Modeling the Cost-Effectiveness of Multi-Drug Resistant Tuberculosis Diagnostic and Treatment Services in Indonesia

David H. Collins and Zina M. Jarrah of
Management Sciences for Health

November 2013

This report was made possible through the support for the TB CARE I provided by the U.S. Agency for International Development (USAID), under the terms of cooperative agreement number AID-OAA-A-10-00020. Management Sciences for Health (MSH) is a partner in the TB CARE I project which is led by Koninklijke Nederlandse Centrale Vereniging tot bestrijding der Tuberculosis (KNCV).

Abstract

Some countries have made great strides in expanding Tuberculosis (TB) control over the last few years, with significant assistance from donors, such as the Global Fund (GF) for Acquired Immune Deficiency Syndrome (AIDS), TB and Malaria. While there is still substantial donor funding for TB programs, these funds are expected to diminish in countries that have improving economies. Even in these countries there may still be a need to scale-up TB services, especially to deal with multi-drug resistant (MDR) TB which represents a major challenge. These countries will need to provide increased domestic funding but in most cases domestic resources will be limited and there will be competing health demands. TB services will, therefore, need to be cost-effective, efficient and affordable.

This will not be possible without a good understanding of the cost-effectiveness of the TB program in general, and of Multi-Drug Resistant Tuberculosis (MDR-TB) services in particular given the high costs of those services. A model has, therefore, been developed to do simple cost-effectiveness comparisons of the provision of the main elements of MDR-TB services - diagnosis and treatment. The model was designed for use by TB control program managers to help them conduct such analysis and has intentionally been made as simple as possible since skills in costing and in the use of such models are often weak. The model was used to cost MDR-TB diagnostic and treatment services at Moewardi Hospital in Surakarta, Indonesia. The 2009 MDR-TB cohort comprised 144 patients, of which 68 were cured and 3 completed treatment and were presumed cured, resulting in a 52% cure rate (Table 2). The remaining patients failed, defaulted, died or were transferred out. This performance reflects the fact that this was the first cohort of MDR-TB patients. The total program cost came to USD 687,512. The individual cost of treating and curing a patient was USD 5,589; the average program cost per patient cured was USD 9,683; and the average program cost per death averted was USD 15,237.

The data are from only one hospital and the prices have not been adjusted to fit the treatment period and so the results are not considered robust enough for international comparisons. This can however be addressed by conducting the same study at the 4 other hospitals in Indonesia, adjusting the prices for inflation and adding an indicator using DALYs.

Recommended Citation

Key Words

Tuberculosis, TB, Multi-Drug Resistant, MDR-TB, Indonesia, Costing, Cost-effectiveness.

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Management Sciences for Health
784 Memorial Drive
Cambridge, MA 02139
Tel: +1(617) 250.9500
Fax: +1(617) 250.9090
www.msh.org

CONTENTS

ACRONYMS

AIDS	Acquired Immune Deficiency Syndrome
ATM	HIV/AIDS, Tuberculosis, and Malaria
CEA	Cost-Effectiveness Analysis
DOTS	Directly Observed Therapy, Short-course *(the Internationally Recommended Standard for Tuberculosis Control)*
DST	Drug Susceptibility Testing
FLD	First-Line Drugs
GF	Global Fund
HIV	Human Immunodeficiency Virus
KNCV	*Koninklijke Nederlandse Centrale Vereniging tot bestrijding der Tuberculosis*
PMDT	Programmatic Management of Drug Resistant Tuberculosis
MDR-TB	Multi-Drug Resistant Tuberculosis
MOH	Ministry of Health
MSH	Management Sciences for Health
NTP	National Tuberculosis Control Program
SLD	Second-Line Drugs
TB	Tuberculosis
TB CARE I	Tuberculosis CARE I Program
USAID	United States Agency for International Development
WHO	World Health Organization
XDR-TB	Extremely Drug-Resistant Tuberculosis

ACKNOWLEDGEMENTS

This study was conducted by Management Sciences for Health (MSH) under the Tuberculosis CARE I Program (TB CARE I) Project of the U.S. Agency for International Development (USAID). It was funded as a Core project since the results are intended for global use.

The authors wish to thank the Director, Dr. Dyah Mustikawati, and staff of the National Tuberculosis Program and other senior officials of the Ministry of Health (MOH). Special thanks are due to Ratna Ekasari of KNCV, the TB CARE I Coordinator for Solo for her strong support and managers and staff of Moewardi Hospital and its Programmatic Management of Drug Resistant Tuberculosis (PMDT) satellite clinics for sharing data. The authors also wish to thank the members of the USAID team who support the TB control program and the GFATM program, their MSH colleagues Julie Rostina, Luiz Avelino Reciolino and Andy Marsden and consultants Firdaus Hafidz, Kiki Tsalatsita and Laura Mayanda. Further thanks are due to Ann Levin who provided helpful comments on the model used for the study. Finally, thanks are due for the support of Indonesia-based KNCV staff, including Dr. Salim Hamid, Linda North, Attin Utoro, Roni Chandra, and Tiar Salman.

The authors of this report are David Collins and Zina Jarrah of Management Sciences for Health in Cambridge, MA, USA. David Collins is a Senior Principle Health Finance Advisor, and Zina Jarrah is a Technical Advisor.

1.0 INTRODUCTION

1.1 Background

In 2009, a World Health Assembly resolution urged World Health Organization (WHO) Member States "to achieve universal access to diagnosis and treatment of MDR-TB and Extremely Drug-Resistant Tuberculosis (XDR-TB)". MDR-TB, or multi-drug resistant tuberculosis, is a major public health concern on a global scale, with an estimated 1 million patients that will need to be detected and put on treatment between 2011 and 2015[1]. WHO estimates that the proportion of newly diagnosed TB cases with drug resistance is 3.7%; and for patients previous treated for TB, this figure rises to about 20%. While the burden of MDR-TB is high, the detection and treatment remains perilously low; an estimated 1 in 5 MDR-TB cases around the world were reported to have been enrolled in treatment[2].

MDR-TB is caused by organisms which are resistant to the most common and effective first-line drugs used to treat TB - isoniazid and rifampicin. This may result as either an infection of the patient by organisms that are already drug-resistant; or MDR-TB may develop in the patient in the course of treatment for TB – especially due to incomplete or incorrect treatment with first-line anti-TB drugs.

Due to the nature of MDR-TB, and each patient's differing experiences with the various anti-TB drugs, a single standardized drug regimen will not necessarily be effective in treating every case. Standard treatment guidelines, outlining the various acceptable options for MDR-TB treatment, have been developed by the WHO[3]. Based on the standard list of drug options, an individualized drug regimen may be created for each patient, based on their drug resistance profile and other considerations. A number of second-line anti-TB drugs have been identified, with suggested dosages and durations for each drug. However, the overall duration of MDR-TB treatment can vary, depending on the patient's acceptance of the drugs, and the time it takes for the patient's conversion from the MDR-TB.

The current WHO guidelines suggest an intensive phase of 8 months for most MDR-TB patients, with the possibility of modifying the duration according to the patient's response to therapy. The total suggested treatment duration for patients newly diagnosed with MDR-TB is 20 months; again, this may be modified based on a case-by-case basis. However, new evidence also suggests that shorter treatment durations may be an option. Results from an observational study in Bangladesh showed much better rates of treatment success using regimens having a duration of 12 months or less compared with those usually achieved when the longer regimens are used[4].

Duration of treatment is not the only variable that may change in the diagnosis and treatment of MDR-TB. Newer and faster methods of drug susceptibility testing, such as GeneXpert, are becoming more readily available in some countries, thereby cutting down the lag time between testing and confirmation significantly. Whereas WHO guidelines propose the use of directly observed therapy (DOT) for the

[1] The global plan to stop TB, 2006-2015 / Stop TB Partnership. World Health Organization, 2006.
[2] World Health Organization, Multi-drug resistant tuberculosis (MDR-TB) 2012 update.
[3] Guidelines for the programmatic management of drug-resistant tuberculosis – 2011 update. World Health Organization, 2011.
[4] Van Deun A, Maug AK, Salim MA, Das PK, Sarker MR, Daru P, Rieder HL. Short, highly effective, and inexpensive standardized treatment of multidrug-resistant tuberculosis. Am J Respir Crit Care Med. 2010 Sept. 1; 182(5): 684–92.

administration of MDR-TB drugs, the location of DOT provision may vary, with patients being treated exclusively at hospitals in some countries, and with the implementation of community DOT in others. MDR-TB patients are typically admitted into specialized inpatient wards at hospitals during an initial period, to ensure that the side effects of the MDR-TB drugs are not too severe. The duration of this initial hospitalization may also vary by country.

Thus, although standardized treatment guidelines for MDR-TB exist, there remain a number of different permutations with regards to the diagnostic methods, drug regimens, duration and location of treatment, and other treatment options. Each of these variables has a different cost structure associated with it and the total cost of treating MDR-TB may vary significantly, depending on each country's approach. With increasing burdens of MDR-TB, and decreasing funding made available for TB programs, it is imperative that the costs and cost-effectiveness of different MDR-TB treatment options be explored.

1.2 Indonesia's TB Control Program

TB prevalence in Indonesia is currently estimated at 289 per 100,000 population, and the country has been designated by the World Health Organization as one of twenty-two High TB Burden Countries (HBCs). At the time of the study approximately 1.8% of all new TB cases and 17% of retreatment cases were believed to develop MDR-TB. Due to Indonesia's high burden of MDR-TB, the rapid detection of rifampicin resistance by GeneXpert is being rolled out as a new model for testing of MDR-TB suspects. GeneXpert will also be used as a rapid way to detect TB among Human Immunodeficiency Virus (HIV)-positive TB suspects.

Based on the current algorithm implemented in Indonesia, any suspected MDR-TB patient with rifampicin resistance confirmed by GeneXpert would immediately commence MDR-TB treatment, while waiting for culture and drug susceptibility testing (DST) confirmation of resistance to isoniazid and other first-and second-line drugs (FLD & SLD). Currently, there are five operational sites providing program management of drug-resistant TB (PMDT) in Indonesia – in Jakarta, Surabaya, Malang, Solo, and Makassar. Four others are under construction in Bandung, Bali, Medan and Yogyakarta. Additionally, six priority sites have been selected for GeneXpert roll-out, as well as two prison settings as pilots.

Under the TB CARE I project, MSH is providing support to the Indonesian National TB Control Program (NTP) in the area of TB financing. Various models have been developed and costing and economic studies have been carried out. Indonesia was selected for this study because the NTP wanted to know more about MDR-TB costs and because some of the necessary cost data had already been collected.

2.0 METHODOLOGY

2.1 Purpose

The purpose of this work was to develop a user-friendly model for conducting cost and cost-effective analysis of MDT-TB diagnostic and treatment services and to use it to conduct an analysis in Indonesia. The model was required to be generic, simple and user-friendly so that it could be accessed and used by NTP managers at national and local levels. Prior to developing a model, a literature review was conducted to look at previous models, methods and results.

2.2 Literature Review

Several studies have been conducted of the cost and cost-effectiveness of treating MDR-TB. The results were generally country or site specific and depended on choices of strategies, assumptions used, availability of data and selection of outcomes. Some of these are described briefly below, An additional study that is also described contains a systematic review and meta-analysis of four observational studies of cost-effectiveness of MDR-TB and provides an indication of how these results may be generalized to other settings. It should be noted that direct comparisons of results cannot be made across countries because the context is often different and figures are from different time periods.

- *Feasibility and Cost-Effectiveness of Treating Multidrug-Resistant Tuberculosis: A Cohort Study in the Philippines (2006)* [5]

In this study, Tupasi et al. compare the cost-effectiveness of implementing a pilot DOTS-Plus program in the Philippines with the standard treatment that would be applied in the absence of DOTS-Plus. Two types of costs were considered: the average cost of individual components of treatment (such as drugs and DOT visits) and the average cost per patient treated. Costs were assessed from a societal perspective – both health system and patient/family costs were considered.

A cohort of 117 MDR-TB confirmed patients were enrolled in DOTS-Plus and studied over a period of three years, with six possible outcomes identified: cured, completed treatment, died, defaulted, transferred out / outcome unknown, and failed treatment. Of these patients, 71 were cured/completed treatment (61% cure rate); 12 failed treatment; 18 died; and 16 defaulted. The DOTS-Plus strategy in the Philippines provided patients with individualized drug treatment regimens.

The average cost per patient treated in the DOTS-Plus project was USD 4,192, of which USD 3,355 was health system costs and USD 837 was incurred by the patients and/or their families. Drugs were the main component of this cost, at an average of USD 1,557 per patient. The net increase in total costs associated with the DOTS-Plus strategy was about USD 0.4 million. In the absence of a DOTS-Plus program, the average cost per MDR case was USD 116. The mean cost per DALY gained by DOTS-Plus was USD 179 from the health system's perspective, and USD 242 when all costs were considered. This cost per DALY gained is considered to be cost-effective, according to international benchmarks, such as a cost per DALY gained of less than per capita gross national income (USD 1,080 in the Philippines) or

[5] Tupasi TE, Gupta R, Quelapio MI, et al. Feasibility and cost-effectiveness of treating multidrug-resistant tuberculosis: a cohort study in the Philippines. PLoS Med 2006 Sep; 3 (9): e352

one to three times gross domestic product per capita. Overall, the study demonstrates that treatment of MDR-TB patients with DOTS-Plus is cost-effective, when compared with the standard treatment available in the absence of DOTS-Plus.

Compared with the Cost-Effectiveness Analysis (CEA) study from Peru (see below), the health systems costs in the Philippines were higher (USD 3,355 per patient compared with USD 2,381 in Peru); however, the improved cure rate (61% versus 48%, respectively) resulted in a similar finding of cost-effectiveness, in which about USD 200 per DALY were gained.

- *Feasibility and cost-effectiveness of standardised second-line drug treatment for chronic tuberculosis patients: a national cohort study in Peru (2002)* [6]

In this study, Suarez et al. analyze the cost-effectiveness of standardized second-line drug treatment for chronic TB / MDR patients in Peru. Treatment was provided for free to patients, in addition to providing a weekly food parcel. Cost-effectiveness in this study was assessed from the perspective of the public sector only. The analysis focused on the increase in total costs and effects associated with the use of second-line drugs, as compared with the treatment confined to isoniazid monotherapy in the absence of second-line drugs. Both the average cost if individual components (such as drugs, DOT visit), and the average cost per patient, were considered.

Of the 466 patients enrolled for this study, 298 (87%) had MDR-TB. 255 patients (48%) were cured, 57 (12%) died, 131 (28%) did not respond to treatment, and 53 (11%) defaulted. Of the 413 (89%) of patients who complied with treatment, 225 (55%) were cured.

The average cost per patient treated on standardized second-line drug treatment was USD 2,381, with drugs taking up the main costs (USD 824); in addition, food parcels, DOT visits, and consultations with doctors represented large costs. The total annual cost of the program was estimated at USD 0.6 million, or the equivalent of 8% of the NTP annual budget. The mean cost per DALY was USD 211; this figure was estimated to decrease significantly with an anticipated fall in drug prices in 2002, to USD 165. The cost per individualized treatment was assumed to cost USD 10,000 per patient; or a cost per DALY gained of USD 368 and USD 484. If the drug costs decreased as mentioned, the cost per DALY would drop to USD 200-300. Considering the gross national income per capita of Peru of USD 2,390 in 1999, treatment with second-line drugs (standardized or individualized regimens) was deemed to be cost-effective.

- *Cost-Effectiveness of Treating Multidrug-Resistant Tuberculosis (2006)* [7]

In this study, Resch et al. use a state-transition model for Peru to evaluate the cost-effectiveness of five different treatment strategies. These strategies are as follows: 1) first-line drugs administered with DOTS; 2) standardized second-line drug treatment for retreatment cases; 3) standardized second-line drug treatment for retreatment cases confirmed MDR-TB; 4) drug susceptibility testing (DST) and individualized treatment for retreatment cases; and 5) DST and individualized treatment for all cases. These strategies were evaluated in terms of incremental costs per TB death averted, and costs per QALY saved. Costs were determined from the perspective of the public health-care system.

[6] Suarez PG, Floyd K, Portocarrero J, et al. Feasibility and cost-effectiveness of standardized second-line drug treatment for chronic tuberculosis patients: a national cohort study in Peru. Lancet 2002 Jun 8; 359 (9322): 1980-9

[7] Resch SC, Salomon JA, Murray M, Weinstein MC (2006) Cost-effectiveness of treating multidrug-resistant tuberculosis. PLoS Med 3(7): e241. DOI: 10.1371/journal.pmed.0030241

The authors modeled Peru's TB epidemic over a 30-year horizon, using a starting population of 100,000 and basing case cure rates, drug costs, and other assumptions on previous cohort studies. Several different sensitivity analyses were performed to determine the stability of the base case findings, due to the fact that there is a lot of variation in, and uncertainty about, the effectiveness and cost of MDR-TB treatment.

In Peru, with a population of 27 million, the authors estimate that DOTS-Plus with standardized regimens (Strategy 3) would avert 2,010 deaths, and individualized regimens (Strategy 4) would avert 2,400 deaths, as compared with DOTS alone over a 30-year period. The cost would be USD 17 million and USD 21 million dollars, respectively. Using Strategy 2 would result in an incremental cost of USD 720 per QALY and USD 8,700 per death averted; Strategy 3, USD 990 per QALY and USD 12,000 per death averted; and Strategy 4, USD 11,000 per QALY and USD 160,000 per death averted.

Based on the results, Strategy 4 (DST testing and individualized treatment for retreatment cases) would be optimal for Peru, using three times the per capita GDP as a threshold for cost-effectiveness. (The per capita GDP of Peru was USD 2,360.) Despite the higher cost of individualized treatment, the extra number of lives saved, when compared with standardized treatment, would justify the additional cost. If the parameters changed (such as drug costs, or percentage of cases that are MDR-TB), the optimal treatment strategy would need to be re-evaluated.

- *Cost and cost-effectiveness of multi-drug resistant tuberculosis treatment in Estonia and Russia (2012)*[8]

This study evaluated the cost and cost-effectiveness of MDR-TB treatment in Estonia and Russia (Tomsk Oblast), comparing cohorts enrolled on treatment according to World Health Organization (WHO) guidelines in 2001 and 2002 with cohorts treated in previous years. Costs were assessed from a health system perspective in 2003 in USD; effects were measured as cures, deaths averted and disability-adjusted life-years (DALYs) averted. Cure rates when WHO guidelines were followed were 61% (90 out of 149) in Estonia and 76% (76 out of 100) in Tomsk Oblast, with a cost per patient treated of USD 8,974 and USD 10,088, respectively. Before WHO guidelines were followed, cure rates were 52% in Estonia and 15% in Tomsk Oblast; the cost per patient treated was USD 4,729 and USD 2,282, respectively. Drugs and hospitalization accounted for 69-90% of total costs. The cost per DALY averted by treatment following WHO guidelines was USD 579 (range USD 297- USD 902) in Estonia and USD 429 (range USD 302- USD 546) in Tomsk Oblast. Treatment of patients with MDR-TB can be cost-effective, but requires substantial additional investment in tuberculosis control in priority countries.

- *A systematic review of the cost and cost-effectiveness of treatment for multidrug-resistant tuberculosis (2012)* [9]

In this study, Fitzpatrick and Floyd review the available evidence on MDR-TB cost and cost-effectiveness. From an initial selection of 420 publications in peer-review journals and grey literature, four studies were selected for the final review, from the Philippines, Peru, Estonia and Tomsk Oblast (Russia). The authors extracted cost and cost-effectiveness data from each study, then adjusted the costs to a common year of value (2005) for comparison purposes.

[8] Floyd K, Hutubessy R, Kliiman K et al. Cost and cost-effectiveness of multi-drug resistant tuberculosis treatment in Estonia and Russia. [Eur Respir J] 2012 Jul; Vol. 40 (1), pp. 133-42.

[9] Fitzpatrick C, Floyd K. A systematic review of the cost and cost-effectiveness of treatment for multidrug-resistant tuberculosis. Pharmacoeconomics ISSN: 1179-2027, 2012 Jan; Vol. 30 (1), pp. 63-80; PMID: 22070215

The cost per patient for MDR-TB treatment in Estonia, Peru, the Philippines and Tomsk was USD 10,880, USD 2,423, USD 3,613 and USD 14,657, respectively. Best estimates of the cost per disability-adjusted life-year (DALY) averted were USD 598, USD 163, USD 143 and USD 745, respectively. Key cost drivers were the model of care chosen (hospitalization vs. ambulatory care) and the second-line drugs included in the treatment regimen. In all cases, the cost per DALY averted was lower than GDP per capita, thereby suggesting that MDR-TB treatment is cost-effective.

The authors conclude with the following key points: treatment for MDR-TB can be cost effective in low- and middle-income countries; scaling up treatment for MDR-TB towards the 2015 goal of universal access to care will require additional resources for TB care and control; and outpatient-based models of care can greatly enhance the efficiency of treatment for MDR-TB, and should be used unless there is strong evidence that hospitalization is necessary to achieve high rates of adherence to treatment.

2.3. Model Development

The literature review did not indicate the presence of an existing simple, user-friendly model for conducting MDR-TB cost and cost-effectiveness analysis. The review did, however, provide useful information for the development of this model. The development of the model took into account, therefore, the methods used in conducting the previous studies as well as the WHO guidelines on cost and cost-effectiveness analysis of TB control.

The model was developed to meet the criteria stated previously – it should be generic, simple and user-friendly and easily accessible to the target group, namely TB control program managers. The software utilized was Microsoft Excel, which is widely used and available, can provide an open source tool, has sufficient power, and most TB program managers have some familiarity with it.

The model is customizable to reflect the standard treatment guidelines and MDR-TB algorithm for each country. The user is able to select from a limited number of options to determine the cost-effectiveness of changing the following parameters:

- Diagnosis
- Drug regimen
- Treatment Setting (level of care, inpatient vs. outpatient, length of stay, DOT).

The model can only compare the cost-efficiency of two actual sets of data since the outcomes are not linked to inputs or processes.

The model was designed to only cost diagnostic and treatment strategies (e.g. comparing hospitalized versus ambulatory treatment strategy). Costs related to MDR-TB case-finding, and contact and defaulter tracing are not included. Only financial costs are included and only from the provider perspective. Non-financial costs and patient costs are excluded[10]. Only recurrent costs are included – capital, depreciation and maintenance costs for vehicles, equipment and buildings are not included[11]. Program development and management costs such as policy-making, training and meeting costs are excluded.

[10] If a second version of the model is developed it is recommended that patient costs be included.
[11] The cost of building in infection control is also not included.

The model is only structured to make simple cost-effectiveness comparisons for two scenarios but it should be feasible to add others. In addition, it only shows total costs and outcomes but it should be possible to also calculate and compare incremental costs and outcomes. For outcome measures, the model uses case completion rate, the cure rate and the cost of deaths averted.

The user enters the numbers of cases treated together with the related outcome figures. These can be actual figures or targets. Prices and unit costs are entered for diagnostic tests, drugs, supplies, staffing, inpatient hospitalization (hotel) and patient travel stipends. Laboratory and outpatient overhead unit costs are not included.

The model uses an activity based costing (bottom-up) methodology for all costs and, therefore, all the costs are considered variable. This includes hospital and PMDT clinic overhead costs which are assumed to have been calculated on a 'per patient cost' outside the model.

The model calculates the average, standard cost for one patient diagnosed and treated for each component of diagnosis and treatment e.g., tests, drugs, a consultation. The model also calculates the total cost for the patient cohort.

MDR-TB diagnosis and treatment can cover up to two years and the interventions take place at different times during that period, generally with more costs falling in the first year. Since the costing can only be related to patients who have completed treatment for the purposes of cost-effectiveness, such a costing can only be carried out in the year afterwards. It is not generally feasible to match the cost data with the 2-year time period. It may be most practical to use test and drug prices and salary levels from the mid-point of the cohort treatment period and overhead costs salaries from the last fiscal year before the end of the 2-year period. The costs do not, therefore, match perfectly with the outcomes but unless there have been major price changes during the period they should be good enough for broad estimates and comparisons.

The model was tested in Indonesia using data provided by the National TB Control Program. Since a uniform approach for MDR-TB treatment has been implemented nationwide in Indonesia, we were unable to obtain any actual data for alternative treatment methods that we could use for a comparison (see Limitations, Section 5 of this report). We, therefore, created a what-if scenario for the comparison. If any new diagnoses or treatments are being considered in the country, then comparisons can be made.

2.3 Data Collection

The first step in testing the model was to collect the MDR-TB algorithm and standard treatment guidelines for each of Indonesia's MDR-TB treatment sites. This involved confirming whether all sites use the same algorithm or whether there are any variations in diagnostic and treatment methods. Based on discussions with KNCV staff (the advisor on PMDT at Moewardi Hospital in Solo), all MDR-TB sites use similar diagnosis and treatment methods. As a result, it was decided that data could be collected from Moewardi Hospital and its satellite PMDT clinics, and other hospitals did not require individual visits.

A significant amount of data was collected from Moewardi's MDR-TB program, including drug costs, GeneXpert costs, inpatient/bed day costs, MDR-TB treatment algorithm and satellite clinic activities. Additionally, the costs of culture and DST testing were required, since this is performed at a national reference laboratory. Costs of DOT provision were collected from PMDT satellite clinics, which operate

in coordination with Moewardi to provide regular treatment monitoring services to MDR-TB patients. This includes patient support costs, which are provided to patients to enable their travel to Moewardi for scheduled updates and additional sputum testing.

The costs were for 2011 and were calculated as follows:

- Diagnostic tests – unit prices were either standard or actual, quantities were according to the Indonesian standard guidelines
- Drugs – unit prices according to the Global Drug Facility Stop TB Partnership, quantities were according to the Indonesian standard guidelines
- Staff costs – salaries collected by authors; standard quantities estimated by hospital staff.
- Inpatient hospitalization – data collected by the authors
- N-95 masks – average price per web search, quantity per Indonesian standard guidelines.
- Patient travel stipend – per Moewardi Hospital staff

Patient and outcome data were collected from Moewardi Hospital for 2009 through 2011, and also at the national level via e-TB Manager[12], which tracks all MDR-TB patients, their current status, and eventual outcome. These data included the following: number of MDR-TB cases, number of HIV+ cases, deaths, cures, defaulters, transfers and failed treatments.

Due to the fact that Indonesia did not have any significant differences in MDR-TB diagnosis and treatment methods across the various sites we were not able to complete the comparative part of the model with real data in this test.

To test the cost-effectiveness comparisons in the model, we therefore created a simple what-if scenario. For this we assumed that increasing the patient travel stipend by 50% would decrease the number of defaulters by one-third. These figures were made up and so cannot be used for comparisons in Indonesia or elsewhere.

[12] A model developed by USAID's Strengthening Pharmaceutical Services Project for managing TB information. For more information see <*http://erc.msh.org/toolkit/Tool.cfm?lang=1&CID=2&TID=224*>.

3.0 RESULTS

3.1 Assumptions

This version of the model only includes the costs of diagnosis and treatment. It does not include the costs of prevention, promotion, case finding or defaulter tracing. It only includes recurrent costs for simplicity and because these costs can be used to develop and compare with recurrent budgets. Capital costs (e.g. laboratory equipment) have been excluded. We also excluded program management and development costs such as developing guidelines and conducting training. Furthermore, program costs are not included. Service delivery support costs, such as hospitalization, doctor salaries and patient stipends are included.

For diagnosis, we assume that all suspected MDR-TB patients would be tested with GeneXpert, and then confirmed with either solid or liquid culture combined with drug susceptibility testing (DST). In addition to the DST, a number of baseline laboratory examinations would be given, as well as initial consultations with a doctor.

The drug regimens for MDR-TB patients can vary depending on the patients' drug resistance profiles. We included the standard drug regimen, ethambutol-resistant drug regimen, and drug regimens for patients previously treated with kanamycin and quinolone.

For treatment monitoring, we assume an average inpatient stay of 24 days based on patient data collected from Moewardi Hospital; this includes both the initial visit to monitor the patient for adverse effects, as well as any subsequent hospitalizations. According to the Indonesian treatment algorithm, MDR-TB patients receive DOTS five days a week from the closest PMDT satellite clinic, as well as a doctor's visit each week at the health center. Monthly visits with a specialist are made at the hospital, which may include additional laboratory testing and routine sputum examinations to test for conversion. Patients are also paid a monthly stipend to cover travel costs to the hospital.

As described in the previous section, patient outcome data was collected using the number of MDR-TB cases admitted to Moewardi Hospital. Due to the long length of treatment, the 2009 cohort was the only year that could be used with complete outcome data. The two-year treatment period covered, therefore, 2009 through 2011. We assume that the self-cure rate for MDR-TB patients who are HIV+ is 0%, and that the mortality rate is 100%. For patients who are HIV-, accurate death rates for MDR-TB were not available; in the meantime, the rates for regular TB (20% self-cure rate) were used as a proxy.

The cost data used in the test was from 2011. Since the patient treatment period covered the period 2009 through 2011 the costs are slightly inflated – probably by around 6% or 7% since the treatment costs are higher in the first year.

3.2 Results

As described in the previous section, Indonesia operates a standard MDR-TB treatment protocol, and therefore the cost-effectiveness of two different treatment scenarios could not be compared. Scenario

one in the model uses the actual data collected and these were used to estimate the current cost per MDR-TB case cured, and cost per death averted.

Based on the assumptions described above, the average cost per MDR-TB patient for diagnosis (test reagents and supplies), treatment (drugs), and treatment monitoring was USD 129, USD 1,725, and USD 3,735 respectively. This comes out to a total average cost per MDR-TB treatment of USD 5,589. See Table 1 below for the cost summary, in USD and IDR. Costs were not included for lab or pharmacy maintenance or overhead (facility running costs) and for pharmacy staff.

Table 1: Cost per MDR-TB Patient Treated (2009-11 patient data and 2011 prices)[13].

	USD	IDR
Diagnosis (reagents and supplies only)	129	1,260,460
Treatment (drugs only)	1,725	16,897,072
Treatment Monitoring (including staffing)	3,735	36,585,997
Total	5,589	54,743,529

The 2009 MDR-TB cohort for Moewardi Hospital comprised 144 patients, of which 68 were cured and 3 completed treatment and were presumed cured, resulting in a 52% cure rate[14] (Table 2).

Table 2: Outcome data for MDR-TB Patients, Moewardi Hospital for 2009

	Number	%
Total number of patients in yearly cohort	144	100%
Number of patients cured	68	47%
Number of patients completed treatment	3	2%
Number of patients failed	29	20%
Number of patients died	14	10%
Number of patients defaulted	22	15%
Sub-total excluding transfers out	**136**	**94%**
Number of patients transferred out	8	6%

The total program cost came to USD 687,512. The individual cost of treating and curing a patient was USD 5,589. The average program cost per patient cured was USD 9,683[15]. The average program cost per death averted was USD 15,237.

[13] As noted above these costs are probably inflated by about 6% or 7%.

[14] The cure rate was calculated by taking the total cured and completed patients as a percent of the total cohort excluding transfers out.

[15] This is the total cost of the program divided by the total number of patients who were cured and who completed treatment.

Recognizing that this data is from only one hospital and the prices have not been adjusted to fit the treatment period, the results are not considered robust enough for international comparisons. This can, however, be addressed by conducting the same study at the 4 other hospitals, adjusting the prices for inflation and adding an indicator using DALYs.

A second scenario was created in the model to test its functionality. For this we assumed that increasing the patient travel stipend by 50% would decrease the number of defaulters by one-third. These figures were made up and so cannot be used for comparisons in Indonesia or elsewhere. Using this made-up assumption, the model calculated that:

- The total program cost would increase from USD 687,512 to USD 761,546 (reflecting the increased stipend costs and the cost of fully treating more patients.
- The individual cost per patient per patient cured would increase from USD 5,589 to USD 6,079 (reflecting the increased stipend costs).
- The average program costs per patient cured would increase slightly from USD 9,683 to USD 9,742 (reflecting the increase in stipend costs offset by the higher number of patient cured).
- The average program cost per death averted would decrease from USD 15,237 to USD 14,564 (reflecting the increased stipend costs offset by the higher number of deaths averted)[16].

Table 3: Cost per outcome compared for one actual and one hypothetical option (USD)

	TREATMENT OPTION 1 (USD)	**TREATMENT OPTION 2 (USD)**
Total program cost	687,512	761,546
Average individual cost per patient fully treated / cured	5,589	6,079
Average program cost per patient cured	9,683	9,742
Average program cost per death averted	15,237	14,564

[16] Patients cured less those who would have been expected to self-cure.

4.0 LIMITATIONS

As we have described earlier in this report, the purpose of this exercise was to create a simple MDR-TB CEA model that could be used by district level managers working in National TB Programs in developing countries. Therefore, the initial model prototype is a very simple and generic model based in Excel. To maintain the simplicity of the model, no probabilistic modeling has been done to determine the validity of the cost-effectiveness calculations. The next iteration of the model should include this modeling.

The MDR-TB CEA model calculates impact in terms of patients cured and deaths averted, using the WHO TB Cost and Cost-Effectiveness guidelines. Disability Adjusted Life Years (DALYS) have not been included but can be added in a second version. Also, self-cure rates for MDR-TB have not been taken into account.

Finally, due to the fact that Indonesia uses a single standard MDR-TB treatment, there were no additional actual treatment options to consider for this exercise. We, therefore, populated the second treatment option with a what-if scenario using made-up data. In other circumstances it will be possible to compare two actual scenarios or to conduct other what-if analysis.

5.0 CONCLUSIONS AND NEXT STEPS

The need for serious consideration of the cost-effectiveness of different MDR-TB treatment options has been demonstrated in several studies. WHO estimates that the proportion of newly diagnosed TB cases with drug resistance is 3.7%; and for patients previous treated for TB, this figure rises to about 20%. While the burden of MDR-TB is high, the detection and treatment remains low; an estimated 1 in 5 MDR-TB cases around the world were reported to have been enrolled in treatment.

The main purpose of collecting the data in Indonesia was to test and refine the model. As noted above the data and results are only from one hospital and at one point in time and thus the results are considered limited and insufficiently robust for international comparisons.

It is recommended that data be collected at the other 4 pilot hospitals in Indonesia with a view to producing costs which are comparable with those in other countries and which can be used as a baseline for Indonesia. It is also recommended that a section be added for patient costs so that comparisons of cost-effectiveness are more complete and the tables be expanded to show incremental cost-effectiveness figures. In addition, it is worth adding an outcome indicator for the cost per DALY gained. Also, while this Version 1 of the model is fully functional, it should be used in two more countries with different treatment methods to ensure that it is generic enough for use in all countries.

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