertise), to moderate or advanced infrastructure found in hospitals and some Asian urban clinics.

The Forum also determined the potential health impact of a specific diagnostic tool for each disease⁵, assuming that access to diagnostics is linked to effective interventions.

The big six

A diagnostic test for bacterial ALRIs could save many lives if it reduced unnecessary antibiotic use while encouraging more appropriate use. A new diagnostic test with 95% sensitivity and 85% specificity, accompanied by greater treatment access and minimal infrastructure requirements, could save at least 400,000 adjusted lives (which also account for lives saved due to reductions in over-treatment) a year. A test for severe cases of ALRI requiring hospitalization would also be beneficial, if access to effective hospital care increases globally.

A test for paediatric HIV infection in infants younger than 12 months with 90% sensitivity, 90% specificity, and minimal laboratory requirements, could save about 180,000 disability-adjusted life years (DALYs) over 12 months if 5% of the target population has access to antiretroviral therapy, or around 2.5 million DALYs if 100% has access.

A test for diarrhoeal diseases with 90% sensitivity, 90% specificity, and minimal infrastructure requirements for each of the pathogens *Giardia lamblia*, *Cryptosporidium parvum* and enteroaggregative *Escherichia coli* could reduce the prevalence of stunted growth by 12.5% and save 2.8 million DALYs annually. But this finding depends critically on uncertain assumptions about treatment cost and additional health benefits (such as an improved immune response), both of which require further research.

A paediatric test for malaria with 95% sensitivity, 95% specificity, and minimal infrastructure requirements, could avert more than 100,000 childhood deaths and around 400 million unnecessary treatments annually. A test with no infrastructure requirements

and 90% sensitivity and specificity could avert more than 300,000 childhood deaths and some 450 million unnecessary treatments annually.

For syphilis, a test that is at least 86% sensitive, 72% specific, requires minimal infrastructure, and has either 100% rate-of-return for test results or 100% treatment rate could save at least 138,000 adjusted lives and avert more than 148,000 stillbirths annually. A similar test requiring no laboratory infrastructure could save more than 200,000 adjusted lives and avert 215,000 stillbirths per year.

A diagnostic that requires minimal infrastructure and has 85% sensitivity and 90% specificity for both gonorrhoea and chlamydia could save nearly 3 million DALYs, avert more than

12 million infections, and prevent at least 161,000 related HIV infections among female sex workers in sub-Saharan Africa, China and South East Asia, over 4 years.

A rapid TB diagnostic requiring no laboratory infrastructure that has 97%

specificity, at least 85% sensitivity, and is unaffected by HIV status, could save around 400,000 adjusted lives annually.

In addition to the above tests, diagnostics that can identify and distinguish between multiple diseases with similar symptoms (for example, the acutely ill child who presents with fever) would improve health outcomes.

The Forum has defined the need and impact of diagnostics for six devastating disease groups. Now we challenge scientists, technology developers, funding agencies, policy-makers, international governmental and aid organizations, investors and diagnostic companies to work together to take this forward. A coordinated approach is needed so that appropriate diagnostics can achieve the promised impact. ■

A full list of signatories to this Commentary is available as supplementary information at www.nature.com/nature/journal/v444/n7120/supinfo/444681a.html.

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"The standard diagnostic test for TB, which kills 2 million people each year, misses half of all cases."

1. Lopez, A. D. et al. *Global Burden of Disease and Risk Factors* (Oxford Univ. Press, 2006).
2. WHO *Global Tuberculosis Control* (Geneva, 2004).
3. Mabey, D. et al. *Nature Rev. Microbiol.* **2**, 231–240 (2004).
4. Lon, C. T. et al. *Trans. R. Soc. Trop. Med. Hyg.* **99**, 493–498 (2005).
5. Burgess, D. C. et al. *Nature Suppl.* **S1**(2006).