The costs and cost-effectiveness of tuberculosis control
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Chapter 7

General discussion and conclusion

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DISCUSSION

This thesis has reported on four studies and one review. This chapter discusses its implications for policy makers and researchers in the future. It takes into account additional research published during the time of researching and writing this thesis.

DOTS

The studies presented in this thesis concerning DOTS in Egypt, Syria and Ukraine demonstrate that DOTS is cost-effective in middle income countries. In addition, a further study, published during the time of writing this thesis, found DOTS to be cost-effective in Brazil (1). Furthermore, the World Health Organisation recently conducted a global analysis of the cost-effectiveness of DOTS. This used extrapolated costs for each country combined with an epidemiological model to estimate effectiveness, including the effects of transmission (2). This analysis found that average cost per DALY gained by DOTS ranged from $6 to $15 international dollars in Africa and Asia. The study concluded that DOTS for new smear-positive cases is a highly cost-effective global public health intervention. Finally, in South Africa (3), researchers examined the impact of MDR-TB on the cost-effectiveness of DOTS. This study found that the inclusion of MDR-TB in the transmission models used to estimate DALYs further improved the estimated effectiveness of DOTS, thus strengthening previous results.

Whilst it is clear that DOTS is cost-effective, the studies presented here from Ukraine, Egypt and Syria show that the mode of delivery of TB control (whether through communities, primary, clinics or hospitals) has a significant impact on provider and patients costs. Developing a better understanding of the effect that different health systems models have on the cost-effectiveness of DOTS is essential for planning the expansion of DOTS. In situations where current public health systems do not reach significant proportions of the population, DOTS coverage will be limited, and therefore TB control will fail to achieve its targets. Faced with this situation, some argue that the focus should be on expanding the scale of the public health system, whilst others look to partnerships with communities or with the private sector to expand DOTS.

Several additional studies have been published in the past few years that address this issue. These focus on two areas. Firstly, there are several studies examining whether DOTS can be made more cost-effective when delivered in a community based way in Africa (4-10). These find that, within pilots, effectiveness can be maintained whilst costs are substantially reduced. It would be interesting to see if whether models involving the community remain cost-effective when done at scale. Secondly, there are several studies examining the cost-effectiveness of DOTS implemented through the private sector (11-15). These find that the private sector (including facility and workplace models)
can deliver DOTS in a cost-effective way. In one study from India, the public subsidy required for DOTS through private clinics was found to be significantly lower than the costs of public provision (11). A further study in India, comparing the costs of DOTS and non-DOTS to the private sector, also found substantial cost savings for private providers when adopting DOTS compared to previous practices (12). Combined this studies suggest that private provision of DOTS is at least as feasible and potentially cost-effective as increased public provision.

However, changing the health systems/institutional framework for implementing TB control can be complex. The study presented from Ukraine, shows that economic studies can assist this effort by providing policy makers and health systems specialists with an indication of the economic winners and losers in any institutional change. More studies that examine both the cost-effectiveness and economic benefits of different health systems approaches (at scale) to support TB control objectives are needed, especially from countries where DOTS has already been successfully expanded throughout the existing health system, and a broader range of interests and stakeholders are involved.

In recent years several studies have been published on enhancing the effectiveness of DOTS with new technologies. Most of these have focused on improved diagnostics. The first of these (16) examines the cost-effectiveness of polymerase chain reaction (PCR) in Kenya. This study found that, where there are large numbers of patients, this relatively expensive technology can be cost-effective. A further study in Zambia examined the cost-effectiveness of culture testing (17). Its findings are similar to the ones presented on MDR-TB diagnostics in this thesis for IDLJ culture (i.e. costs of around $35 dollars per test). In addition, it found that liquid and solid media compare are both cost-effective. However, like the PCR study above costs vary considerably depending on the throughput of the machines used for liquid culture (MGIT). The study presented in this thesis also shows that prevalence is a key determinant of cost-effectiveness. The question now facing future researchers is therefore not whether it is potentially cost-effective to employ these new diagnostic technologies, but when/where to employ them.

One approach to answering this question is modeling. In 2008, a study was published modeling the incremental cost-effectiveness of a hypothetical new point-or-care TB diagnostic test in South Africa, Brazil and Kenya (18). This study assumed set prevalence rates and concluded that price and specificity were key determinants of cost-effectiveness of diagnostic technologies for TB. The cost of false positives was found to be a significant element in overall costs, due to cost of avoidable treatment. As increasing funds are being invested in new technologies to enhance DOTS, these decision analysis models will be an important area for development in the future. Those funding new TB control
technologies will need to assess when and where a technology is likely to be cost-effective and produce estimates of demand for these technologies.

MDR-TB
The study presented in this thesis examining the cost-effectiveness of MDR-TB diagnostics, is one of several recent studies looking at the cost-effectiveness of controlling MDR-TB. Following the first study of MDR-TB treatment in Peru (19) two more studies examining the cost-effectiveness of MDR-TB have been published (20-21). A further study from Peru compares different ways of diagnosing and treating MDR-TB (20). It uses a dynamic state-transmission model to examine the transmission benefits of MDR-TB treatment, estimating outcomes for a population of 100,000 people. It finds that using a combination of drug susceptibility testing followed by either locally standardised second-line drugs or individualised treatment for previously treated cases is significantly more cost-effective than; a) DOTS (including retreatment); b) providing locally standardised drugs for previously treated cases (without testing); or c) individualised treatment after drug susceptibility testing for all cases. The study authors conclude that the treatment of MDR-TB using second-line drugs is highly cost-effective in Peru, and is likely to be so in a wide range of other settings. Finally, a study from an MDR-TB pilot in the Philippines (21) reports that MDR-TB diagnosis and treatment were found to be cost-effective, even where the drugs costs were significantly higher than those used in Peru and patient costs were included.

The combined findings of these studies suggest that the diagnosis and treatment of MDR-TB is likely to be cost-effective, and this may be further enhanced by the development of new technologies. Whilst broadly this conclusion has not been challenged, these studies have attracted a number of letters in scientific journals (22). These responses highlight a number of issues. Firstly, it has been suggested that these studies are not independent, as they are conducted, supported or funded by a small group of technocrats at the global level. Secondly, there is concern that these findings cannot be generalized to other settings as these pilots are not sufficiently robust enough to justify scaling up MDR-TB diagnosis or treatment. In particular, attention has been drawn to their small-scale, external funding and the use of the best clinicians and scientists. Finally, there has been a concern that a focus on MDR-TB will distract limited resources away from the main public health priority treating drug susceptible smear-positive TB (i.e. DOTS).

This last issue highlights a common problem in applying economic evaluations. Economic evaluations simply demonstrate the potential cost-effectiveness of MDR-TB treatment. In the real world, rather than attracting additional funding for TB control, additional interventions may pull resources away from the existing strategy i.e. (first line treatment) DOTS. This consequence needs to be better addressed in the discussion of research results in the future. In
particular, the resource requirement implications of cost-effectiveness studies need to be made more explicit. As resources (particularly human resources) are fixed in the short-run, it should be clear that investments need made over a sufficient time scale. Finally, now the pilots have established potential cost-effectiveness, further research should be focused on establishing the feasibility and cost-effectiveness of MDR-TB in routine and real-life settings to provide the basis for more accurate estimates of true resource requirements.

**TB/HIV**

The study on TB/HIV patient costs from Ethiopia presented in this thesis argues that the early detection of the TB and HIV has both public health and economic benefits to households. This is complemented by a recent study, conducted in South Africa, which concludes that the ProTEST package of TB/HIV services (which includes the expansion of VCT and linking of TB/HIV services) is cost saving from a health service perspective (23). Despite these positive indications, the same study shows whilst TB services can substantially improve the case detection of HIV, using VCT to detect TB cases seems to be less successful. Further studies from different settings are still required to confirm these findings.

More broadly as DOTS coverage increases it is likely that more attention will be paid to trying to identify low cost methods of active forms of TB case detection in high prevalence HIV settings. This issue is explored in a recent study modeling the population wide benefits of different interventions to control TB in high prevalence HIV settings (24). This study finds that improving the TB case detection rate is potentially the most cost-effective approach to TB control in high prevalence HIV settings. This finding is based on the assumption that the unit costs of case detection will increase 2-4 times when activities to improve case detection rates to 70% are implemented. TB treatment, a combination of case detection and treatment, and the treatment of latent TB infection (with IPT) also were found to be cost-effective, confirming previous studies. ART was significantly less cost-effective. Further studies are required to confirm these findings. Whilst there is no doubt that case finding is essential to TB control, a key issue now will be to verify the preliminary cost estimates of enhanced case detection.

**Estimating the resource needs of scaling up TB/HIV interventions**

The studies presented or referred to in this thesis demonstrate that there are a variety of cost-effective interventions available to control TB. Furthermore, several new interventions or enhancements to current interventions to control TB are likely to become available the coming years. In order to support the scale-up of these interventions, economists working in TB control are now becoming increasing concerned with how to finance them. Whilst this thesis does not focus on health care financing, the review contained in the final chapter examines the resource implications of scaling up cost-effective TB/HIV interven-
tions. This review highlights several of the methodological issues involved and areas that require further research. However, in reality, financial planning capacity within Ministries of Health, let alone TB services, in many countries remains weak. Supporting the development of simple tools that TB services can use to estimate their resource needs are required. The WHO has been assisting in this effort in its production of its annual TB control report and other activities over the past few years, however efforts remain focused on TB-specific costs.

The review presented in this thesis draws attention to the estimation of the systems costs required to scale up TB control interventions. The review found that most estimates of systems costs were made by simple ‘rule of thumb’ calculations. Estimates of long term costs of the investments in human and physical health systems capacity, based on different health systems modalities of scaling up TB control, are now required. As the Ukraine and Ethiopian study both illustrate, obtaining a better understanding on who bears the costs of expanding TB control interventions can be used to support the necessary systems reform. In addition, investments in the long term systems development costs for TB control may help address skepticism about the feasibility of adopting new technologies in weak health systems. In summary, the economic research focus in the future TB control needs to move beyond filling the gaps in knowledge regarding the cost-effectiveness of different interventions, to a thorough examination of the (costed) system implications of expanding these interventions.

CONCLUSION

Directly Observed Treatment Strategy remains the cornerstone for TB control. The studies presented in this thesis demonstrate that DOTS expansion in middle income countries may face institutional rigidities, but is feasible and cost-effective. The study into the MDR-TB highlights the potential cost-effectiveness of new cost technologies to tackle this disease; particularly if they are proved successful in preventing future transmission and spread of this dangerous disease. All the cost-effectiveness studies in this thesis highlight the importance of the cost to the patient in accessing and adhering to TB treatment. In the case of Ethiopia this cost is significant compared to annual household income. Attention needs to be give to mitigating these costs when planning services, particularly for the very poor. Finally the last part of this thesis examines the use of the cost information in the financial planning of TB services. Whilst the cost-effectiveness of many TB control interventions is well established, there is still significant work to be done to plan and estimate the resource requirements required to implement and scale-up both TB and HIV interventions. A particular area of concern is the estimation of systems costs of TB control expansion.
REFERENCES


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