

Post-2015 Development Agenda

India Perspectives



Tuberculosis

SPEAKERS AND CONTRIBUTORS

Anna Vassall

Anna Vassall is Senior Lecturer in Health Economics at the London School of Hygiene and Tropical Medicine. She is a health economist with around twenty year of experience in economic analysis. Her first degree is in economics. She then worked in the NHS supporting funding/contracting. She then took an MSc in Health Planning and Financing at the LSHTM, thereafter working for DFID as a health economist in the UK and Pakistan. This was followed by a period at Royal Tropical Institute (KIT) Amsterdam working on health planning and financing, aid effectiveness and the cost-effectiveness of tuberculosis and reproductive health in a wide range of low and middle income countries. Thereafter she directed and provided economic support to European Community and World Bank funded health sector reform and development projects in Yemen, East Timor, Syria and Sudan. Her PhD is in the economic evaluation of tuberculosis control. She has worked as an academic since 2010 (at LSHTM) specializing in research into the economics of HIV and TB, with a particular focus on health services and systems. Her current research interest is the costs and economic evaluation of HIV, TB and Sexual Reproductive Health. She has a keen interest in 'real world' evaluation methods and incorporating a broader health systems perspective in economic analysis. She has also published on health services financing, in particular the role of development assistance finance

Table of Contents

Summary: White Paper Report by Anna Vassall **1**
White Paper Report by Anna Vassall **3**

Summary: White Paper Report by Anna Vassall

Over 2 million Indians developed tuberculosis (TB) in 2013, and around 278,000 people in the country die from the disease every year: about 30 an hour. TB not only affects health, but the loss of earnings and cost of treatment forces many people deeper into poverty. The main focus of this study for the Copenhagen Consensus is the reduction of deaths from TB.

Many people have a latent TB infection. Of these, about 5% develop active TB within 18 months, while a further 5% will develop it sometime later in life. Most cases respond well to a standard combination of drugs, but some are multi-drug resistant (MDR-TB) largely because of poor initial treatment. About 2.2% of new cases in India are multi-drug resistant, with many more emerging if more than one course of treatment is needed.

Early detection of TB is important to reduce transmission, but finding those with the active disease is difficult because many of the symptoms are similar to those for other common diseases. As in most countries, India relies mainly on people presenting themselves to health services when they are ill. However, a particular problem in the country is that nearly half of TB sufferers first visit private practitioners who are not able to diagnose and treat the disease properly.

Multiple visits may be needed and there is an average delay of two months in receiving proper treatment. One result is that only 58% of all cases are notified to the Revised National Tuberculosis Control Programme (RNTCP). Engaging public and private health provision ensures that private practitioners become more effective, and expanded engagement is a critical part of a strategy to reduce deaths and further transmission.

TB is most commonly diagnosed using smear microscopy of sputum samples, although a particular issue in India is that some private practitioners use ineffective diagnostic techniques that are more expensive and produce many false positives. However, even microscopy may miss many active cases, particularly for those also infected with HIV, and the more expensive Xpert MTB/RIF test is now recommended by the World Health Organisation. This test also identifies those at most risk from MDR-TB.

About 6% of TB sufferers in India are also HIV infected, but this group accounts for 13% of all deaths. Routine referral of those diagnosed with TB to HIV diagnosis and treatment services is recommended by the Indian government for the nine states where HIV infection is most common.

Most cases of TB are treated with a standard combination of drugs in two phases over six months, and generally this can be carried out effectively in the community. Over 90% of TB cases can be cured with proper monitoring and high adherence to taking the full course of medicine; in India the success rate is about 88%. Treatment of MDR-TB is much more complex and expensive, may take two years and may require hospitalisation. Only about half the sufferers starting treatment are cured.

TB is a particular problem for poor families. Over three quarters of TB patients are from households with an income of less than a dollar a day per person, but it costs about \$145 for treatment (nearly half a year's income for one person). The average sufferer (across all social groups) also loses about \$500 in income.

However, treating TB can be highly cost-effective. Between 1997 and 2006, scaling up of TB control saved 1.3 million lives and a total of over 29 million life-years of disability or death. The overall increase in economic well-being was valued at \$88 billion for the ten year period, and each dollar spent generated \$115 worth of benefits.

Although the World Health Assembly has proposed a post-2015 target of reducing deaths from TB by 90%, widespread general population screening would be needed to achieve this, and the cost of this is unknown. However, a substantial reduction of up to 70% is feasible, saving about 180,000 deaths a year by 2025.

It currently costs about \$215 (13,500 rupees) to treat a TB patient in India, including general health service costs. This increases to \$7,500 (half a million rupees) for a case of MDR-TB. More public-private engagement would be cost-neutral, but a further \$9-15 would be needed for each month of treatment for social support and to ensure the full course of medicine is taken. Extra money is also needed for improved diagnostic testing. Overall, to reduce deaths by 70% by 2025, there would be an additional cost of \$180 million (five billion rupees) a year on top of current spending of \$250 million.

Depending on the assumptions made about the valuation of life and the discount rate, each rupee spent would give benefits of between 11.9 and 71.9 rupees, making a very strong case for improved TB control in India.

White Paper Report by Anna Vassall

Tuberculosis is a serious public health issue in India. According to the World Health Organisation (WHO) over 2 million Indians developed Tuberculosis (TB) in 2013 [1]. Around 278,000 people die from TB in India every year. This means that every hour, around thirty people die of TB in India, despite effective treatment being available. Despite this death toll, India has made considerable progress towards controlling TB, and TB incidence has been reducing in recent years. Nevertheless much more needs to be done to prevent further unnecessary deaths.

The economic case for sustaining this commitment and investment in TB control in India is compelling. Put simply, TB treatment is low cost and effective, and this combination results in substantial economic return. Moreover, the delivery of high quality TB services can also prevent the spread of the disease to others and slow the emergence of multidrug-resistant TB (MDR-TB), a dangerous and costly form of TB. Investment in TB is also important from a poverty reduction perspective, where the costs of accessing treatment, nutritional decline and loss of earnings may force many of those with TB into poverty.

This short report presents the economic case for maintaining investment in TB control post 2015 in India. The report first provides an overview of the targets for TB, the disease and the main TB control interventions. It then outlines the costs and benefits of investment in the different TB control interventions in India; arguing that TB control should be a priority investment in India's post 2015 development agenda. Our starting point for this presentation is the global post 2015 strategy, supported by the World Health Assembly. This declaration aims to end the global TB epidemic, with targets to reduce TB deaths by 90% and new TB cases by 80% by 2030, while ensuring no family is burdened with catastrophic expenses due to the disease. We focus here on the target to reduce deaths from TB.

TB control: what can be done?

In simple terms the disease of TB has two stages. The first is *latent TB* infection, when a person first becomes infected with TB. Of those infected, approximately 5% develop *active TB* disease (become TB cases) within 18 months, followed by a further 5% risk of developing active TB disease over a lifetime. Left untreated, active TB can be fatal. Active TB can be broadly divided into two types: TB which is drug-sensitive – responding well to a standard combination first line treatment; and, multi-drug resistant TB (MDR-TB) which is resistant to two or more drugs in the first line standard TB regimen. The treatment of MDR-TB has poor outcomes, is complex and can be costly [2-4]. While MDR-TB can be spread and circulated among populations, its origins lie in the misuse, poor delivery and adherence of TB treatment [5]. In India around 2.2 % of all new TB cases have MDR-TB, with many more cases found in those who need more than one course of TB treatment.

Identifying those who develop active TB is complex. The symptoms of (active) pulmonary TB include cough, fever, night sweats and weight loss, many of which are similar to symptoms of common diseases. However, ensuring early detection of active TB cases is fundamental to reducing transmission. As with most TB programmes, India relies primarily on 'passive case finding' to identify cases of active TB. This strategy is based on the expectation that those with TB symptoms will present at health services for their symptoms, and that health facilities and staff are sufficiently equipped and skilled to recognise and act on them. A key challenge in India is that almost half of those with TB first visit private practitioners with their symptoms. These private practitioners are often unaware of the appropriate diagnostic procedures for TB and may not treat TB correctly. This challenge results in an average delay before receiving appropriate TB treatment of just under 2 months; with those with TB making an average of 2.7 of often costly health care visits before

diagnosis [6]. As a result of these delays, only 58% of all TB cases are notified to the Revised National Tuberculosis Control Programme (RNTCP) in India.

However, in recent years, India has moved towards more intensified methods of collaborating with private sector in order to identify (and ensure effective treatment) of more of those with TB. Different models of engagement are being explored; many of which have been found to be cost-effective. For example, one study found that the cost-effectiveness of public provision of TB services was around the same as engaging with the private sector; but, if the public sector did not engage, then the cost-effectiveness of TB treatment in the private sector was much reduced [7]. Further expanding public private engagement is therefore a critical element of the strategy to reach the global TB targets; thereby, not only reducing deaths from TB, but also reducing the onward transmission of TB.

The most common method of diagnosis of TB globally is smear microscopy. This is recommended by the WHO and is widely used as a low cost method of TB diagnosis. Those who have positive smear test, are described as having 'smear positive' TB, and are the most infectious of TB patients. In India, a range of other tests may also be used. One particular issue is that private practitioners may use diagnostic tests that may not be accurate, thus generating unnecessary cost. If used instead of sputum microscopy, these tests generate thousands of additional false-positive TB diagnoses at approximately four times the cost of smear microscopy [8].

However, microscopy is far from a perfect test, and may miss substantial numbers of those with active TB [9, 10]. This is a particular issue for those also infected with HIV (6% of all TB cases in India). Since 2011, the WHO therefore recommends the Xpert MTB/RIF assay for widespread use in the diagnosis of TB. Xpert MTB/RIF increases chances that a case of TB can be diagnosed [11], however the cost per test is considerably higher than that of smear microscopy [12]. It also allows for the identification of those at most risk of MDR-TB. The rollout of Xpert MTB/RIF is therefore being considered in India, particularly for those cases at a higher risk of MDR-TB. While the impact of this rollout on TB incidence generally is less than improving public private engagement, it may contribute to a reduction in the incidence of MDR-TB [13].

Around 13% of deaths from TB in India, occur in those with HIV; as TB is more deadly in those who are co-infected. To improve the outcomes of those co-infected with TB and HIV, it is essential to ensure that those diagnosed with TB, are referred and have access to effective HIV diagnostic and treatment services. Indian guidelines recommend routine referral for HIV testing of all tuberculosis (TB) patients in the nine states with the highest HIV prevalence, and selective referral for testing elsewhere. A recent study examining the cost-effectiveness of this policy found that the referral of all patients with active TB in India for HIV testing would be both effective and cost-effective; and that while effective implementation of this strategy would require investment, routine, voluntary HIV testing of TB patients in India should be adopted [14].

The treatment of drug susceptible TB involves delivering a standard regimen of TB treatment usually for six months, divided into two phases; an intensive phase for two months and a four month continuation phase. During both phases treatment must be adhered to maximise treatment success and prevent drug resistance developing. In the last twenty years the WHO has recommended the Directly Observed Treatment Strategy (DOTS), moving away from the hospitalisation of TB. This has substantially reduced costs. With this good treatment monitoring, and high adherence, TB treatment can be very successful (at over 90% of people cured), and in India, treatment success is around 88% [1]. Treatment success may be further improved through proper support to patients (see section on social and nutritional support below).

MDR-TB however provides additional challenges. Microscopy cannot identify new drug-resistant TB, but (as stated above) Xpert MTB/RIF can identify cases of rifampicin-resistant TB, a strong indication that a patient has MDR-TB. Culture based tests also are used to diagnose MDR-TB, but are not currently widely available in India. Unfortunately, this complex process of diagnosis means that currently many TB cases are not tested for MDR-TB, and of those that are (and are found to be positive), just under 60% start treatment in India. The treatment of MDR-TB is far more complex than first-line treatment and may require hospitalisation. It can take 24 months or longer. Treatment is also costly and once started on treatment, MDR-TB treatment success in India is lower than many other countries with only around 50% of those starting treatment being cured. Strengthening diagnostic systems and providing models of MDR-TB care that are high quality, but also ensure that patients receive integrated care will therefore be key in the coming few years to reduce both deaths and the transmission of MDR-TB in India going forward.

Finally, the social determinants of TB cannot be overlooked in India. Poverty is key to care seeking behaviour and treatment default. Moreover, poor nutrition can substantially worsen treatment outcomes. TB and its treatment can still cause poor households substantial economic loss, primarily from loss of earnings while feeling unwell, thus further exacerbating this cycle of poverty, and making treatment adherence a challenge. As with other countries in South Asia, studies in India have found that TB disproportionately affects the poor. The RNTCP highlights that around 64% of those treated from TB come from the poor economic strata. [15]. A further study found that 77% of TB patients were from households with a per person income of less than US\$1 per day – but yet the average cost to the patient of being treated for TB was US\$145 – around 50% of the annual per person income [16]. Other studies have focused on lost income and found that across all TB patients (rich and poor) the average loss of income was around US\$ 500 per person – a substantial productivity loss for the economy. [17]. The costs to households of MDR-TB are likely to be considerably higher. Hence improved social and nutritional support to those with TB and their families may also be a key intervention to further improve both the health and poverty impact of TB control in India.

In summary, the short report above highlights the fact that strengthening TB control to achieve the post-2015 targets requires continued sustained investment in TB services, particularly in continued efforts in case detection – if deaths from TB are to be further reduced. Particular attention needs to be given to engagement with the private sector. It is also essential to ensure the appropriate and high quality treatment of MDR-TB cases. Social and nutritional support may prove important in improving both diagnostic and treatment success. All of this will require strengthening of the health systems. Programmatic, management and information support to all these services need to have the capacity to enable and support these investments; and ensure that funding flows and is spent in an efficient manner.

Costs and Benefits of reaching TB control targets in India

Despite the fact that considerable effort needs to be made, TB control has high economic returns for every Rupee invested. As described above, there are a wide range of studies that examine the costs and cost-effectiveness of the different elements of TB diagnosis and treatment in India – all of which support the current policies/ guidelines of the RNTCP. In addition, a recent study examined the economic costs and benefits of scaling up TB control between 1997 and 2006. This study found that the scale-up of TB control in India has resulted in a total health benefit of 29.2 million disability-adjusted life years (DALYs) over this period, including 1.3 million deaths averted. The total gain in economic well-being from TB control is estimated at US\$88.1 billion over the 1997-2006 10-year period. This generated a return of US\$115 per dollar spent [18].

Looking forward, we refer to the TB Targets work done by the TB Modelling and Analysis Consortium (TB-MAC) – that brings together groups which model the TB epidemic globally. Despite the cost-effectiveness of current interventions, work by this group suggests that the future looks less optimistic in terms of continuing the gains made. In particular it may not be possible to achieve a drastic reduction in deaths (90% by 2030) in a cost-effective manner using current diagnostic and treatment tools by 2030. The only intervention that was found to do this was widespread general population screening for TB. The costs of this approach are unknown. However, on the positive side, this work found that substantial reductions in TB deaths can be achieved for high economic gain; with the estimates of reductions in deaths through current tools ranging from a 60 to 70% reduction in deaths, or about 180,000 fewer deaths per year, by 2025. This would still be a considerable success and may be accelerated thereafter, if new tools to fight TB become available. This work was presented at last year’s global TB conference and uses multiple infectious disease models – and combines these with cost data from India to make estimates of the cost-effectiveness of these investments – and we use these calculations to estimate the benefit cost ratios of increased investment in TB control until 2030 here.

The estimates of costs that we are draw upon are provisional – and a formal announcement of final costs will be made at a later date, nevertheless they provide some indication of the likely magnitude of the cost benefit ratio of TB control in India going forward – and help us outline the potential economic return of TB control. In brief, we estimate that it currently costs around US\$215 (around 13,500 rupees) to treat someone with TB in India using previous studies. This is higher than estimates using TB programme expenditures [19]; and is a top end estimate, including general health service costs. For MDR-TB this increases significantly to around US\$7500 (around 500,000 rupees), although this depends on amount of hospitalisation involved. In addition many other costs need to be considered, these include the costs of engagement with the private sector and the costs of improving service quality and performance. We assumed that the while the public private engagement would increase the national TB programme (public sector) budget, overall the cost of treatment would remain neutral. We added a US\$9-15 dollar additional cost per treatment month in terms of social support and adherence. Finally, we made an adjustment to reflect the costs of laboratory strengthening for drug susceptibility testing and Xpert MTB/RIF expansion to previously treated cases.

Based on the above we estimate the costs of reaching the TB target of reducing deaths by 70% in 2025 to be around US\$ 180 million (around 5 billion rupees) per year *in addition to current spending* of around US\$ 250 million. It should be noted that this cost reflects additional expenditures per person with TB, but also reflects an expected reduction over time of the number of TB cases. Based on the findings of the modelling work done by TB-MAC, we estimate that the annual reduction in TB mortality and incidence following this investment, will result in around 2,590,000 DALYs averted per year (discounted at 3%).

| | | Annual Benefits (USD million) | | | | Benefit for every Rupee/USD spent | | | |
|-------------------------|--|-------------------------------|--------|--------|--------|-----------------------------------|-------------|-------------|-------------|
| | | 3% | | 5% | | 3% | | 5% | |
| Target | Annual Incremental Costs (USD million) | DALY L | DALY H | DALY L | DALY H | DALY L | DALY H | DALY L | DALY H |
| Reduce TB deaths by 70% | 180 | 2590 | 12950 | 2140 | 10702 | 14.4 | 71.9 | 11.9 | 59.5 |

We place an economic value on these DALYs averted saved using the Copenhagen Consensus recommended methods from of using an economic value of US\$1000 (63,500 rupees) and US\$5000 (320,000 rupees). We find that the economic return per rupee spent ranges from around 11.9 to over 71.9 making TB control a sound economic investment post -2015. We therefore conclude that the economic case for TB control in India remains very strong – and improved TB control should be a core part of the post-2015 development effort in India going forward.

References

1. Organisation, W.H., *Global Tuberculosis Report 2014*. 2014, World Health Organisation: Geneva, Switzerland.
2. Fitzpatrick, C. and K. Floyd, *A systematic review of the cost and cost effectiveness of treatment for multidrug-resistant tuberculosis*. *Pharmacoeconomics*, 2012. **30**(1): p. 63-80.
3. Orenstein, E.W., et al., *Treatment outcomes among patients with multidrug-resistant tuberculosis: systematic review and meta-analysis*. *Lancet Infect Dis*, 2009. **9**(3): p. 153-61.
4. Johnston, J.C., et al., *Treatment outcomes of multidrug-resistant tuberculosis: a systematic review and meta-analysis*. *PLoS One*, 2009. **4**(9): p. e6914.
5. Dye C, W.B., *Criteria for the control of drug-resistant tuberculosis*. *Proc. Natl. Acad. Sci. U.S.A*, 2000 **97**(14): p. 8180-8185.
6. Sreeramareddy, C.T., et al., *Delays in diagnosis and treatment of pulmonary tuberculosis in India: a systematic review*. *Int J Tuberc Lung Dis*, 2014. **18**(3): p. 255-66.
7. Floyd, K., et al., *Cost and cost-effectiveness of PPM-DOTS for tuberculosis control: evidence from India*. *Bull World Health Organ*, 2006. **84**(6): p. 437-45.
8. Dowdy, D.W., K.R. Steingart, and M. Pai, *Serological Testing Versus Other Strategies for Diagnosis of Active Tuberculosis in India: A Cost-Effectiveness Analysis*. *PLoS Med*, 2011. **8**(8): p. e1001074.
9. Davis, J.L., et al., *Diagnostic accuracy of same-day microscopy versus standard microscopy for pulmonary tuberculosis: a systematic review and meta-analysis*. *Lancet Infect Dis*, 2013. **13**(2): p. 147-54.
10. Steingart, K.R., et al., *Fluorescence versus conventional sputum smear microscopy for tuberculosis: a systematic review*. *Lancet Infect Dis*, 2006. **6**(9): p. 570-81.
11. Denkinger, C.M., et al., *Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysis*. *Eur Respir J*, 2014. **44**(2): p. 435-46.
12. Pantoja, A., et al., *Xpert MTB/RIF for diagnosis of tuberculosis and drug-resistant tuberculosis: a cost and affordability analysis*. *Eur Respir J*, 2013. **42**(3): p. 708-20.
13. Salje, H., et al., *The importance of implementation strategy in scaling up Xpert MTB/RIF for diagnosis of tuberculosis in the Indian health-care system: a transmission model*. *PLoS Med*, 2014. **11**(7): p. e1001674.
14. Uhler, L.M., et al., *Cost-effectiveness of HIV testing referral strategies among tuberculosis patients in India*. *PLoS One*, 2010. **5**(9).
15. Muniyandi, M., et al., *Socio-economic dimensions of tuberculosis control: review of studies over two decades from Tuberculosis Research Center*. *J Commun Dis*, 2006. **38**(3): p. 204-15.
16. Pantoja, A., et al., *Economic evaluation of public-private mix for tuberculosis care and control, India. Part I. Socio-economic profile and costs among tuberculosis patients*. *Int J Tuberc Lung Dis*, 2009. **13**(6): p. 698-704.
17. John, K.R., et al., *Costs incurred by patients with pulmonary tuberculosis in rural India*. *International Journal of Tuberculosis and Lung Disease*, 2009. **13**(10): p. 1281-1287.

18. Goodchild, M., et al., *A cost-benefit analysis of scaling up tuberculosis control in India*. Int J Tuberc Lung Dis, 2011. **15**(3): p. 358-62.

19. Floyd, K., et al., *Domestic and donor financing for tuberculosis care and control in low-income and middle-income countries: an analysis of trends, 2002-11, and requirements to meet 2015 targets*. Lancet Glob Health, 2013. **1**(2): p. e105-15.