

Economic Cost of Non-Adherence to TB Medicines Resulting from Stock-Outs and Loss to Follow-Up in the Philippines

INTRODUCTION

One of the key elements of successful tuberculosis (TB) control programs is adherence to treatment, and this is a cornerstone of most international and national policies and guidelines. Non-adherence is often due to patient-related factors, but can also be a result of provider issues, such as stock-outs of TB medicines. Non-adherence results in increases in length and severity of illness, deaths, disease transmission, and drug resistance. These have economic consequences in terms of costs and loss of income for patients and their families and also costs to the health system.

Non-adherence is commonly due to treatment interruption, which may be for short intermittent periods of a few days or for longer periods of weeks or months, and may even end up as complete discontinuation of treatment. Interventions to prevent treatment interruption are aimed at both patients and providers. On the provider side, actions include ensuring proper prescribing practices and management of side effects, providing good quality medicines, and preventing stock-outs. On the patient side, these include interventions to encourage patients to continue treatment even when they feel better, use medicines as directed, and remove barriers such as transport costs. These actions are believed to be a good investment, but the economic savings have not been well and clearly defined. The Philippines is among 22 countries considered to have a high burden of TB, including multidrug-resistant (MDR) TB. The Philippines Department of Health (DOH) has an

extensive TB program with directly observed treatment short (DOTS) courses for TB and programmatic management of drug resistant TB for MDR-TB. In addition, the DOH has strategies and procedures in place to ensure and improve treatment adherence, including supervised treatment, patient compliance incentives, and supply chain management strengthening. This is not always easy, however, especially in a large, decentralized country where health care services are largely managed at local levels and stock-outs and loss to follow-up (LTFU) have been challenges.

In recent years, National Tuberculosis Control Program (NTP) data and several studies have indicated problems with stock-outs of some TB medicines and with LTFU. Both of these problems result in treatment interruption.

At the request of the NTP and USAID, a study was conducted to determine the health, mortality, and economic impact of stock-outs and LTFU to justify greater investment in addressing these challenges.



*Child with MDR-TB undergoing treatment in the Philippines.
 (photo: WHO/HM Dias)*

METHODOLOGY

Three case studies were selected on the assumption that these would probably have had the greatest impact: stock-outs of drug-sensitive TB (DS-TB) category 1 medicines; LTFU of DS-TB patients; and LTFU of MDR-TB patients.

Data were obtained from three sources: a global literature review, a review of NTP documents and records, and interviews with an expert panel of doctors, pharmacists, and NTP staff. Algorithms were developed based on the information received (figure 1), and these were modeled in a spreadsheet-based tool developed by SIAPS to analyze the impact.

The models quantify the likely impact of the treatment interruption in terms of subsequent treatment or non-continuation of treatment and in terms of provider costs, household out-of-pocket costs, and productivity losses. The models show the additional health and cost outcomes of each specific type of treatment interruption, excluding the health and cost outcomes that would have been incurred if treatment had not been interrupted.

RESULTS

DS-TB medicine stock-outs

Based on the results of a sample patient survey conducted in early 2014, as many as 2,663 DS-TB patients may have been unable to obtain medicines from the public sector for a month or more. The likely impact of these stock-outs is that 266 of these patients would have developed MDR-TB because of poor-quality private sector treatment, poor adherence, or discontinuation of treatment (table 1). And these 266 patients are likely to have infected an additional 63 people with MDR-TB. In addition, 588 patients and persons infected by those patients are likely to have died.

The total additional economic cost resulting from the stock-outs is likely to have been as much as USD 21 million, comprised of USD 1.5 million for additional service delivery costs and USD 19.5 million for additional household costs (out-of-pocket costs and productivity losses) (table 2). This works out to a cost of approximately USD 8,000 per patient who interrupted treatment, meaning that an investment of up to that amount to prevent the stock-out for one patient would have resulted in a net saving to society.

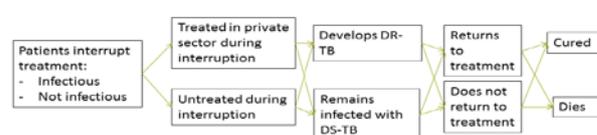


Figure 1. Conceptual framework for treatment interruption

DS-TB patients lost to follow-up

In 2014, 8,870 DS-TB patients were reported by the NTP as lost to follow-up. The likely impact of this LTFU is that 887 of these patients would have developed MDR-TB through poor-quality private sector treatment, poor adherence, or discontinuation of treatment. And those 887 patients are likely to have infected an additional 245 people with MDR-TB. In addition, 1,958 patients and persons infected by those patients are likely to have died.

The total additional economic cost resulting from this LTFU is likely to have been as much as USD 72.2 million, comprised of USD 5.8 million for additional service delivery costs and USD 66.4 million for additional household costs. This works out to a cost of approximately USD 8,000 per patient who interrupted treatment, meaning that an investment of up to that amount to prevent LTFU for one patient would have resulted in a net saving to society.

MDR-TB patients lost to follow-up

A study of a 2012 cohort of MDR-TB patients found that 29% were lost to follow-up. We applied that percentage to the 2,680 MDR-TB patients treated in 2014, which gave an assumption that 777 MDR-TB patients would have been lost to follow-up. The likely impact for the 777 patients is that 330 would have developed XDR-TB through poor-quality private sector treatment, poor adherence, or through discontinuation of treatment. And those 330 patients are likely to have infected an additional 19 people with XDR-TB. In addition, the MDR-TB patients who were still

infectious at the time of interruption are likely to have infected an additional 474 persons with MDR-TB. Plus, 233 people are likely to have died as a result of the LTFU.

The total additional economic cost resulting from this LTFU is likely to have been as much as USD 12.9 million, comprised of USD 4.5 million for additional service delivery costs and USD 8.4 million for additional household costs. This works out to approximately USD 17,000 per patient who interrupted treatment, meaning that an investment of up to that amount to prevent the LTFU for one patient would have resulted in a net saving to society.

Table 1. Impact of treatment interruption on morbidity and mortality

Number of	DS-TB stock-outs of 1 month	DS-TB LTFU of 3 months	MDR-TB LTFU of 5 months
Patients whose treatment was interrupted	2,663	8,870	777
Patients who develop MDR-TB as a result of the interruption	266	887	0
Patients who develop XDR-TB as a result of the interruption	Not estimated		330
Additional persons who develop DS-TB as a result of the interruption ¹	0	0	0
Additional persons who develop MDR-TB as a result of interruption	63	245	474
Additional persons who develop XDR-TB as a result of interruption	Not estimated		19
Persons who die as a result of the interruption	588	1,958	233

Table 2. Estimated economic impact of treatment interruption

	DS-TB stock-outs of 1 month	DS-TB LTFU of 3 months	MDR-TB LTFU of 5 months
Number of patients whose treatment was interrupted	2,663	8,870	777
Total estimated additional cost			
Provider cost	\$ 1.5 million	\$ 5.8 million	\$ 4.5 million
Household cost	\$ 19.5 million	\$ 66.4 million	\$ 8.4 million
Total	\$ 21.0 million	\$ 72.2 million	\$ 12.9 million
Estimated additional cost per affected patient			
Provider cost	\$ 573	\$ 655	\$ 5,733
Household cost	\$ 7,309	\$ 7,485	\$ 10,875
Total	\$ 7,882	\$ 8,141	\$ 16,608

¹ In both of the DS-TB case studies, the opinion of the expert group was that none of the patients with DS-TB should be infectious at the time of the treatment interruption and, therefore, no additional people would be infected as a result of the interruption.

CONCLUSIONS

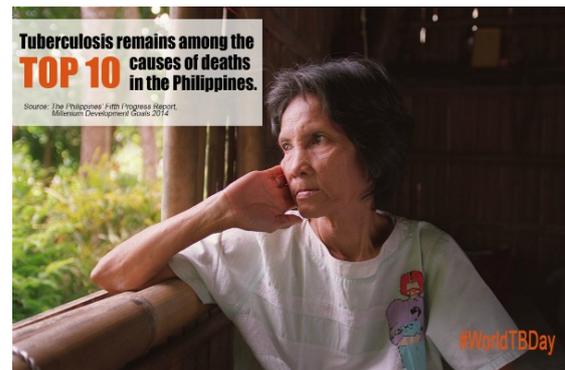
The results of the three case studies show that TB treatment interruption can have a significant impact on morbidity and mortality, causing many people to develop MDR-TB and XDR-TB, resulting in many new infections and deaths. The economic impact on the health services, families, and society in general is equally devastating, running into many millions of US dollars.

These results are only approximate estimates because some of the assumptions were based on estimates provided by an expert panel in the absence of data. However, it is likely that the above figures are actually underestimated, partly because we did not take into account that some patients who had become non-infectious before interrupting treatment but did not return to treatment would have become infectious again at some stage. We also did not take into account that some of the persons who would have developed MDR-TB would have later developed XDR-TB.

The global literature review found that little research has been done on the impact of treatment interruption, and additional research would, therefore, be highly beneficial,

Further Reading

1. Collins, D, et al. The Economic Cost of Non-adherence to TB Medicines Resulting from Stock-Outs and Loss to Follow-Up in the Philippines. Arlington, VA: SIAPS; 2016.
2. Podewils LJ, et al. Patterns of Treatment Interruption among Patients with Multidrug-Resistant TB (MDR TB) and Association with Interim and Final Treatment Outcomes. PLoS ONE 2013;8(7): e70064. doi:10.1371/journal.pone.0070064
3. Soucy Brown M et al. Philippine Tuberculosis Supply Chain Options Analysis: Technical Report. Arlington, VA: SIAPS; 2015
4. Tupasi T, et al. Factors Associated with Loss to Follow-up during Treatment for Multidrug-Resistant Tuberculosis, the Philippines, 2012–2014. Emerging Infectious Diseases www.cdc.gov/eid, Vol. 22, No. 3, March 2016.



both in the Philippines and globally to provide a more robust evidence base.

The results of the analysis indicate that prioritization should be given to improving supply chain management to prevent stock-outs; reduce DS-TB patient LTFU through better education and case management, especially in regions where it is high; and reduce MDR-TB LTFU through improved case management, including better management of medicines, because adverse side effects are a major reason for LTFU.

It is clear from these case studies that the cost of treatment interruption in the Philippines is significant and that investing additional resources to resolve the causes of these problems is likely to be extremely worthwhile.

ABOUT SIAPS | The Systems for Improved Access to Pharmaceuticals and Services (SIAPS) program works to assure access to quality pharmaceutical products and effective pharmaceutical services through systems-strengthening approaches to achieve positive and lasting health outcomes. SIAPS is funded by the US Agency for International Development (USAID) and is implemented by Management Sciences for Health.

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