

Factor Associated with Treatment Initiation of Multidrug Resistance Tuberculosis in  
Jakarta, Indonesia: A Mixed-Method Study  
by

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Thesis submitted in partial fulfillment of  
the requirements for the degree of  
Master of Science, in the Department of  
Global Health in the Graduate School  
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2021

ABSTRACT

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## **Abstract**

Background: Indonesia has one of the highest TB burdens in the world and is one of ten countries that accounted for 77% of the global gap between treatment enrollment and the estimated number of new cases of MDR/RR-TB in 2019. However, there are knowledge gaps about how the delay of MDR-TB treatment initiation might affect this situation. Therefore, this study aimed to examine challenges of implementing MDR-TB treatment initiation in a Programmatic Management of Drug-Resistant Tuberculosis (PMDT) national referral hospital in Indonesia. Method: This study used mixed methods to collect both quantitative data through hospital records of MDR-TB patients and qualitative data through interviews with patients and health workers. Result: The median time between diagnosis and treatment initiation was 26 days, and was associated with co-morbidities, MDR-TB knowledge, and support assessment. This study also revealed the complex situation of people affected with MDR-TB with lack of social support and health system challenges during the MDR-TB treatment initiation process. Conclusion: The results of this study revealed the challenges of the treatment initiation process from the complex perspectives of the patients, the aspects of the health system that need to be improved, and the importance of social support starting from diagnosis.

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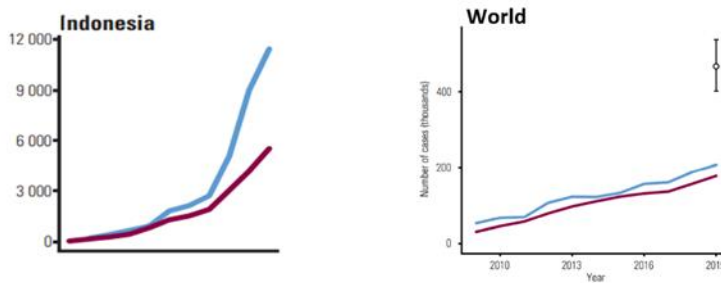
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# 1. Introduction

## 1.1 *Multidrug-Resistant Tuberculosis in Indonesia*

Tuberculosis is a major public health problem across the world. The main challenge at present is the increase in drug-resistant tuberculosis, especially multidrug-resistant strains, as defined as resistance to at least two main types of TB drugs: isoniazid and rifampicin (WHO, 2014).

Indonesia has the second-highest national burden for TB globally and is part of the top 20 countries with the highest burden of MDR-TB in the world. In 2019, WHO estimated 24,000 new cases of RR/MDR-TB in Indonesia. While Indonesia made good progress on increasing both detection and enrolment of MDR-RR-TB cases, Indonesia still experiences a huge gap between the number of cases detected and the number enrolled in treatment compared with the average global ratio (Figure 1) (WHO, 2020). Based on the JEEM Report, there were 2,483 TB cases reported in 2017, but only 1,848 cases were enrolled (74,4%) for treatment the same year, which indicates a great disparity between diagnosis and treatment enrolment (WHO, 2017). In addition, reduction in attrition after diagnosis through prompt initiation of treatment of MDR-TB patients is crucial to prevent the transmission of disease and reduce related morbidity and mortality. This has become a key opportunity for ending TB (Soeroto et al., 2019b).



**Figure 1: Number of MDR/RR-TB Cases Detected (blue) and Enrolled on MDR-TB Treatment (maroon) 2009-2019**

## **1.2 National TB Program in Indonesia**

Indonesia has made effort to eliminate TB by creating a National TB Program (NTP) (IndonesiaMoH, 2018). As a part of NTP, Indonesia adopted WHO recommended Programmatic Management of Drug-Resistant Tuberculosis (PMDT) as the guideline for effective service delivery and management of MDR-TB in Indonesia (KemenkesRI, 2013; WHO, 2014).

PMDT services are offered in some health care facilities in centralized locations called "PMDT Referral Hospitals" with Direct Observe Therapy (DOT). In Indonesia, there are 360 PMDT hospitals in 34 provinces. The PMDT hospitals are equipped with facilities such as a microbiological and pathological laboratory, a 24-hour emergency room, outpatient services, and isolated inpatient services. The respiratory intensive care unit continuously supports the drug-resistant TB department at the hospital (RSUP Persahabatan, 2020; WHO, 2014, 2017).

An MDR-TB suspect commonly comes or is referred to a PMDT Treatment Center or treatment satellite site. Diagnoses of MDR-TB were based on one specimen designated for rapid molecular testing (with Gen Expert test or Line probe assay) and two sputum specimens (taken in the morning) assigned for sputum smear examination, culture examination, and susceptibility testing with Lowenstein-Jensen (LJ). These tests are utilized as a reference in the case of discrepancies in susceptibility testing results from the Gen-expert outcome. If results indicate rifampicin resistance (RR), standard MDR-TB treatment should be initiated. Patients' status is registered as TB-RR and continues with bacterial culture checks and Mycobacterium tuberculosis (Mtb) identification (MoH, 2016). Moreover, WHO also reported that 99% of RR cases are diagnosed with MDR-TB in Indonesia (WHO, 2020).

The procedure for baseline assessment, after the diagnosis of MDR-TB, has been well established based on initial preparations consisting of initial evaluation and pre-treatment screening, which should be completed before commencing treatment. This step is necessary for initial assessment to prevent side-effects from second-line anti-TB drugs and prepare MDR-TB patients and their families for the required mentality needed to undergo treatment based on DOT guidelines (WHO, 2014). The steps of the baseline assessment regulated by the Indonesia PMDT guidelines (KemenkesRI, 2013) consist of:

- i. Physical examination
- ii. Psychiatric examination

- iii. Supporting baseline examination, which includes:
  - a. Microscopic sputum examination, culture, and susceptibility test for Mtb
  - b. Complete blood count, including haemoglobin (Hb) levels, and leukocyte counts
  - c. Blood chemistry tests (Renal test : Urea, creatinine; Liver test: SGOT, SGPT; Blood sugar; Electrolyte; and Uric acid)
- iv. Thyroid Stimulating Hormone test (if necessary)
- v. Pregnancy test for women of childbearing age
- vi. X-ray of chest/ thorax
- vii. Hearing test (audiometric examination)
- viii. Electrocardiogram (ECG) examination
- ix. HIV test (if HIV status is unknown)
- x. Medication observers are determined for MDR-TB patients, which can consist of health workers or trained health experts as well as relatives of the patient.

All RR-TB/MDR-TB patients should receive ambulatory treatments immediately while considering the patient's clinical conditions. There are no clinical criteria that cause RR-TB/MDR-TB patients to be excluded from treatment. Based on the decision of team clinical experts (TAK) with input with the PMDT team, some patients could undergo the

inpatient treatment for a maximum of 2 weeks with certain disease criteria, such as psychiatric disorder, liver disorder, diabetes mellitus, and severe malnutrition(KemenkesRI, 2013; Rumende, 2017).

Currently, MDR-TB diagnosis and treatment cost are free under NTP, outside of national insurance coverage (JKN). However, this program does not include additional costs such as drugs and lab work for comorbidities, such as diabetes. Doctors also often recommended supplements and vitamins to improve the treatment outcome, which must be paid for out of pocket since it is not covered by NTP. However, the NTP programs provide a cash transfer for those who are already confirmed as MDR-TB patients of IDR 750,000/month (US\$ 53), (Soeroto et al., 2019a; WHO, 2017). However, despite the efforts from the NTP, there remain challenges for program implementation, especially for the treatment initiation process for people with MDR-TB.

Previous research and interventions have been conducted in the diagnosis or treatment stage of MDR-TB in Indonesia (Asyary & Mahendradhata, 2019; Lina et al., 2016; Ruru et al., 2018; Soeroto et al., 2019b; Surya et al., 2017). However, there is still a lack of research in explaining the huge gap between the case detection and treatment enrollment of MDR-TB patients. One study in West Java, Indonesia, mentioned that the phenomenon of delay of treatment initiation could lead to loss to follow-up of MDR-TB treatment enrollment (Soeroto et al., 2019b).

### **1.3 Research Purpose**

This study examined challenges of implementing MDR-TB treatment initiation in a PMDT national referral hospital, known Persahabatan Hospital, Jakarta, Indonesia, with the following objectives:

- i. To understand the phenomenon of delay in MDR-TB patients' treatment initiation after diagnosis.
- ii. To identify biological, psychological, and social factors associated with MDR-TB treatment initiation after diagnosis.
- iii. To explore the health system challenges faced by healthcare workers to initiate the treatment for MDR-TB.
- iv. To develop evidence-based policy recommendations by exploring the patient experience of treatment initiation for MDR-TB.

## **2. Methods**

### **2.1 Study Design**

This study used a mixed-methods approach to collect and analyze both quantitative and qualitative data. Quantitative data consisted of 188 medical records and documents of patients, who registered in the study hospital between 1 Jan – 31 Dec 2019. Qualitative data involved conducting interviews for a subset of ten patients and seven health workers in Persahabatan Hospital.

Quantitative methods were employed to measure the time between the establishment of a TB diagnosis and treatment initiation and to identify factors associated with the length of this time. Qualitative methods were used to explore additional factors related to delay, including the experiences and challenges patients face during treatment initiation, as well as other relevant factors from a health worker's perspective. The study has benefitted from the utilization of qualitative methods that complement the quantitative data collected. This aligns with the study objectives to comprehensively understand the factors related to treatment initiation within the specified study population.

### **2.2 Setting**

The study was conducted at Persahabatan Hospital in Jakarta, Indonesia. Persahabatan Hospital is a public national referral respiratory teaching hospital and has been recognized as one of the most renowned PMDT referral hospitals in Indonesia



among 360 PMDT hospitals in 34 provinces across the country. In addition to the hospital's well-equipped facilities such as a microbiological and pathological laboratory, a 24-hour emergency room, outpatient services, and isolated inpatient services, the respiratory intensive care unit supports the drug-resistant TB department at the hospital. Persahabatan hospital has acquired more than 13.214 MDR-TB suspects since 2009 and has successfully treated approximately 1.776 MDR-TB confirmed cases. On average, the drug resistant TB department in the hospital accommodates around 70-90 patients daily from diverse backgrounds, with 25-30 new MDR-TB cases each month(RSUPPersahabatan, 2020).

## ***2.3 Quantitative Methods***

### **2.3.1 Study Population**

The subjects for the quantitative portion of the study comprised of MDR-TB adult patients, aged 18 or above, who completed the baseline assessment and initiated their treatment in Persahabatan Hospital from 1 January to 31 December 2019.

Data analysis included patients who were diagnosed in 2019 and had initiated treatment in Persahabatan Hospital with matching data according to the hospital's databases. An MDR-TB patient in this study was defined as an individual with confirmed results of at least rifampicin resistance by GenXpert MTB/RIF. The exclusion criteria for this study were: a) extrapulmonary TB; b) pregnancy; c) unmatched data across the hospital's records and community psychosocial assessment.

According to explanations from the data officer from Persahabatan Hospital, there are several possible reasons for unmatched (n=642) data:

- 1) Patients did not initiate treatment in Persahabatan Hospital
- 2) Patients moved to another hospital
- 3) Patients died before starting treatment
- 4) Patients were not reached by LKNU
- 5) Diagnostic changes
- 6) Initial loss to follow up

### **2.3.2 Data Sources**

Quantitative methods used secondary data sources. First, we used electronic records, which consisted of the suspect registration database (TB06) and the treatment registration database (TB03) provided by the Persahabatan Hospital data officer. Second, we used paper format records, which consist of a treatment monitoring card (TB01) whose medical records were manually entered into Microsoft Excel by research assistants and the Principal Investigator (PI) in Persahabatan hospital. Moreover, we also used electronic records of psychosocial assessment databases provided by case manager from Lembaga Kesehatan Nadhatul Ulama (LKNU) who assisted Persahabatan Hospital for psychosocial support of the patients.

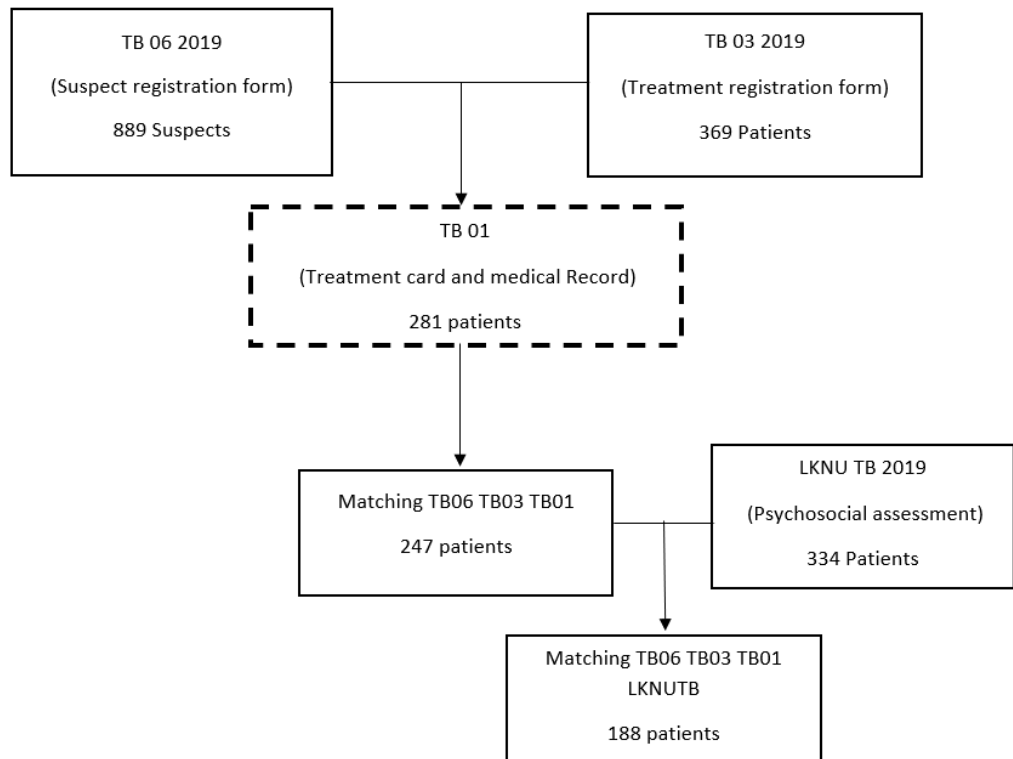
The main information from each database consisted of TB 06 (date of results for GenXpert, sex, birthdate); TB 03 (date of result GenXpert, date of treatment initiation,

sex, birthdate); TB 01 (TB History); Medical Record (married status, work status, comorbidities, date of baseline assessment, insurance); Psychosocial Assessment (knowledge assessment, adherence assessment, accessibility and social assessment).

### **2.3.3 Data Collection Procedures and Variables**

Research assistants were recruited before conducting the fieldwork and were given an orientation discussing the research overview, design, and data collection from the PI.

The data collection processes are as follows. First, the PI is provided with the TB06 and TB03 databases in MS Excel format from the hospital data officer. Data were matched based on name, sex, address, and birthdate of the patients, and were further processed to become the "master database." The compilation of all databases for this study consisted of TB01, TB03, TB06, and Psychosocial Assessment. Next, TB01 and medical records in Persahabatan Hospital were manually entered into the "master database" in MS Excel format by the PI and research assistants, assisted by the hospital data officer. Finally, the collected data were merged and matched based on previous medical records concerning psychosocial assessment in an electronic database provided by the case management officer. In total, there were 188 patient records considered in this study for further statistical analysis, succeeding a proper uncluttering and coding of raw data. (Figure 2)



**Figure 2 : Data Collection Scheme**

In this study, treatment initiation delay was the dependent variable. Treatment initiation delay was defined based on the median number of days between the initiated treatment and GenXpert diagnosis confirmation. The cut-off was determined by the median, after consideration of previous similar studies (Evans et al., 2017; Htun et al., 2018; Tefera et al., 2019). Furthermore, this study used the biopsychosocial model to determine factors associated with treatment initiation, with biological factors, social factors, and psychological factors as the independent variables (Sarafino, 2011).

The biological factors consisted of MDR-TB comorbidities status and TB history of the patients. TB history was classified as new (a patient who has received no or less

than one month of anti-TB treatment), relapse (a patient who previously completed treatment for TB), and loss to follow-up or failure (a patient from treatment after loss to follow-up, after failure of first treatment with first-line drugs, after failure of retreatment regimen with first-line drugs, and other previously treated patients).

Contributing social factors consist of if the patient has medical insurance, if the patient is the head of their household, marital status, professional status, duration of seeking healthcare, and initial support assessment. The initial support assessment is a classification determined by the TB case manager that determines whether patients require maximal or minimal support from the support program.

Psychological factors include the patient's MDR-TB knowledge (definition and symptoms, causes of MDR-TB, possibility of MDR-TB being cured, duration of treatment, MDR-TB drugs and their side effects, transmission, prevention of infection, protocols to be conducted if any patients' relatives acquire TB symptoms, and the patient's confidence to complete the MDR-TB treatment program).

## **2.4 Qualitative Methods**

### **2.4.1 Participants**

This study used purposive sampling methods to select two groups of participants: MDR-TB patients and healthcare workers who are a part of the implementation of treatment initiation in Persahabatan Hospital. The inclusion criteria for participants of MDR-TB patients were: a) over the age of 18 years old, b)

experiencing more than one month's waiting time for treatment initiation, and c) willingness to participate in this study. Participating health workers needed to be involved in the MDR-TB treatment initiation processes in Persahabatan Hospital for a minimum of 3 months to be considered for inclusion in the study. In-depth interviews were conducted with ten MDR-TB patients and seven health workers: one specialized doctor, one interning doctor in the MDR-TB department, one nurse, two data officers, one case manager, and one patient supporter.

#### **2.4.2 Procedures**

Alongside the PI, the peer educator organization in Persahabatan Hospital, also known as Pejuang Tangguh (PETA), provided assistance in recruiting MDR-TB participants based on the eligibility list provided from the hospital database. Patients were approached by the PI via WhatsApp messenger with assistance from 6 peer educators. The PI also personally approached all the health worker participants from the MDR-TB Department in Persahabatan Hospital. The PI shared information about the study and asked them if they would be interested in participating. If participants agreed, they were asked when and how they would be able to interview. All interviews and recruitment were conducted in Bahasa Indonesia (local language).

All interviews were conducted by the PI following a semi-structured topic guide. The patient interview topic guide covers five domains of interest: 1) Characteristics of the patient, 2) TB History and diagnosis experiences, 3) Treatment

initiation experiences, 4) Psychological factors related to treatment initiation, 5) Social factors related to treatment initiation. Interviews with health workers cover three domains of interest: 1) Procedure of treatment initiation, 2) Enablers and obstacles of treatment initiation, 3) Current support and suggestions for implementing treatment initiation.

Nine MDR-TB patient participants were interviewed via telephone call and one participant was interviewed in the open corner waiting area at the hospital, as preferred by the patient. At the beginning of the interview, the principal investigator read the informed consent form to the participant, gave participants time to ask questions regarding the interview, and asked for consent verbally. Seven health worker participants agreed to participate in this study; six were interviewed in a private room in the hospital, and one was interviewed via voice call. The PI provided a paper copy of the informed consent form and gave time to read the consent agreement and provide clarification for interviews in person. If the participants agreed, they signed the consent paper.

For in-person interviews, a research assistant assisted the PI by making notes during the interview. The notes consist of main or important points during the interview. Interviews were typically 30-45 minutes long. All in-depth interviews were audio-recorded, with participants' consent. After the interview, participants got a package of daily goods as compensation for their time.

## **2.5 Analysis**

Quantitative analysis involved categorical variables that were summarized by counts and percentages, and the differences between groups were compared using chi-square ( $\chi^2$ ). The binary logistic regression model was fitted by considering treatment delay as an outcome of interest. Then, the association of factors with waiting time of treatment initiation was analyzed with Poisson multivariate regression analysis. Crude and adjusted rate ratio with a 95% confidence interval (CI) were used to determine the strength of association between the dependent and independent variables.

Qualitative analysis involved the transcription of all the interviews in Bahasa Indonesia (local language) and translation to English by the team of research assistants, with supervision from the PI. This study used an applied thematic analysis approach (Guest et al., 2011). The PI read all the transcripts and drew out a set of themes underpinning the basis of the analysis while considering the study objectives. Each theme also was defined to ensure the understanding of themes during the coding process. Then, the PI applied the theme list to code the interviews using Nvivo12 (Bazeley & Jackson, 2013). Following the coding, the PI examined the code text through analytic memos and discussed the contents with research advisors, which was used to synthesize the findings, structure the results, and identify representative quotes. The



goal in this study was not to obtain theme saturation but to acquire a range of perspectives from the participants.

## **2.6 Ethical Review**

This study has already been approved by the ethical review boards at Duke Kunshan University and Persahabatan Hospital. Moreover, in order to comply with the participants' right to informed consent, the researchers also collected a signed and dated paper-based or verbal informed consent from all participants after they received an explanation about the research and before data collection began. Furthermore, all digital records were stored in a digitally secure location only accessible to the research team. There was no risk of physical harm. The participants could stop and drop out of the interview at any time if they were not comfortable with any questions.

### 3.Result Section

#### 3.1 Quantitative Analysis

Table 1 Characteristics of Study Participants in Quantitative Study

| Variable                   | MDR-TB Patients   |
|----------------------------|-------------------|
| Count (%) or Mean $\pm$ SD |                   |
| Age, years (n=187)         | 42.32 $\pm$ 13.94 |
| Age Classification         |                   |
| 18-30 years old            | 46 (24,6)         |
| 31-56 years old            | 108 (57,75)       |
| Over 56 years old          | 33 (17,65)        |
| Sex (n=188)                |                   |
| Male                       | 104 (55,32)       |
| Female                     | 84 (44,68)        |
| Work Status (n=176)        |                   |
| No work                    | 83 (47,16)        |
| Informal sector            | 44 (25,00)        |
| Formal sector              | 49 (27,84)        |
| Married Status (n=179)     |                   |
| Single                     | 42 (23,46)        |
| Married                    | 126 (70,39)       |
| Divorced                   | 11 (6,15)         |
| Medical Insurance (n=188)  |                   |
| Yes                        | 183 (97,34)       |
| No                         | 5 (2,66)          |
| Co-Morbidities (n=186)     |                   |
| DM                         | 61 (32,80)        |
| HIV                        | 6 (3,21)          |
| Others                     | 27 (14,52)        |

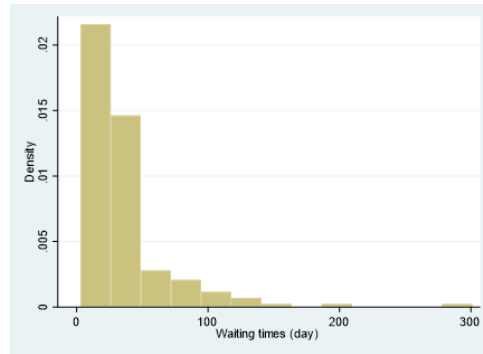
Abbreviations: TB, tuberculosis; MDR-TB, multidrug resistant tuberculosis; SD, standard deviation, DM: diabetes mellitus; HIV, human immunodeficiency viruses

In total there were 188 patient records included in this study. Table 1 shows the MDR-TB patient characteristics in Persahabatan Hospital in 2019. Most of the patients were of productive age, from 31-56 years old (n= 108; 57.75%), followed by age range 18-30 years old. In terms of work status, most patients were not working (42.16%, n=83), yet there were 19 participants in this group who were still of school age (18- 24 years old). In terms of comorbidities, there were 77 people (41.4 %) who had comorbidities, and diabetes mellitus (DM) was the most major comorbidity (32.8% n=61). Additionally, most patients were already married (n=126 ; 70.39%) and had medical insurance (n=183 ; 97.34%).

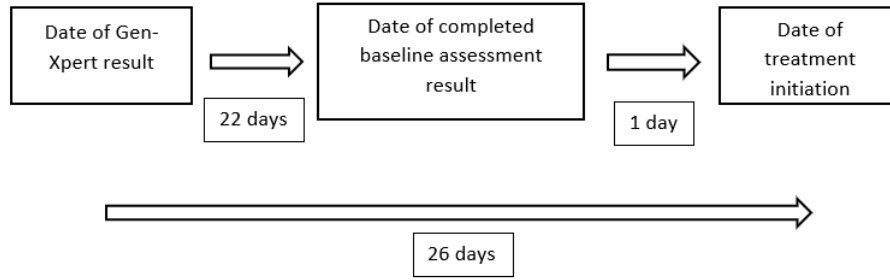
**Table 2: Waiting Time of Treatment Initiation for MDR-TB**

| Variable  | Patient with presumptive MDR-TB<br>Count (%) or Median, IQR |
|---|---|
| Waiting Time ( Gen-Xpert result to Baseline result) (n=150)     | 22 (15-36)  |
| Waiting Time (Baseline result to Treatment Initiation ) (n=153) | 1 (1-4)   |
| Waiting Time (Gen-Xpert result to Treatment Initiation) (n=188) | 26 (16-37.5)  |
| <14 days  | 29 (15.43)  |
| 14 days – 30 days   | 89 (47.34)  |
| 31-60 days  | 46 (24.47)  |
| More than 60 days   | 24 (12.77)  |
|   |   |

Abbreviation: IQR, inter-quartile range



**Figure 3 Distribution of Waiting Time for Initiation MDR-TB Treatment**



**Figure 4 : Median Time of Treatment Initiation Flow Chart**

Figure 4 shows that the median time of patient enrollment in MDR-TB treatment was 26 days after diagnosis, with 22 days median time for patients to complete the baseline assessment and 1-day median time between completing the baseline assessment and initiating the treatment.

Table 2 describes the count and percentage of patients who experienced long waiting times to enroll in the treatment. There were 156 (82,98 %) patients who experienced treatment delay for more than 14 days and 87 (46.28%) patients who experienced waiting time for more than 26 days. Moreover, we found that the

distribution of waiting time was normally distributed, fitting a Poisson curve very closely (Figure 3). Therefore, we used Poisson regression for further analysis.

**Table 3: Univariate Analysis of Factors Related with MDR-TB Treatment Initiation Delay (>26 days)**

| Variable  | Below the median (%) | Above the median (%) | Total (%)   |
|---|----------------------|----------------------|-------------|
| Count (%) or Mean $\pm$ SD                                  |                      |                      |             |
| <b>Waiting time treatment initiation</b>                    |                      |                      |             |
| <b>Characteristic</b>                                       |                      |                      |             |
| Age, years  | 42.33 $\pm$ 13.94    |                      |             |
| Age Classification (n= 187)                                 |                      |                      |             |
| 18-30 years old   | 22 (47.83)           | 24 (52.17)           | 46 (24,6)   |
| 31-56 years old   | 58 (53.70)           | 50 (46.30)           | 108 (57.75) |
| Over 56 years old   | 20 (60.61)           | 13 (39.39)           | 33 (17.65)  |
| Sex (n= 188)  |                      |                      |             |
| Male  | 59 (56.73)           | 45 (43.27)           | 104 (55.32) |
| Female  | 42 (50.00)           | 42 (50.00)           | 84 (44.68)  |
| <b>Biological Factors</b>                                   |                      |                      |             |
| Co-Morbidities (n= 186)                                     |                      |                      |             |
| Yes   | 37 (48.05)           | 40 (51.95)           | 77 (41.4)   |
| No  | 62 (56.88)           | 47 (43.12)           | 109 (58.6)  |
| TB History (n= 188)   |                      |                      |             |
| New   | 28 (53.85)           | 24 (46.15)           | 52 (27.67)  |
| Relapse   | 47 (55.95)           | 37 (44.05)           | 84 (44.68)  |
| Loss to follow-up / Failure                                 | 26 (50.00)           | 26 (50.00)           | 52 (27.65)  |
| <b>Psychological factors</b>                                |                      |                      |             |
| MDR-TB Knowledge score <sup>a</sup>                         | 5.47 $\pm$ 2.50      |                      |             |
| MDR-TB Knowledge classification <sup>b</sup> (n= 188)       |                      |                      |             |
| Low   | 27 (47.37)           | 30 (52.63)           | 57 (30.32)  |
| Medium  | 23 (47.92)           | 25 (52.08)           | 48 (25.54)  |
| High  | 51 (61.45)           | 32 (38.55)           | 83 (44.14)  |
| Are you sure could finish the treatment? (unsure)* (n= 188) | 45 (45.00)           | 55 (55.00)           | 100 (53.19) |
| <b>Social Factors.</b>                                      |                      |                      |             |
| Medical Insurance (yes) (n= 188)                            | 99 (54.10)           | 84 (45.90)           | 183 (97.34) |
| Head of household (Yes) (n= 188)                            | 20 (46.51)           | 23 (53.49)           | 43 (22.87)  |
| Married Status (n= 179)                                     |                      |                      |             |
| Single  | 22 (52.38)           | 20 (47.62)           | 42 (23.46)  |
| Married   | 70 (55.56)           | 56 (44.44)           | 126 (70.39) |
| Divorce   | 3 (27.27)            | 8 (72.73)            | 11 (6.15)   |
| Work Status (n= 176)  |                      |                      |             |
| No work   | 43 (51.81)           | 40 (48.19)           | 83 (47.16)  |
| Informal sector   | 27 (61.36)           | 17 (38.64)           | 44 (25)     |
| Formal sector   | 24 (48.98)           | 25 (51.02)           | 49 (27.84)  |
| Time journey to healthcare* (n= 188)                        |                      |                      |             |
| >1 hour   | 30 (56.60)           | 23 (43.40)           | 53 (28.19)  |
| 1-2 hours   | 45 (46.39)           | 52 (53.61)           | 97 (51.6)   |
| >2hours   | 26 (68.42)           | 12 (31.58)           | 38 (20.21)  |
| Initial Support Assessment (Need Max) (n= 188)              | 32 (50.00)           | 32 (50.00)           | 64 (34.04)  |

<sup>a</sup> Accumulative of TB Knowledge score<sup>c</sup> Knowledge MDR-TB consist of : symptoms, causes, is the disease is curable?, the drugs, side effects, duration of treatment, is the disease infectious, how the transmission, prevention of infection, what should you do if there is relative have TB symptoms : Low (Total Score : 0-3), Medium (Total Score : 4-6), High (Total Score : 7-10)

Table 3 shows the univariate analysis on factors related to MDR-TB treatment initiation, comparing patients with a total delay of  $\leq 26$  days with patients with a total delay of  $> 26$  days. We found that 51.95 % of patients with comorbidities, around 52% of patients with low and medium MDR-TB knowledge, 55% of patients unsure if they could finish the treatment, and 52% of patients who traveled 1-2 hours to the hospital experienced delayed treatment initiation of  $> 26$  days

Further, Table 4 shows the multivariate analysis with Poisson regression. In the crude analysis, the waiting time of treatment initiation was associated with TB History, confidence to finish the treatment, medical insurance, head of household, marriage status, work status, and time of journey to the hospital.

Then, the adjusted analysis revealed that MDR-TB patients with comorbidities had 47 % longer relative change in mean waiting time (25.4 days) after adjustment for age and TB history compared to patients without comorbid diseases.

Patients with low knowledge had 31% longer relative change and those with medium knowledge had 24% longer relative change in waiting time than the mean of patients who had high knowledge of MDR-TB. We also found that the results from the initial support assessment had a smaller impact since patients who had maximal support assessment had only 11 % longer relative change in mean waiting time compared to patients who had minimal support assessment.

**Table 4: Multivariate Poisson Regression Analysis Factors Associated with MDR-TB Treatment Initiation**

| Variable  | CRR (95% CI)            | ARR (95% CI)                       |
|---|-------------------------|------------------------------------|
| <b>Age Classification</b>                           |                         |                                    |
| 18-30 years old                                     | 0.991 (0.9178 – 1.0698) |                                    |
| 31-56 years old                                     | 1.051 (0.984 – 1.123)   |                                    |
| Over 56 years old (reference)                       | 34.1 Days               |                                    |
| <b>Sex</b>  |                         |                                    |
| Male  | 0.959 (0.913 – 1.006)   |                                    |
| Female (reference)                                  | 35.8 days               |                                    |
| <b>Biological Factors</b>                           |                         |                                    |
| <b>Co-Morbidities</b>                               |                         |                                    |
| Yes   | 1.371 (1.306 – 1.439)*  | 1.466 (1.389 - 1.547) <sup>b</sup> |
| No (reference)                                      | 30.4 days               | 25.4 days                          |
| <b>TB History</b>                                   |                         |                                    |
| New (reference)                                     | 33.5 days               |                                    |
| Relapse   | 1.009 (0.951 – 1.072)   |                                    |
| Loss to follow-up / Failure                         | 1.145 (1.073 – 1.221)*  |                                    |
| <b>Psychological factors</b>                        |                         |                                    |
| <b>MDR-TB Knowledge score</b>                       |                         |                                    |
| MDR-TB Knowledge score                              | 0.956 (0.946 – 0.965)   |                                    |
| <b>MDR-TB Knowledge classification <sup>c</sup></b> |                         |                                    |
| Low   | 1.309 (1.236 – 1.385)*  | 1.314 (1.239 - 1.380) <sup>f</sup> |
| Medium  | 1.250 (1.177 – 1.328)*  | 1.244 (1.169 - 1.325) <sup>e</sup> |
| High (reference)                                    | 30.2 days               | 30.3 days                          |
| <b>Confidence to finish the treatment</b>           |                         |                                    |
| Unsure  | 1.184 (1.128 – 1.244)*  |                                    |
| Sure (reference)                                    | 31.8 days               |                                    |
| <b>Social Factors</b>                               |                         |                                    |
| <b>Medical Insurance</b>                            |                         |                                    |
| No  | 0.8133 (0.689 – 0.960)* |                                    |
| Yes (reference)                                     | 35.1 days               |                                    |
| <b>Head of household</b>                            |                         |                                    |
| Yes   | 1.096 (1.036 – 1.159)*  |                                    |
| No (reference)                                      | 34.2 days               |                                    |
| <b>Married Status</b>                               |                         |                                    |
| Single  | 0.871 (0.820 – 0.927)*  |                                    |
| Married (reference)                                 | 36.3 days               |                                    |
| Divorce   | 1.046 (0.946 – 1.156)   |                                    |
| <b>Work Status</b>                                  |                         |                                    |
| No work   | 1.072 (1.011 – 1.137)*  |                                    |
| Informal sector                                     | 0.829 (0.772 – 0.891)*  |                                    |
| Formal sector (reference)                           | 35.5 days               |                                    |
| <b>Time journey to hospital</b>                     |                         |                                    |
| >1 hour   | 39.4 days               |                                    |
| 1-2 hours   | 0.896 (0.849 – 0.946)*  |                                    |
| >2hours   | 0.707 (0.657 – 0.762)*  |                                    |
| <b>Initial Support Assessment</b>                   |                         |                                    |
| Need Maximal support                                | 1.180 (1.123 – 1.240)*  | 1.11 (1.052- 1.176) <sup>d</sup>   |
| Need Minimal support                                | 32.9 days               | 20.6 days                          |

Abbreviation: CI, confidence interval, CRR, crude rate ratio, ARR, Adjusted rate ratio; \*statically significant P-value < 0.05

<sup>b</sup>Adjusted with Age and TB History; <sup>c</sup> Adjusted with Work Status and Age; <sup>d</sup> Adjusted with Age, Co-morbidities, MDR-TB knowledge score, patient as head of household, and confidence of patient to start the treatment

## **3.2 Qualitative Analysis**

This study presents the qualitative data in four subsections. The first subsection is the characteristics of patients who experienced delayed treatment initiation and health workers. The second subsection is the steps of treatment initiation identified by patients and health workers. The third subsection is health system challenges in treatment initiation from health workers' perspectives. The last subsection is the patient's life changes after diagnosis of MDR-TB related to the treatment initiation process.

### **3.2.1 Characteristics of samples**

The qualitative participants included 10 MDR-TB patients who experienced delay in the initiation of treatment and 7 health providers who provide MDR-TB care. Table 5 shows MDR-TB patient characteristics. The mean waiting time was 70 days (range 31 to 226 days). The majority of participants were still ongoing treatment (n=8) when we conducted the interview. Most of them were married (n=8) and one of the participants was widowed with one child. The mean age was 33 years old (range 22-44 years old). There were four males and six females and only 3 participants worked in formal sectors.

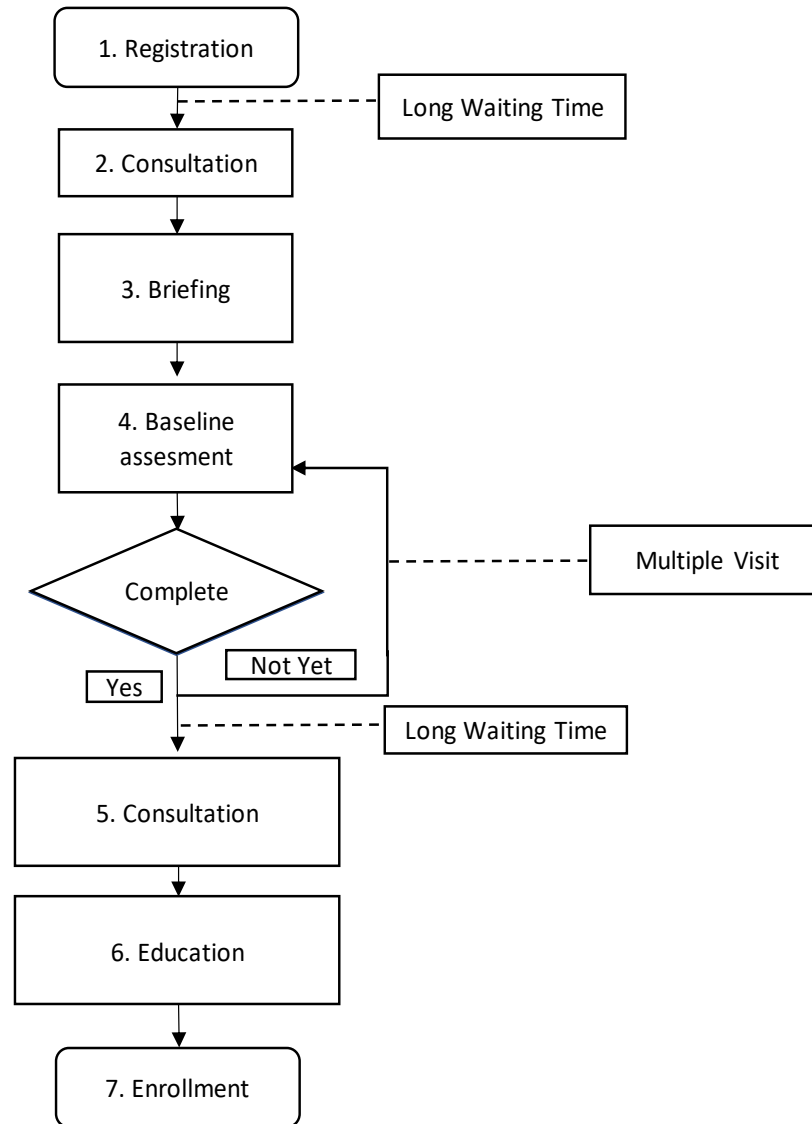


**Table 5: Characteristic of Patients Who Experienced Delay Treatment Initiation (>30 Days)**

| Code | Sex | Age | Married                | Head of family | Work status | Co-morbidities | Day of Delay | TB history | Treatment Status    |
|------|-----|-----|------------------------|----------------|-------------|----------------|--------------|------------|---------------------|
| PT1  | M   | 44  | married                | Yes            | Non-formal  | DM             | 31           | Yes        | On treatment        |
| PT2  | F   | 24  | Single                 | No             | Formal      | No             | 46           | Yes        | Completed treatment |
| PT3  | F   | 26  | Married                | No             | Housewife   | No             | 91           | Yes        | On treatment        |
| PT4  | F   | 33  | Married                | No             | Formal      | No             | 72           | Yes        | On Treatment        |
| PT5  | M   | 40  | Married                | No             | Non-formal  | DM             | 41           | No         | On treatment        |
| PT6  | M   | 35  | Married                | Yes            | Not work    | Epididymitis   | 226          | No         | On treatment        |
| PT7  | F   | 37  | Married                | No             | Formal      | No             | 40           | Yes        | On treatment        |
| PT8  | F   | 22  | single                 | No             | Housewife   | No             | 73           | Yes        | Completed treatment |
| PT9  | F   | 37  | Married                | No             | Housewife   | Hypertension   | 37           | Yes        | On treatment        |
| PT10 | M   | 35  | widowed with one child | No             | Non formal  | DM             | 45           | No         | On treatment        |

Furthermore, MDR-TB health workers who participated came from a variety of roles and years of work experience in the MDR-TB division. The participants consisted of two data officers, one case manager, one nurse, one internship specialist doctor, one specialist doctor, and one peer educator. The mean period of work experience was 4 years (range 0.5 to 7 years working time). To maintain confidentiality of the health workers, we could not describe more detail about their characteristics.

### 3.2.2 Treatment Initiation Process



**Figure 5 Treatment Initiation Process and Challenges**

This study summarized MDR-TB treatment initiation pathways in Persahabatan Hospital, based on interviews with health workers (Figure 1). The figure illustrates the process of treatment initiation from the point when a person who is diagnosed with

MDR-TB first registers at the hospital to start their treatment until they enroll in treatment. The process is described in detail below, supported with examples from patient interviews, including their experiences and the challenges they faced.

### **Step 1-3 (Registration, Consultation and Briefing)**

First, a person diagnosed with MDR-TB needs to register at the registration desk at the MDR-TB division in the hospital. Patients need to bring their gen-expert results from the primary healthcare or previous hospital. If patients are a primary or new patient (never had previous TB History), they need to have two results from GenXpert tests. But if the patients have previous TB history, they can conduct a GenXpert test in Persahabatan Hospital with average waiting time for the result around 3 - 7 days.

“The duration of (GenXpert) should be up to one week, but an average of three days. The waiting time mostly because the large number of samples in the lab. Not only from this hospital but often the sample from other facility healthcare. Then, around 3 days for patient to start the baseline assessment” (HW1)

After patients fill the registration form, they need to wait in the waiting room at the hospital (Picture 1) before they can get a consultation with an on-site doctor<sup>1</sup>.

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<sup>1</sup> Doctors who standby in the MDR-TB Division, which commonly consists of 3-4 internship specialized doctors that regularly changes.

As for challenges, all patients in this study complained how they need to wait a long time only to have a short consultation with the on-site doctor. As one patient explained, if you come late in the morning, you will wait longer to have a consultation with a doctor because of too many patients.

“You need to go to hospital really early in the morning. Because if you come later you need to wait really long to meet the doctor. We (patient) know that the nurses and doctors busy and there are many patients here, however, they need to consider that we are sick, confuse and tired” (PT7)



**Picture 1 MDR-TB Waiting Room in Persahabatan Hospital**

Then, during the consultation, the doctor will educate patients with MDR-TB about the process of initiating the treatment. However, the on-site doctor only has limited time to educate and fill the consultation report considering there were many patients in the queue, which were additional challenges.

“If I want the patient consul to pre-enrollment, there are a lot of things written, now it's also like I have to say "Sir, wait a minute, I'll write first, then after writing, I'll definitely explain this I want to check this, check this. , this consultation ... is written clearly and it takes time and the difficulty is there, then it's like that, the problem is only there”. (HW 5)

After the consultation, a nurse will check the records of patients and direct patients to the registration desk to determine the baseline assessment schedule.

#### **Step 4 Baseline Assessment**

In the baseline assessment process, the registration desk will coordinate with patients to schedule the assessment. The baseline process consists of physical examination, psychiatric examination, supporting examination (microscopic sputum examination, complete blood test and blood chemistry test), thyroid hormone (if necessary), pregnancy test (for childbearing age women), thorax X-ray, hearing test, ECG examination and HIV test. All patients in this study reported that in this phase, they needed to go to the hospital multiple times to take the assessment since the schedule of the assessment is not available every day. Consequently, many patients reported that they experienced difficulties matching the schedule of the assessment with their own or those of people who accompany them, as the challenges. Moreover, one patient shared her experience of delay in scheduling baseline assessment due to a national holiday. Here, one of the patients explained how she needed to wait a long time to start the treatment.

“At Persahabatan Hospital, I immediately directed to take some tests. The tests were cardio test, sputum, blood, everything. In one month, I had not received any drugs. I did the tests back and forth at Persahabatan Hospital. The lab results did not out in one month. They were out after months, except the sputum test’s result. It took so long which made my family confused (...)” (PT 9)

Furthermore, health workers reported that some assessment results are available immediately or the next day after the assessment for the Ear Nose and Throat (ENT),

and Eye Test. But assessments related with the internist division such as X-ray or blood tests commonly take a longer time.

“(...) For example, ENT (ear nose and throat) test only takes a day, it is only available on Tuesday, then eye test on Thursday. So, we cannot join them (baseline assessment) all in one day. So, it will probably, Friday for heart test, ENT on Tuesday, eye test on Thursday. If it is in a sequence, they can go to internist division on Wednesday, then eventually enroll to the treatment (...)” (HW3)

### **Step 5-7 (Consultation, Education and Enrollment)**

After all the results from baseline assessment are available, except the culture sputum test, patients will have consultations regarding their baseline assessment. Under the supervision of specialist doctors, usually, the on-site doctor will determine if the patient can initiate the treatment or not. Moreover, some patients in this study reported that they needed to postpone the treatment initiation because of their comorbidities.

“But it turned out that we could not, the patient’s (Pak Edi) hearing is not really good, so he couldn’t get injection (...) Unfortunately, this patient has diabetes. I think what made the process became long was the diabetes, but the TB itself must not be that complicated. Because as he got his diabetes medicine, the doctor gave him the TB medicine immediately.” (PT10)

Then, the doctor will give education about the treatment, and ask the patient to sign the agreement for adherence to the treatment. The nurse will also re-inform and ensure the understanding of the patients. In the meantime, the nurse also coordinates with the case manager for socio-psychological assessment of the patients. The assessment will be utilized to determine if the patient needs maximal or minimal support from the peer supporter.

“The Case Manager's first assignment is to assess the patient's psycho-social condition as well as what kind of psychology the patient, so the case manager determines the minimum and maximum criteria of social support for MDR-TB patients.” (HW 2)

Finally, patients can start the MDR-TB treatment immediately based on patient preference. Moreover, most of the health workers reported that on average, patients need around 1-2 weeks for the whole process of treatment initiation.

“If the family is cooperative, the patient is cooperative, the patient's clinical is good and he really wants to go to treatment, (...), they could start for around 1- 2 weeks, which needs like five times visit to here (hospital)” (HW 4)

Despite this, in the quantitative analysis, we found that the median period for the entire treatment initiation process in this hospital was 26 days.

### **3.2.3 Health System Challenges**

#### **Human Resources**

Human resources were an important aspect for treatment initiation implementation. In this study, patients reported that most of the health workers are friendly and helpful, yet they are still lacking in the number of staff, which might create waiting time and delay in the treatment initiation process.

“(…) simply not from the hospital, the hospital was running according to the procedure, maybe there was only a shortage of expert experts such as ENT, eyes. It's only served once a week, right? Which makes the length of time sometimes there are services once a week or twice a week, because the queue is too full. (HW2)

As the health workers also explain, it is difficult to search for people who are willing work in MDR-TB divisions, since they need to follow health and safety protocol,

such as wearing N95 masks all day, which can be quite uncomfortable, and risk getting infected with MDR-TB.

On the other hand, even though health workers felt a positive working environment in the MDR-TB hospital, some of the health workers believed they need routine capacity building and training to adapt to new TB programs or update their skills to handle the complexity of MDR-TB situations. In addition, health workers also often face difficult situations from patients such as anger and temperamental attitudes, or even patients who ask for money from health workers.

### **Management and Coordination**

Based our interviews with health workers, coordination between the health workers is one of main challenges for implementing treatment initiation in Persahabatan Hospital. MDR-TB divisions consist of many health worker roles, such as data officer, nurse, case manager, on-site (interning) doctor, and specialist doctor. Currently, the health workers are using WhatsApp as their tool for daily coordination, since there is not any specific Standard Operational Procedure (SOP).

“The main obstacle is coordination because we cannot work alone. Even though we work different fields, we still have the same goal.(...) we mostly use WA (WhatsApp’s) for coordination,(...) Yes. There is no SOP about it (the coordination)” (HW 1)

Health workers also reported that a common problem they often experience is miscommunication across stakeholders. For example, the MDR-TB division commonly has difficulty reaching the internist division to ask about assessment results, since the



data officer cannot go directly to the internist division due to safety protocol. Furthermore, the case manager also reported that often there are missed communications between cadres and peer educators to handle and approach the patients. Therefore, the care manager also independently created informal monthly meetings with the peer supporters and cadres to resolve issues. In addition, there is no formal system to coordinate between nurses and peer supporters, so usually nurses will directly contact the peer supporter.

### **3.2.4 Life Changes After Being Diagnosed with MDR-TB**

Besides the health system challenges for treatment initiation, this study also found that most patients experienced a “life changing” situation, (e.g., weak physical condition, loss of productivity, and stigmatization) after being diagnosed with MDR-TB, which correlated with the treatment initiation process. This study identified biological, psychological, and social changes to life perceived by MDR-TB patients who experienced delay in treatment initiation.

#### **Biological Aspects**

Most patients in this study experienced weak physical condition when they were initially diagnosed with MDR-TB. They felt overwhelmed while carrying out the treatment initiation process, especially when they needed to wait around 2 hours and make multiple visits for the baseline assessment.

“My family’s reaction was feeling bad because I have to go to Persahabatan Hospital every day to take the medicine. In the beginning, I also

went back and forth for x-ray test, and took every kind of tests. The wait also took long, they sympathize when they looked at my condition, how I was so skinny at that time." (PT 5)

Other patients also reported that they postponed the treatment due to their comorbidities. For example, for diabetes, they need to undergo diabetes treatment around one week before starting the TB treatment. Moreover, health workers also noted that implementation of treatment initiation is difficult since most of the patients had weak physical condition and comorbidities. Yet, there are still limited forms of support or assistance, for example, wheelchairs, oxygen, or special waiting rooms for those who need it.

### **Psychological Aspects**

When patients were initially diagnosed with MDR-TB, most of the patients said that they were feeling hopeless and were shocked that they got this disease. Several shared their concern that MDR-TB is a deadly disease, difficult to cure, and a situation that will become a burden for their family. Other patients also noted that they were distressed at having to substantially change their lives. For example, when diagnosed with MDR-TB, some of the patients distanced themselves from their families or withdrew from their jobs.

"(...) I am afraid to stay close with family, I always wear a mask all day, because I am afraid of transmitting my disease to others. Even though, they (her family) remain the same with me, but I think, because they not really know about the disease." (PT 4)

Even though there was not any direct report that psychological burden led to delay of treatment initiation, the level of stress and hopelessness that patients reported could contribute to such an attitude. The treatment initiation process also could be a stressful situation since most of the patients reported that they did not know about MDR-TB before the initial phases of the treatment process. As one of the patients described, he felt frustrated during the process of treatment initiation.

“It was frustrating too, how come it took so long even though I only wanted to take medicine, but it turned out that the procedure was like that from the hospital. Yes, I was immediately given directions from A to Z and continued to make a letter of agreement” (PT 8)

This situation is also supported by health workers’ statements that they often experience angry patients due to long waiting time or long procedures for baseline assessment for the treatment initiation process.

### **Social Aspects**

All patients reported some degree of impact to their social lives after being diagnosed. Some patients shared their experiences on how society or even health workers were treating them with stigma due to their disease. For example, their neighborhood prohibited them to participate in community discussions, or the health workers asked the patients to wait outside of the waiting room when they went to primary healthcare. Moreover, some of the patients also worried about telling their friends or colleagues about their disease and kept distant from them.

Furthermore, MDR-TB also made the patients lose their jobs or productivity. Some of them were not able to work due to their weak physical condition, others withdrew or were laid off from their jobs because they worried about infecting other people. This situation really impacts their financial condition, also considering the cost of transportation and additional medical services, especially for those who are from lower economic conditions or act as the head of their household.

“Oh, regarding financial condition, it is very hard to me. Especially my income was originally not much. Moreover, I do not work for now, so my wife is working. It is my financial issue. Maybe it’s also an obstacle to my friends who are also infected with TB when I heard their story.” (PT 5)

Patients also reported the importance of family support. Most of the patients said that their families really support them through the process. Even a few patients became dependent on other family members, especially for financial support and accompanying them to undergo the process of treatment initiation.

“ I am really shocked when got this disease again, yet my family encourage me to take the treatment again, even though the disease worsens (...) since my family who financially and morally support me for the mobilization back and forth to the hospital “  
(PT 4)

## **3. Discussion**

### ***3.1 Main Finding***

The quantitative results from 188 patient records included in this study showed that there were long delays between patient diagnosis and treatment initiation. On average, patients initiated their treatment 26 days after they got diagnosed, and 46.28% (87 patients) experienced delays longer than 26 days due to a long procedure for completion of the baseline assessment (average 22 days) before they could initiate the treatment. The delay of treatment initiation of MDR-TB was longer in patients with comorbidities, lower MDR-TB knowledge score, and classified need for maximal support based on the initial support assessment.

Furthermore, the qualitative results supported and explained the quantitative results. First, all patients complained about the complexity of the baseline assessment and some patients postponed their enrollment due to weak physical condition and comorbidities. Second, the health workers emphasized the importance of improving human resources, management, and coordination procedures, as well as social support for patients, considering the negative "life changing" situation of patients when diagnosed with MDR-TB. Currently, there is no official social support during the early period of the treatment initiation process.

### **3.2 Interpretation**

Based on this study, the duration of treatment initiation was shorter than previous research from a PMDT hospital in West Java, Indonesia, in 2015-2016 (45 days vs 26 days)(Soeroto et al., 2019b). This might be due to integrated community services in PMDT Hospitals in 2018. (WHO, 2018 ). However, the result was longer compared to other countries such as China (9 days) (Zhang et al., 2015), Ethiopia (8 days) (Tefera et al., 2019), and Bangladesh (10 days) (Rifat et al., 2015). Therefore, Indonesia still needs to reduce the delay between diagnosis and enrollment to 7 days based on the Indonesia NTP recommendation (IndonesiaMoH, 2018; MoH, 2016).

To achieve the NTP recommendation with only 7 days waiting time, we should recognize the complex conditions of people who are diagnosed with MDR-TB(Morris et al., 2013; Sarafino, 2011). First, for the biological factors, other studies also found similar results with this study as to the relationship between comorbidities and the treatment initiation process. Patients with comorbidities may also have weak physical condition and complications, as a result, it is necessary to handle and monitor the conditions of patients which may cause a delay in treatment enrollment, as we found in this study. (Htun et al., 2018; Stagg et al., 2016; Tefera et al., 2019). Moreover, these conditions also led to more complications in administrative procedures(Ivdity Chikovani, 2019; Thomas et al., 2018). Besides biological conditions, other studies also found that most patients felt afraid and lost hope when they were diagnosed with MDR-TB, which is in line with this

study's findings (Bhattacharya et al., 2018; Charyeva et al., 2019; Morris et al., 2013; Zhang et al., 2015).

Another obstacle for the treatment initiation process was low knowledge of MDR-TB among the patients. Many patients lacked basic knowledge about MDR-TB and did not know the procedure of the MDR-TB treatment process after diagnosis with MDR-TB, which made patients feel frustrated during the treatment initiation process. Many studies also found that patients' knowledge and ambition are important aspects of treatment efficacy, as the appropriate knowledge and ambition for combatting TB have been the main drivers for patients starting and finishing the treatment. (Cramm et al., 2010; Hoa et al., 2003; Paramasivam et al., 2016; Tupasi et al., 2016; Zhang et al., 2015).

Although the treatment initiation process is already included in NTP guidelines and supported by the International Donor and Civil Organization, there is no national plan to standardize the management and formal coordination mechanisms (WHO, 2018), which leads to miscommunication during the treatment initiation process, as we found in this study.

Another issue was the quantity and quality of human resources, considering the dynamic situation of MDR-TB programs and system information across the years in Indonesia (Indonesia MoH, 2018; WHO, 2017). Competence and capacity of human resources are important aspect of providing quality TB services, as mentioned in a previous study in China. However, there were many challenges to providing adequate

human resources such as lack of training and capacity building, lack of protective equipment, and low compensation, similar to this study. (Ehsanul Huq et al., 2018; Guo, 2018; Htun et al., 2018; Sagbakken et al., 2008). As a result, lack of coordination and human resources creates long queues and unnecessary multiple visits to the hospital, which could lead to delayed treatment. As several studies in developing countries mentioned, reducing waiting time for admission and commencement of treatment reduces treatment delay over time (Rifat et al., 2015; Tefera et al., 2019; Zhang et al., 2015).

Furthermore, the health workers in this study also mentioned the importance of social support. In addition to improving human resources, management, and coordination procedures, increasing involvement for patient social support is necessary. Negative impacts of "life changing" situations of patients when diagnosed with MDR-TB include loss of productivity and income and financial burden for patients from low socioeconomic status (Gebhard, 2018). Currently, MDR-TB diagnosis and treatment cost are free under NTP, outside of national insurance coverage (JKN). However, this program does not include additional costs such as drugs and lab work for comorbidities, such as diabetes, which must be paid for out of pocket or insurance, since it is not covered by NTP, and it leads to more complications in administrative procedures. Furthermore, currently, there is no official social support in the early period after diagnosis, it is only available after patients initiate the treatment, since the NTP only provide cash transfer



only for those who are already confirmed as MDR-TB patients of IDR 750,000/month (US\$ 53)(Fuady et al., 2018; LKNU, 2019; WHO, 2017, 2018 ; Winter et al., 2018).

### **3.3 Recommendation**

This study has revealed more information about MDR-TB procedures at one of the most renowned PMDT referral hospitals in Indonesia. This data can be used to inform future policy and practice. There are several aspects of the process that could be improved on hospital, CSO, and national levels.

#### **Persahabatan Hospital**

To prevent confusing patients during the treatment process, the hospital should provide information regarding procedures, pathways, and average waiting times of the MDR-TB process through information boards around the pulmonary ward, on a website, or through social media. To prevent the miscommunication between MDR-TB staff and non-MDR-TB staff, especially for internists working in the lab, the hospital needs to strengthen coordination through routine staff meetings between the MDR-TB staff and the lab staff. They may also benefit from establishing formal communication channels through the hospital information system or online databases such as Google Drive. To reduce the waiting time of patients for consultation with a doctor, the hospital could provide online registration or booking for consultations. Considering that some patients do not have access to a computer or smartphone, they should also provide a

peer supporter to assist the online registration. A peer supporter system will also be helpful to prevent the early loss to follow-up and long delays in treatment initiation.

### **Community or Civil TB Organizations who provide peer support (CSO)**

Moreover, to prevent early loss to follow-up and delay of treatment initiation, it is also the responsibility of the peer supporters to collaborate with the hospital and begin peer support promptly after the registration stage. When strengthening the resources of the CSOs, it is important to establish internal capacity-building courses such as financial planning, micro-entrepreneurship, and grant writing. The resources could further be used to provide safety protocols or health insurance for the peer supporters, as well as psychosocial capacity building. To improve the quality of services provided by peer supporters, it is important to establish routine coordination meetings (once a week) with PMDT teams.

### **National Tuberculosis Program**

To reduce the long delay of treatment initiation and the gap between case detection and enrollment, it is important for NTP to provide national guidelines regarding psychological and social aspects of MDR-TB diagnosis as part of NTP guidelines and action plans, as recommended by WHO. The PMDT hospital should be required to provide not only psychological disorder assessment by a doctor, but also psychological counseling by a psychologist to assist patients facing the life-changing situation of MDR-TB diagnosis (Winter et al., 2018).

First, NTP should regulate the collaboration between PMDT hospitals and local TB CSOs starting from the registration period to provide social support for patients to reduce early loss to follow up. Moreover, with this condition, NTP could collaborate with TB CSOs directly to provide cash transfers for MDR-TB patients starting from the patient registration period.

Second, NTP needs to raise awareness about MDR-TB facts and procedures in the public and within the hospitals, through social media, brochures, posters, or in the information board, especially regarding the pathway of treatment initiation until patients complete the treatment. This information includes, but is not limited to, the process flow, estimation of waiting time, and location of each part of the process. Having adequate information about basic knowledge and procedures of MDR-TB is a right for people affected with TB (STPI, 2019a, 2019b), particularly to be prepared for the treatment initiation process.

Third, we highly encourage the NTP to collaborate with TB CSOs, such as TB Survivor organization, to strengthen social support for MDR-TB patients starting at diagnosis, and to establish national TB social support guidelines to strengthen coordination across stakeholders. These actions should be supported with the provision of routine training and capacity building not only for health workers in the PMDT hospital but also with peer supporters to cope with complex conditions of MDR-TB

patients' lives (Lina et al., 2016; Morris et al., 2013; van de Berg et al., 2018; Walker et al., 2018).

Furthermore, NTP needs to strengthen and simplify the integration mechanism, administration, and information system for TB with other services, especially for TB co-morbidities such as DM and HIV. These actions reduce the complexity of the MDR-TB treatment initiation process and prevent delay or loss to follow-up (Winter et al., 2018).

### ***3.4 Strength and Limitation***

Strengths of this study include its mixed methods, in which qualitative components explain and complement the findings from the quantitative component. Including wide perspectives from different stakeholders closely involved in treatment initiation in Persahabatan Hospital, the data is suspected to have reached saturation based on triangulation from different stakeholders.

With IDIs, the interviewer created personal, deep data collection for each of the interviews and collects detailed information for each of the stakeholders. Data collection by the Indonesian native principal investigator with prior qualitative training maximized comfort and trust for the participants. Participant comfort was also maximized through flexible time and location of the interviews.

This study also had some limitations. This study only included and addressed patients who experienced delay in the treatment initiation process, but did not have information about patients who experienced early loss to follow up between diagnosis

and treatment initiation. For quantitative data, we used secondary data. As a result, this study lacked control over data quality and limited variables available. Since the data was collected by someone else and not created for research purposes. Moreover, in this study found 642 unmatched data across the database. This happens due to weak information integration system across the TB database and dynamic situation of MDT-TB patients, such as diagnostic changes, initial loss to follow up, patient died before starting treatment, patients were not reached by LKNU (case manager) or move to other hospital. This study was also conducted with a small sample size and only in one referral hospital, so generalizability across the larger population of Jakarta is limited.

Furthermore, most of the patients were interviewed through phone calls, so the interviewer was not able to ascertain non-verbal cues from participants during interviews. Recall bias of the patients may also be a concern because many of the patients who were willing and able to be interviewed were toward the end stage of treatment. Also, because most patients were interviewed via phone call, there were some network issues during the call, which may have led to the interviewer mishearing words or misunderstanding.

## **4. Conclusion**

This study aimed to examine the challenges of implementation of MDR-TB treatment initiation in a PMDT national referral hospital, known as Persahabatan Hospital, Jakarta, Indonesia. The result of this study revealed the challenges of the

treatment initiation process from the complex perspectives of the patients, aspects of the health system that need to be improved, and the importance of social support starting at diagnosis. With this important consideration, we hope there will be more awareness about MDR-TB treatment initiation procedures. Moreover, the collaboration between NTP, PMDT hospitals, and CSOs for MDR-TB social support since diagnosis is essential. With these actions, the NTP can reduce delayed treatment initiation and prevent early period loss to follow up in Indonesia.

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