Cost-effectiveness of Xpert MTB/RIF and investing in health care in Africa

The Xpert MTB/RIF assay is an accurate test for the diagnosis of tuberculosis when an adequate sputum sample can be obtained; even in smear-negative tuberculosis the sensitivity is about 67%.[1,2] Although the assay turnaround time is under 2 h, depending on the health-care setting, time to tuberculosis treatment can be 2 weeks or more in a substantial number of patients.[3] The technology has now been endorsed by WHO as a frontline test for tuberculosis in populations where there is a high incidence of HIV.[4] Indeed, several countries in Africa are rolling out Xpert MTB/RIF.[5] However, for expanded and sustained uptake, governments and policy makers require information about the cost-effectiveness of the technology to allow for appropriate planning and allocation of health-care resources. Cost-effectiveness must be balanced against affordability and sustainability. Thus, although the diagnostic accuracy of the technique is not in doubt, questions remain about the cost-effectiveness of the technology given that the overall number of patients treated for tuberculosis can remain unchanged[6] and given the high rates of empirical treatment in resource-poor health-care settings.[7]

Modelling studies have estimated that the implementation of Xpert MTB/RIF, either in addition to or as a replacement to smear microscopy, will be cost-effective for the diagnosis of tuberculosis and mutidrug-resistant (MDR) tuberculosis in countries with a high burden.[8–11] The incremental cost of each disability-associated life-year averted by Xpert implementation (the incremental cost-effectiveness ratio [ICER]) is below the WHO-defined "willingness to pay" threshold for all settings modelled by Vassal and colleagues,[10] and the findings of Menzies and colleagues suggest that Xpert implementation could, through improved case-finding and treatment, substantially reduce tuberculosis illness and death.[11]

However, these studies differed in their assumptions about disease transmission, rates of MDR tuberculosis, duration and effect of future disease burden, downstream effects of antiretroviral therapy, and how the relevant health-care system models were constructed. Thus, further data are required about the cost-effectiveness of different algorithmic strategies on health-care systems in Africa. In this issue of *The Lancet Global Health*, Ivor Langley and colleagues[12] assess the cost-effectiveness of different diagnostic strategies on cost-effectiveness within the context of the Tanzanian health-care system. These strategies included a combination of conventional smear microscopy (Ziehl Nielson staining), LED microscopy (conventional versus same day), full roll-out of Xpert MTB/RIF, and LED microscopy followed by targeted Xpert in smear-negative cases (the latter two strategies in either all HIV-infected persons or only those known be HIV-infected).[5] They found, using an integrated modelling approach, that full roll-out of Xpert MTB/RIF was the most cost-effective option with the potential to substantially reduce national tuberculosis burden, and that targeted use of Xpert MTB/RIF after microscopy in HIV-infected people was a less cost-effective approach. The latter was less cost-effective because of the reduced likelihood of preventing death and reduction in the potential gain in life-years owing to the shortened lifespan in HIV-infected people.

However, there are several limitations to these findings. Current diagnostic practice, especially the frequency, timing, and accuracy of clinical diagnoses or empirical tuberculosis treatment, is highly setting-specific, dependent on adherence to the WHO algorithm for smear-negative tuberculosis,[13] and can reduce the cost-effectiveness of diagnostic interventions.[7,14] Langley and colleagues' estimated sensitivity of smear-negative tuberculosis in Tanzania (52%)[15] is lower than that from a recent meta-analysis,[16] and the authors also assumed excellent specificity (95%). In South Africa, for example, most smear-negative patients seem to be "detected" through empirical treatment, and, as seen in Uganda and Kenya,[17,18] less than half of notified cases are microbiologically confirmed, suggesting that significant overtreatment is occurring.[6]

Furthermore, patient-level costs were not included and these are known to be substantial and influence default, particular in tuberculosis-endemic countries.[19] The targeted use of Xpert MTB/RIF after smear microscopy was only explored in HIV-infected participants and not

HIV-uninfected people. The ICER also differed substantially from other studies.[10] However, this must be understood within the context of different assumptions about transmission, future disease burden, and antiretroviral therapy, among other factors. MDR tuberculosis was not considered in the transmission component and therefore one wonders about applicability to other settings with high rates of MDR tuberculosis, such as South Africa. However, the higher rates of MDR tuberculosis would probably have made the Xpert MTB/RIF strategy even more cost-effective in this context.

One could further debate many nuances of the internal workings of the models and their external validity in replicating or predicting outcomes in the priority areas for tuberculosis intervention, but perhaps it is not reasonable to ask too much of a single study. We would argue that sensitivities of the model to particular assumptions warrant further discussion, and be interpreted not just as limitations but as flags that inform programmatic implementation.

Despite these limitations, several of which are acknowledged by Langley and colleagues,[12] the study adds important information to the current knowledge base, and not only confirms but quantifies the cost-effectiveness of Xpert MTB/RIF in the Tanzanian setting. It further provides crucial information about the magnitude of investment that must be made by African governments for full roll-out of Xpert MTB/RIF. Tuberculosis is now the commonest cause of death in many African countries and has a significant effect on national gross domestic products (GDPs). It therefore makes economic sense to invest in health-care systems and to roll out technologies such as nucleic acid amplification tests. However, knowledge translation is now required to affect the decision making process at programmatic level, and thereafter monitor post-implementation operational and epidemiological indicators. However, the potential gains of Xpert MTB/RIF can only be realised if several other operational and logistic aspects of the health-care system, as a whole, are addressed including communication and transport infrastructure, capacity of the national treatment programme, and investing in efficient reporting systems, among others, so that the impact of Xpert MTB/RIF can be realised on the ground.

Most importantly, however, it is time for governments and policy makers to invest in health care so that the potential gains of newer technologies such as Xpert MTB/RIF can be translated into reduced morbidity and mortality, and positively affect the GDPs of African economies. There are several indications that Africa is entering a golden age of economic prosperity and it is hoped that investment in health-care systems and infrastructure will parallel this boom. The data by Langley and colleagues inform this agenda.

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