

Conference Paper

# The Economic Burden and Non-Adherence Tuberculosis Treatment in Indonesia: Systematic Review

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## Abstract

Until today, Tuberculosis (TB) is still taking part as a world health problem, especially in The South East Asia Region. TB in South East Asia contributes almost 50% of the worldwide burden. Indonesia is one of the regional countries that provide to the statistics, and the World Health Organization (WHO) enlisted it in the 30 High-TB-Burden Countries. The high number of TB in Indonesia mostly caused by a lack of case registration, non-adherence of treatment, and lost to follow-up. This study conducted an overview of systematic review based on Prisma Protocol to systematically and objectively focus on the economic burden as a risk factor of non-adherence of TB treatment in Indonesia. Relevant literature was searched from PubMed, Science Direct, Google Scholar and reviewed abstracts and full-text article based on eligibility criteria. Seven studies included in this review after selected using inclusion and exclusion criteria. The studies revealed a consistent association between economic burden as a risk factor of non-adherence of TB treatment. In conclusion, financial burden was significant with non-adherence of TB treatment and most of TB patient who stopped the treatment should spare their family spending into TB treatment and this often constitutes to more considerable financial risk for them.

**Keywords:** Tuberculosis, Economic burden, Non-adherence, Indonesia

## 1. Introduction

One of the untreated infectious diseases that contribute to the high rate of death is Tuberculosis (TB). TB is an infectious disease caused by *Mycobacterium tuberculosis* that commonly affects the lungs. TB patients have symptoms of a phlegm cough with blood for two weeks or more, shortness of breath, weakness, weight loss and decreased appetite, night sweat, and fever for more than one month [1].

By 2015, a new case of TB across the world was estimated to be 10.4 million in which Southeast Asia region contributed 46.5% (> 4.7 million) to the world's TB case burden. Indonesia ranks second after India, with 1.02 million new cases in 2015. Meanwhile, the death rate from TB disease in Indonesia is 45 per 100.000 populations [2].

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One of the things that need to be aware of and most challenging in the treatment of TB disease is the resistance of *Mycobacterium tuberculosis* to INH and Rifampicin called multi-drug resistance (MDR-TB). WHO states that only 52% of MDR-TB were successful in the treatment of TB across the world, and less than 49% were successful in the treatment of MDR-TB in the Southeast Asia region. Globally, 250.000 people died from TB drug resistance, and only 37% of MDR-TB cases were detected. The MDR-TB case in Indonesia was 32.000 in 2015 and the ranked second in Southeast Asia. As many as 71% of MDR-TB was confirmed and did follow the treatment, while the rest refused the treatment or died. Meanwhile, only 51% of MDR-TB patients had a successful result in a treatment program [2].

Results of *Riset Kesehatan Dasar (Riskesdas)* Year 2013 illustrate that the magnitude of TB problems between groups in each characteristic shows differences. In the age group, the highest prevalence is in the 65-74-year age group. Unemployed TB patients were the greatest prevalence when compared with TB patients who worked as employees, entrepreneurs, farmers/fishers/laborers, and others. In the education group, the highest incidence of TB patients is in the non-school education group, and as the level of education goes higher, the prevalence goes lower [1].

Increases in TB cases are thought to be caused by various causes, such as improper diagnosis, inadequate treatment, HIV endemic infections, population migration, self-medication, increased poverty, and insufficient health services [3]. WHO states in Aditama [4] that non-adherence to TB treatment that may lead to treatment failure caused by the degree of poverty of the sufferer, difficulties in reaching health facilities, lack health workers, expensive drug prices, and convoluted procedures. TB ensues in poverty and creates poverty; in fact, the poor will have a five-time higher chance of getting TB. Some barriers to TB control in South East Asia Region include failure to address poverty, undernutrition and risk factors that will become exposure to TB [2].

Non-adherence with TB treatment provided by the government becomes one of the challenges in implementing TB treatment programs in Indonesia. Non-adherence of treatment by TB patients may be affected by many things. This review will focus on the economic burden of tuberculosis patients which result in non-adherence of TB treatment in Indonesia.

## 2. Methods

### 2.1. Overview

This study is a systematic review of the literature on the economic burden and non-adherence TB treatment in Indonesia. Study results reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA). An outline of the evidence searches and study inclusion provided as shown in Figure 1.

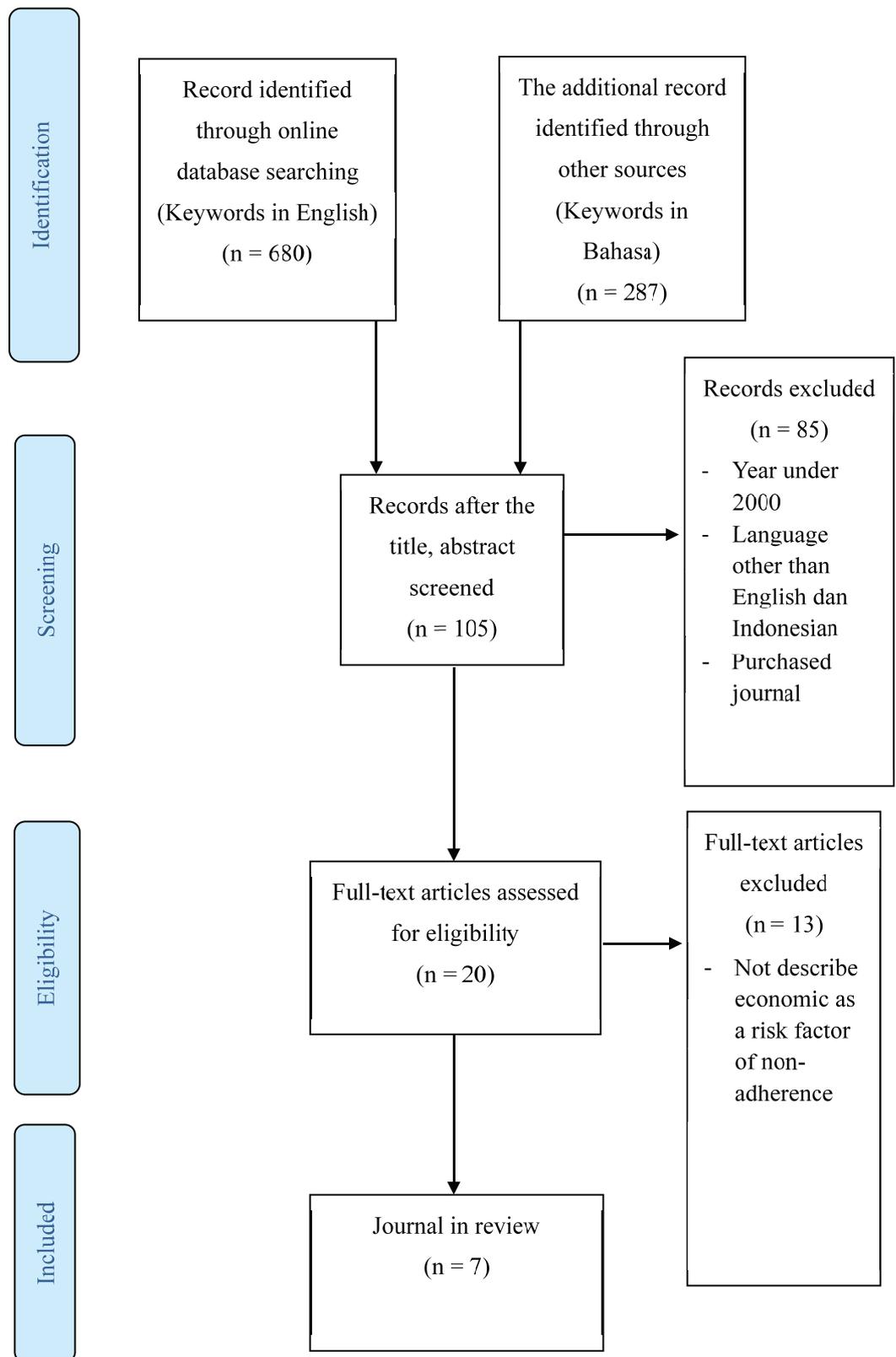


Figure 1: Preferred Reporting Items for Systematic Review and Meta-Analysis Flow Diagram [15].

## 2.2. Data sources and study eligibility

The literature conducted publications after 2000 in PubMed, ScienceDirect and Google Scholar using keywords: “Economic Burden” OR “Non-Adherence Treatment” OR “TB” AND “Indonesia.” Searches were not restricted by not using study design filters and cross-referenced the citations from relevant systematic reviews and excerpts of recovered articles. The literature searches screened in duplicate by using study eligibility criteria.

## 2.3. Study inclusion criteria

Inclusion criteria of documents that consider appropriate to do systematic review were as follows: a journal, an original study, and systematic analysis, reported in English and Bahasa Indonesia, said the economic burden of TB treatment, and study location in Indonesia.

## 2.4. Study exclusion criteria

Exclusion criteria were as follows: publication before the year 2000, magazines used a language other than English and Bahasa Indonesia and purchased journals.

## 3. Results

This study identified seven eligible studies from Indonesia and resumed in conclusion as shown in Table 1. Based on studies reviewed, for research design, the researcher used cross-sectional and cohort. The studies showed there are factors affecting non-adherence in TB, including economic status. TB treatment costs in all countries mostly were much higher than diagnostic values. In Indonesia, right prices (out of pocket) for treatment were more senior than indirect costs (foregone income) related to treatment. The highest cost element in Indonesia during TB diagnosis was for transportation, food supplements, laboratory tests and administration fees for MDR-TB patients [5].

Though most of TB diagnosis and treatment services are free, patients had other direct and indirect costs and affected financially for most patients. MDR-TB patients estimated costs for diagnosis and treatment were 3.4-13.9, higher than other TB patients and MDR-TB patients more often lost their jobs.

Based on Rutherford, M.E. et al. [6], self-employed (HR 2.47, 95%CI 1.15-5.34) predicted to treatment default than those in the highest income bracket. Patients with longer travel time and higher travel costs not associated with an increased rate of default. Those who paid >200.000 IDR (approx. 15 US\$) were 0.24 (95%CI 0,06-0,91) times more likely to default rather than those who spent >100.000-200.000 IDR and those who paid nothing. The study revealed that TB poor patients in Central Java went directly to government facilities which diagnosis is free. Patients whose eligible for government health insurance were more likely to be adherent.

TABLE 1: Journals in Review.

Title	Author	Year of publish	Method	Variable	Analysis	Result	Suggestion
The Socio-economic Impact of Multidrug Resistant Tuberculosis on Patients: Results from Ethiopia, Indonesia and Kazakhstan	- Susan van den Hof - David Collins - Firdaus Hafidz - Demissew Beyene - Aigul Tursynbayeva - Edine Tiemersma	2016	Cross-sectional Survey	- Age - Sex - Treatment Type and Phase - Socioeconomic status - Ethnicity - Distance to health facilities - Costs related to the diagnosis and treatment	Data were analyzed in Microsoft Excel, STATA/SE 11.1 for Windows, SPSS v20 IBM.	Although MDR-TB diagnosis and treatments services are free for patients, patients have other direct and indirect costs. The financial impact was significant for most MDR-TB patients and was higher than other TB patients in all three countries.	Financial burden in TB patients especially MDR-TB patients should be a priority for Indonesia's government. Besides, countries' willingness and ability also has an influence to worked out into a strategy and how this strategy can be implemented.
Risk Factors for Treatment Default Among Adult Tuberculosis Patients in Indonesia	- M.E Rutherford - P.C Hill - W. Maharani - H. Sampurno - R. Ruslami	2013	Cohort Study	- Demographics - Patient household head - Patient health seeking behaviour - Clinic Accessibility - TB knowledge - Social support - Previous experience - Perceived stigma and experience with clinical staff and facilities	Data were double-entered an Access database. To assess the relationship between risk factors and patients default using Cox's proportional hazard regression. Final results from univariate and multivariate analysis were displayed with 95% CI and P < 0.05 was considered significant.	Patients with government health insurance were more likely to be adherent than patients with greater wealth. Poor clinic accessibility, lack of social support, health service satisfaction has a significant impact on default rates. Transport cost to clinic were not associated with increased rates of non-adherence TB treatment	Indonesia's government should consider about health insurance and accessibility to health care as an important factor to reduce the number of non-adherence TB treatment.

Title	Author	Year of publish	Method	Variable	Analysis	Result	Suggestion
Costs to Health Services and the Patient of Treating Tuberculosis: A Systematic Literature Review	- Yoko V. Laurence - Ulla K. Griffiths - Anna Vassal	2015	Systematic Literature Review	- Tuberculosis - Cost treatment	Costs were converted in the local currency, US\$, and OANDA's average annual exchange rate. The relationship between provider costs and country gross net income was assessed using Pearson's correlation coefficient.	Cost treatment data for MDR-TB are limited. The financial burden of illness is greater in poorer countries without universal health coverage	Researchs and data about cost as a risk factor of non-adherence TB treatment in Indonesia are urgently needed.
Factors that Influence Treatment Adherence of Tuberculosis Patients Living in Java, Indonesia	- Bagoes Widjanarko - Michelle Gompelman - Maartje Dijkers - Marieke J van der Werf	2009	- Qualitative - Quantitative	- Structural factors (side effects and duration) - Patient factors (poverty and gender) - Social context (stigma) - Health service factors	- Exploratory, comparative, and qualitative descriptive to identify structural factors, patient factors, social support, and health service factors. - Statistical analysis using Chi-square to compare factors associated with (non) adherence.	Most TB patients stopped treatment because they were starting to feel better, lack of money, side effects of pills, getting bored of treatment, the behavior of health care staff, social support.	The number of default TB treatment in Indonesia expected will increase rapidly. Some comprehensive efforts and coordination between stake holders are needed to prevent default TB treatment.

Title	Author	Year of publish	Method	Variable	Analysis	Result	Suggestion
Financial Burden for Tuberculosis Patients in Low-and Middle-Income Countries: A Systematic Review	- Tadayuki Tanimura - Ernesto Jaramillo - Diana Weil - Mario Raviglione - Knut Lonroth	2014	Systematic Review	- Direct medical costs - Direct non-medical costs - Indirect costs	The focus of the analysis was on the distribution of the magnitude and components of cost.	20% of the total cost was due to direct medical costs, 20% to direct non-medical costs, and 60% to income loss. Cost as percentage of income was particularly high among poor people and MDR-TB. Income loss often constitutes the largest financial risk for patients.	Direct and indirect costs should be considered by government as a burden for TB patients. On the other hand, affordable health services and health insurance are needed to enable access, reduce delays and non-adherence, and to compensate direct and indirect costs.
Patient Adherence to Tuberculosis Treatment: A Systematic Review of Qualitative Research	- Salla A. Munro - Simon A. Lewin - Helen J. Smith - Mark E. Engel - Atle Fretheim - Jimmy Volmink	2007	Systematic Review of Qualitative Research	- Organisation of treatment - Financial burden of treatment - Knowledge, attitudes, and beliefs about treatment - Law and immigration - Personal characteristics and adherence behaviour - Side effects - Family, community, and household support	Included studies are assessed using a pre-determined checklist and data were extracted independently onto standard form. On the other hand, to synthesize the findings using Noblit and Hare's method of meta-ethnography/	There are four major factors that interact to affect adherence to TB treatment: structural factors, social context, health service factor, and personal factor.	Further research is needed to address structural barriers to treatment adherence.

Title	Author	Year of publish	Method	Variable	Analysis	Result	Suggestion
Social Aspects of Patients with Pulmonary Tuberculosis in Indonesia	- E. Karyadi - CE West - RHH Nelwan - WMV Dolmans - JVM van der Meer - JW Schultink	2002	Research project	- Demo-graphic and socio-economic - Living conditions, TB contact, and smoking habits - Social consequences due to TB - Role of family of TB patients	Independent t-test was used to test the differences of nutritional status among groups based on social consequences of TB. ANOVA was used to assess the difference of nutritional status among patients with no occupation. SPSS was used for all statistical analysis.	TB patients have social problems related to their illness which may influence their adherence of TB treatment. Most TB patients had poor nutritional status and lived in crowded environment, jobless, negative attitude from their neighbors and relatives. Patients were supported by their families, both financially and socially. Around 71% patients were in families with median monthly income per head that was below poverty line.	Priority should be given to developing program aimed at minimizing economic burden.

An Indonesian study [7] reported that productivity losses of US\$12 per patient. Widjarko, B et al. [8] there are several factors that influence treatment adherence in Java, Indonesia such as personal characteristics; costs and financial burden; knowledge, beliefs, attitudes about TB; role of the traditional healer; community and household support; stigma attached to tuberculosis; and health care service factors. Although TB treatment in Indonesia is free, 30% of patients who live in rural areas had to pay much for transportation to primary health care. Forty percent of non-adherent patients told that costs played an important factor in deciding whether they adhered to the treatment. The average income of non-adherent patients in private hospitals was three times lower than the adherent patients, but this difference was less apparent in public hospitals.

Forty-nine studies in low-and-middle-income countries [9] revealed that the proportion of direct medical costs out of total cost ranged from 0-62%, direct non-medical prices ranged from 0-84% and indirect costs from 16-94% of total cost. Transportation cost (range 11-96%) and food costs (range 0-89%) were the most significant cost that contributes to direct non-medical expenses in 16 studies. The total cost for MDR-TB patients was remarkably higher than drug-susceptible TB. Several studies revealed that having TB had consequences for work and effects on adherence, TB treatment posed an economic barrier because they often worked out of town, impact to their family

livelihoods. Some patients explained that TB treatment interruption by noting the costs of treatment, such as hospitalized fee, Rontgen fee, and transport costs. Conflicts between treatment, the hidden cost of treatment, and income could push patients into poverty and this possibility as a reason for non-adherence treatment. In societies where depend on family for financial support, poverty reported as a significant reason for non-adherence treatment [10].

Productivity losses comprised 98% in low-and-middle-income countries [7]. In another study on which most patients become unemployment in the most productive years of their lives, the researcher found an unemployment rate about 57% and the families of TB patients former had a lower median income than families without TB patients former [11]. Because of this situation, their extended family bears the financial burden.

## 4. Discussion

In the studies reviewed, the financial impact was significant for most TB patients although diagnosis and treatment services are supposed to be free on the other hand direct and indirect cost increased while patients' income was decreased [5,7-11]. Transport cost to the clinic not associated with increased rates of non-adherence TB treatment in another study [6]. Most TB patients referred to the closest clinic to their homes. TB is a giant poverty producing mechanism and neglecting TB in one region will let poverty reign. Besides, the relationship between disease and poverty like a vicious cycle. A sick person is forced to have expensive clinical treatment and other fees that follow. As a result, the poor became poorer and decided to stop the medication and get worse [4].

Economic loss caused by TB can be seen in four aspects [4], health consumption effects is the loss in the form of decreased consumption of goods/health services due to illness or death; social interaction and leisure effects is the disadvantage of social interaction and lack of leisure time to relax; short term production effects, is medical expenditure to get treated and loss of productive work days and the loss of opportunity to take care of family properly; and long term production consumption effects can see in the form of consumption demographical effects and workforce supply.

In line with those studies reviewed, a pilot study in Indonesia conducted by KNCV TB Foundation [12] shows total approximated median patients costs for TB diagnosis and treatment were around 1.5 million rupiahs. While total approximated median TB-MDR patients' prices were 15 times higher at about 22 million rupiahs. Patients told that TB had affected their family financially, so they had different strategies to pay the expenses during the diagnosis and treatment such as borrowing money and selling property/asset. On the other hand, patients reported a lower income at the time of interview than before the diagnosis of TB and the more significant drop in median household income occur among MDR-TB patients. TB patients face a considerable financial impact due to their treatment and become extraordinary to MDR-TB patients and family. A too high financial burden may cause patients to default from treatment.

About 75% of TB cases arise during people's most productive years between the ages of 15 and 54, while people who are infected by TB are often unproductive and unable to work which affected their family members [13]. The impact of TB usually measured as

the direct costs of treatment to health services, which include the costs of medicines, personnel, and facilities. While additional costs come from food required for TB patients and the costs of travel to health services [14].

The total patient's costs while seeking diagnosis and treatment include food, travel, and accommodation would have been approximately US\$ 7.9 million. TB and MDR-TB patients will lose their productivity due to the inability to be economically productive. The study assumed that TB and MDR-TB treated patients are unable to work for 81 days and 180 days after starting treatment due to illness and time spent to obtain daily care. While, untreated TB and MDR-TB patients would be unable to work until they self-cure or die, on average which is assumed to be three years. The total number of years of life lost related to 2011 new cases are likely around 1.9 million and productive years of experience failed to be 1.5 million. While the total economic burden will be roughly US\$ 2.1 billion and it will be higher each year related to the number of new TB cases [13].

Another study in Indonesia showed TB patients will lose 13 years of life and patients who receive treatment are estimated to miss about two months' work from illness and untreated TB patients will lose about twelve months' work. TB will cause psychological and social costs; their circumstances may reject TB patients and lose their job. Besides, discrimination for TB patients which can result in anxiety, depression, and reduce their quality of life. High direct TB treatment costs for patients often take more than a month before diagnosis made, extensive use of X-rays, prescription of expensive supplements, and cooperation among providers [14].

The limitation of this systematic review is that only a few studies could about economic burden/poverty that has an effect on non-adherence TB treatment in Indonesia and just reviewed journal and research accessible on a database online with English and Indonesian language. The content of discussion will be well if more publications about the relationship between economic burden and non-adherence TB treatment. Another possible limitation is that this systematic review only concludes the financial burden affecting non-adherence TB treatment based on the conclusion of the research articles and then qualitatively review of significance variables, without doing a meta-analysis to combine the results of multiple scientific studies.

## 5. Conclusions

This systematic review found a consistent positive association between economic burden and non-adherence TB treatment in Indonesia. The financial burden of TB patients will affect patients' productivity resulting in decreased income. This can be rough especially for TB patients who are the only one earner in the family. Also, long duration of treatment may also result in TB patients not being able to work so that they may be dismissed or getting deduction payment by the employer. Costs incurred by patients such as transportation costs, food expenses, and dietary supplements, and accommodation costs during TB treatment are also determinants of non-adherence of TB treatment. Thus, affordable health services including social protection schemes, are needed to enable access, reduce delays and to compensate for the direct and indirect costs of TB treatment.

## Competing Interest

Authors have no competing interest in this systematic review.

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