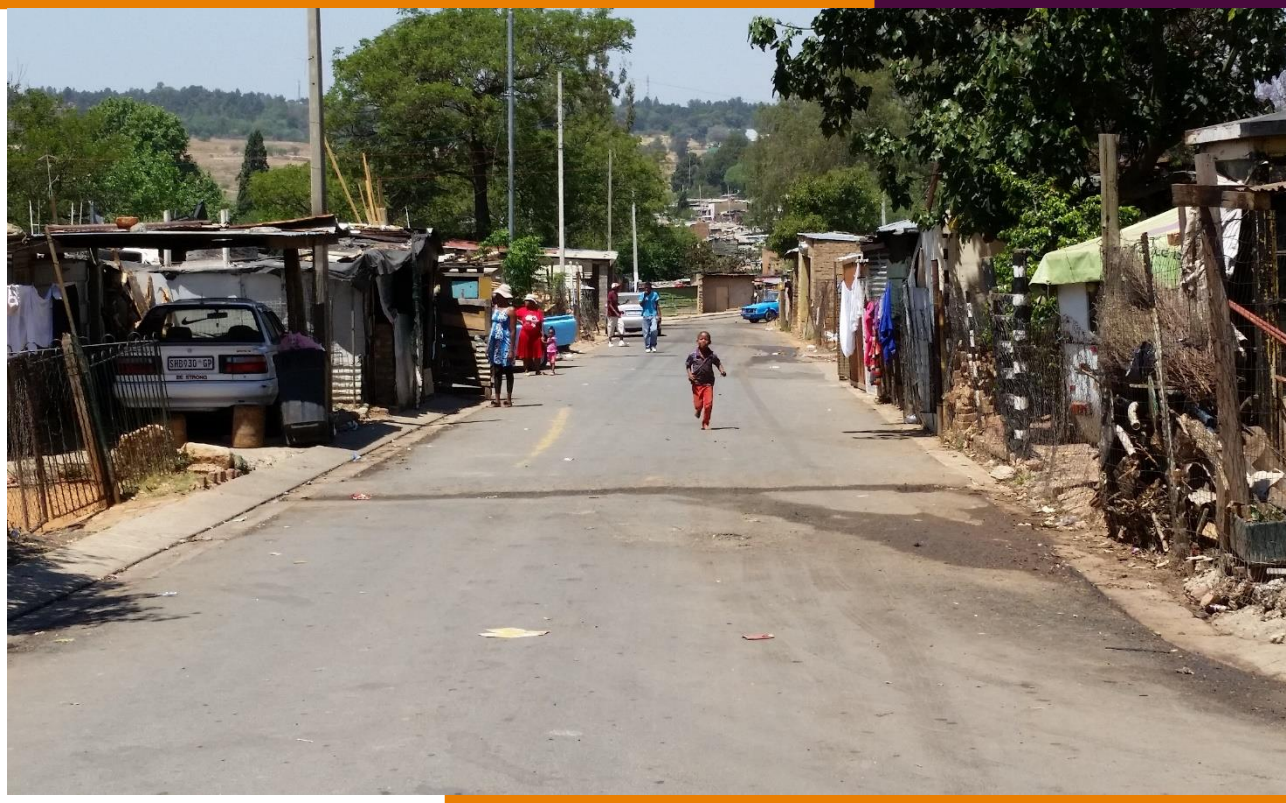
POST-2015 CONSENSUS

Post-2015 Development Agenda

South Africa 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

Tuberculosis is a serious public health issue in South Africa. About 450,000 people develop the disease every year, and 270,000 of those are also living with HIV. TB is South Africa's leading cause of death. About 89,000 people die from it every year; that's ten people every hour. Effective treatments are available and the country has made considerable progress in fighting the disease, but much more is needed to bring it under control.

The post-2015 agenda being finalised by the international community introduces some ambitious targets to end the global epidemic, and the current South African government has gone beyond these. The government is now committed to screening 90% of those at risk of contracting TB, ensuring that 90% of suspected cases are correctly diagnosed and treated and ensuring that 90% of those treated are cured.

Many people carry a latent infection, with only 5% going on to develop active TB within eighteen months and the same percentage at risk of developing TB later in life. Most cases are drug-sensitive and respond well to standard treatment with a combination of drugs, but failure to complete a proper course of treatment encourages the development of multi-drug resistant TB (MDR-TB), which is difficult and costly to treat and has poorer outcomes. Around 1.8% of new cases of TB in South Africa are multi-drug resistant.

HIV infection is a key factor in the TB epidemic. HIV sufferers have a higher risk of contracting TB and a greater chance of dying. In 2013, almost one million HIV-positive people were screened for TB, but more needs to be done to reach more of the over six million living with HIV. Preventive treatment for those with latent TB is relatively low-cost and can be delivered with HIV treatment (anti-retroviral drugs). But, despite several million people being eligible, only 340,000 were receiving this treatment according to 2014 figures.

Diagnosis is quite complex (particularly for those living with HIV), since many symptoms are similar to those for other common diseases. South Africa has moved towards more intensive and active methods of identifying cases, for example by screening all those attending primary health clinics. The aim is to move from identifying fewer than 70% to 90% of all cases.

Diagnosis using a microscope to screen sputum samples is cheap and the most common method used. However, it may miss substantial numbers of sufferers and more expensive techniques are needed to improved detection rates, particularly of those living with HIV, and find cases of drug-resistant infection. South Africa was one of the first countries to roll out the WHO-recommended Xpert MTB/RIF assay.

But screening is not the only factor. Ways must be found to ensure that patients return for results and also complete their treatment. Over 90% of people can be cured, but the rate is only 77% in South Africa. Treatment of MDR-TB is much more complex and costly (with possibly over half the South African budget for TB going on this). The success rate, at 45%, is also lower than for many other countries.

Poverty contributes to the problem by making people less likely to seek care and finish treatment, and poor nutrition can also reduce the chances of being cured. The average cost of a complete episode of TB can be almost 4,000 Rand, including loss of earnings, which is a major burden for poor families.

Currently, it costs about 2,500 Rand to treat a straightforward case of TB, rising to about 115,000 for treating MDR-TB. Reaching the target of reducing deaths by 90% would cost about 5 billion Rand per year in additional spending. Making this investment between 2016 and 2035 would give a total of 450,000 additional years of life to South Africans.

Valuing a year of life at $5,000 (60,000 Rand) means that each Rand invested would be worth around 5 Rand in benefits (extra years of life). This is probably an under-estimate for a country like South Africa, and does not take account of indirect economic benefits. In any case, tackling the TB epidemic would be a sound economic investment.

White Paper Report by Anna Vassall

Tuberculosis is a serious public health issue in South Africa. According to the World Health Organisation (WHO) around 450,000 South Africans developed Tuberculosis (TB) in 2013, (of these around 270,000 were living with HIV) [1]. Around 89,000 people die from TB in South Africa every year. Tuberculosis therefore accounts for just under 10% of the total deaths in South Africa annually and is South Africa's leading cause of death. Every hour, around ten people die of TB in South Africa, despite effective treatment being available. Despite this death toll, in the face of an HIV epidemic, South Africa has made considerable progress towards controlling TB in recent years, and TB incidence has been reducing in recent years. Nevertheless much more needs to be done.

The economic case for sustaining this commitment and investment in TB control in South Africa 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 those with TB into poverty.

This short report presents the economic case for maintaining investment in TB control post 2015 in South Africa. 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 the different TB control interventions in South Africa; arguing that TB control should be a priority investment in South Africa'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. The Minister of Health has been a leading force in expanding these targets and the current government has stated a strong commitment to: screen 90% of those vulnerable to TB; ensure that 90% those suspected of having TB are correctly diagnosed and initiated on treatment; and, ensure that 90% of those who are treated are cured.

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 South Africa around 1.8% of all new TB cases have MDR-TB, with many more cases found in those who need more than one course of TB treatment.

One of the key factors driving the TB epidemic in South Africa is HIV and hence those living with HIV are a priority for further TB control improvement [6]. According to the UNAIDS Global Report 2014 there are

an estimated 6,300,000 people living with HIV in South Africa. Unfortunately, the risk of developing active TB increases substantially following HIV infection [7]. HIV also substantially increases the risk of mortality from TB. However, the presentation of TB in those living with HIV is atypical, meaning that TB in those living with HIV can be difficult to diagnose [6]. South Africa has been a leader in rolling out TB/HIV collaborative activities to address these multiple challenges. In 2013, almost 1 million of those persons living with HIV were screened for TB. However much more needs to be done, to ensure that those living with HIV are linked into TB services, if the post-2015 targets are to be reached.

For those with latent TB, who are co-infected with HIV, the WHO recommends the use of preventative therapy to reduce the risk of developing active TB. The optimal treatment regimen for latent TB is still being evaluated, but currently the WHO recommends a 6-9 months treatment of one TB drug (isoniazid) [8]. Alternative or complementary strategies for some population groups are 36 months to lifelong treatment for persons living with HIV [9], or shorter course combined therapies (for example a 3 month combination of two TB drugs isoniazid and rifapentine [10]). Preventative therapy is a relatively low-cost intervention, which can be delivered alongside HIV treatment. Yet, despite, several million persons living with HIV being eligible for preventative therapy for TB in South Africa, the WHO reported only around 340, 000 persons living with HIV receiving preventative therapy in South Africa in its 2014 report, so this remains a key area for improvement.

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, South Africa traditionally relied 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. However, more recently, recognising that this approach will be insufficient to fully tackle the TB epidemic, South Africa moved towards more intensified and active methods of identifying those with TB. One approach is to screen all those who attend primary health clinics [11], another is focus on groups who may be particularly vulnerable to infection with TB. This approach is a key part of the strategy to help move South Africa from its current achievement of identifying just under 70% of TB cases to its target 90%; 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. However, microscopy is far from a perfect test, and may miss substantial numbers of those with active TB [12, 13]. This is a particular issue for those also infected with HIV. While X-ray and other methods can help, they are often not regularly performed to a high quality. 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 [14], however the cost per test is considerably higher than that of smear microscopy [15]. In 2012, South Africa took the courageous step of being one of the first countries globally to roll-out Xpert MTB/RIF. Unfortunately, while the roll-out was a success in many ways, it has to date proved insufficient to preventing deaths for TB [16]. Although Xpert remains a key part of the TB response, it is being increasingly recognised that it is only part of the solution to ensuring that 90% of those with TB are successfully diagnosed.

One of the reasons Xpert alone is proving insufficient are challenges with the linkage from diagnostics to receiving treatment in South Africa. While many patients provide samples to be tested for TB, they often

fail to return for the result, and are not therefore placed on appropriate treatment. More effort needs to be placed on ensuring adherence at this crucial stage in TB care; and to develop effective and low cost methods to trace those who default. Moreover, while Xpert is more accurate at detecting TB than microscopy, it still is not 100% accurate, meaning that too many of those with HIV are still missed, and still fail to get appropriate treatment in time. Again, more effort needs to be placed in ensuring that those with HIV receive the necessary additional testing, even where the initial Xpert test is negative, if more deaths are to be prevented.

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), but in South Africa, treatment success is around 77% [1]. Treatment default remains too high. Importantly, even for those staying on treatment death rates are higher than they need to be, because not all who also need HIV treatment are place on treatment in time. Increased efforts to ensure patient retention during treatment, and ensure access to anti-retroviral therapy (ART) is therefore required to reduce the relatively poor TB treatment outcomes in South Africa. South Africa is making steps in this direction, for example the employment of lay health workers to help supervise TB treatment, but more work therefore has to be done to ensure systematic linkages between providers of community based care and health facilities; and ensure effective linkage within health facilities to HIV services.

MDR-TB also provides additional challenges. Microscopy cannot identify new drug- resistant TB, but Xpert MTB/RIF can identify cases of rifampcin-resistant TB, a strong indication that a patient has MDR-TB. Culture based tests also are used to diagnose MDR-TB. Unfortunately, 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 extremely costly, with some estimating that over half of the budget for TB in South Africa being spent on MDR-TB. As with TB more generally, many of those with MDR-TB never make it onto treatment. The reasons are unclear, and are likely to be a combination of patient default and lack of access to appropriate care. Once started on treatment, MDR-TB treatment success is lower than many other countries with around 45% of those starting treatment being cured. As with TB more generally, key explanations are a high default rate during treatment and ensuring that patients also receive timely HIV treatment. Providing models of MDR-TB care that are high quality, but also ensure that patient receive integrated care will therefore be key in reducing both deaths and the transmission of MDR-TB in South Africa going forward.

Finally, the social determinants of TB cannot be overlooked in South Africa. 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 challenge. A recent study found at that the average cost of a complete episode of TB care to be around in South Africa to be over US$325 (almost 4,000 rand)[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 TB control in South Africa.

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 those living with HIV in

South Africa – if deaths from TB are to be further reduced. Particular attention needs to be given to diagnosing TB in those living with HIV and reaching other high risk communities. It is also essential to ensure the appropriate and high quality treatment of MDR-TB cases. For linkage to care and treatment, ensuring a high quality of adherence support remains essential. 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 South Africa

Despite the fact that considerable effort needs to be made, TB control has high economic returns for every Rand invested. There are wide range of studies that examine the costs and cost-effectiveness of TB prevention, diagnosis and treatment in South Africa. The National Department of Health has been working intensively over the last few months, to formalise the Minister's political commitment to TB, with a sound estimate of the resource requirements of achieving the TB Targets. These estimates are work in progress and this report does not want to pre-empt them. Instead our aim here is to support this effort, and provide a very approximate rate of economic return for TB control in South Africa in the context of the broader development effort.

To do this, we build on work done by the TB Modelling and Analysis Consortium (TB-MAC) – that brings together groups the model the TB epidemic globally. Recent work conducted by this consortium finds that the reaching the TB Targets in South Africa is achievable. This work was presented at last year's global TB conference and uses multiple infectious disease models – and combines these with local cost data from South Africa to make estimates of the cost-effectiveness of these investments [18-21].

The estimates of costs that we are draw upon are provisional – and a formal announcement of final costs will be made at a later data, nevertheless they provide some indication of the likely magnitude of the cost benefit ratio of TB control in South Africa. They are based on recent extensive data collection around TB treatment costs across South Africa, conducted by the Aurum Institute and the University of Cape Town. In brief, this recent research estimates that it currently costs around US$210 (around 2500 rand) to treat someone with TB in South Africa. For MDR-TB this increases significantly to around US$9500 (around 115,000 rand), although this depends on amount of hospitalisation involved. In addition many other costs need to be considered, these include the costs of screening in the community and at facilities, the costs of preventative therapy, and the costs of improving service quality and performance. In particular, the costs of screening all those who need it can be substantial, and as of yet are difficult to estimate. Finally, costs of supporting health systems, expanding programme and laboratory strengthening are also required.

Based on the above this short report estimates the costs of reaching the TB target of reducing deaths by 90% to be around US$ 422 million (around 5 billion rand) per year in addition to current spending. This will be considerably higher in the first years, where intensified case detection, active community work to screen all vulnerable groups may be required. There is considerable uncertainty around these costs, as the Ministry is just embarking on these screening programmes, and over time the costs of screening may reduce as providers develop efficient approaches.

Based on the findings of the modelling work done by TB-MAC, we estimate that the reduction in TB mortality and incidence following this investment, will result in around 450, 000 additional years of life for South Africans for the annual investment described above per year between 2016 and 2035.

		Benefits (ZAR million)				Benefit for every Rand spent			
		3%		5%		3%		5%	
Target	Costs (ZAR million)	YLL L	YLL H	DALY L	DALY H	DALY L	DALY H	DALY L	DALY H
Reduce TB deaths by 90%	4,977	5,378	26,889	4,446	22,231	1.1	5.4	0.9	4.5

We place and economic value on these life years saved using the Copenhagen Consensus recommended methods from of using an economic value of US$1000 (12,000 Rand) and US$5000 (60,000 Rand). The value of US$1000 is extremely low for South Africa, where the WHO recommends using the GDP per capita valuation of US$6617. **Therefore for only the top end estimates of benefit for every Rand spent should be considered in this case, and may be considered by some as an underestimate of true economic benefit.**

Nevertheless, referring to these estimates we find that the economic return per Rand spent ranges from around 4.5 to over 5.4, making TB control a sound economic investment post -2015. We therefore conclude that the economic case for TB control in South Africa is strong – and improved TB control should be a core part of the post-2015 development effort in South Africa. However, more work needs to be done to develop the most cost-effective TB strategy and we commend the National Department of Health for taking important steps in this direction with the development of the Investment Case.

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. Zumla, A., et al., Tuberculosis. N Engl J Med, 2013. 368(8): p. 745-55.

7. Wells CD, C.J., Nelson LJ, Laserson KF, Holtz TH, Finlay A, et al, HIV infection and multidrug-resistant tuberculosis: the perfect storm. J. Infect. Dis., 2007. 196 Suppl 1: p. S86-107.

8. Martinson, N.A., et al., New regimens to prevent tuberculosis in adults with HIV infection. N Engl J Med, 2011. 365(1): p. 11-20.

9. Samandari, T., et al., 6-month versus 36-month isoniazid preventive treatment for tuberculosis in adults with HIV infection in Botswana: a randomised, double-blind, placebo-controlled trial. Lancet, 2011. 377(9777): p. 1588-98.

10. Sterling, T.R., et al., Three months of rifapentine and isoniazid for latent tuberculosis infection. N Engl J Med, 2011. 365(23): p. 2155-66.

11. Bassett, I.V., et al., Intensive tuberculosis screening for HIV-infected patients starting antiretroviral therapy in Durban, South Africa. Clinical Infectious Diseases, 2010. 51(7): p. 823-829.

12. 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.

13. 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.

14. 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.

15. 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.

16. Theron, G., et al., Do high rates of empirical treatment undermine the potential effect of new diagnostic tests for tuberculosis in high-burden settings? Lancet Infect Dis, 2014. 14(6): p. 527-32.

17. Foster, N., et al., The economic burden of TB diagnosis and treatment in South Africa. Soc Sci Med, 2015. 130: p. 42-50.

18. Cunnama, L., et al., Using top-down and bottom-up costing approaches in low- and middle-income countries: the case for using both to assess the incremental costs of new technologies at scale. Health Economics, 2015. [Submitted for this supplement].

19. Hausler, H.P., et al., Costs of measures to control tuberculosis/HIV in public primary care facilities in Cape Town, South Africa. Bulletin of the World Health Organization, 2006. 84: p. 528-536.

20. Sinanovic, E., et al., Cost and cost-effectiveness of community-based care for tuberculosis in Cape Town, South Africa. Int J Tuberc Lung Dis, 2003. 7(9 Suppl 1): p. S56-62.

21. Sinanovic, E., et al., Impact of reduced hospitalisation on the cost of treatment for drug-resistant tuberculosis in South Africa. Int J Tuberc Lung Dis, 2015. 19(2): p. 172-8.