Variation of Tuberculosis Prevalence across Diagnostic Approaches and Geographical Areas of Indonesia

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ความชุกของวัณโรคที่แตกต่างกันระหว่างวิธีการตรวจวินิจฉัยและพื้นที่ภูมิศาสตร์ของประเทศอินโดนีเ ชีย

น.ส.อเวร่า โนวิวานิ

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ความชุกของวัณโรคที่แตกต่างกันระหว่างวิธีการตรวจวินิจฉัยและพื้นที่ภูมิศาสตร์ของประเทศอินโดนีเซีย. (Variation of Tuberculosis Prevalence across Diagnostic Approaches and Geographical Areas of Indonesia) อ.ที่ปรึกษาหลัก : Asst. Prof.กฤษณ์ พงศ์พิรุฬห์, MD, MPH, PhD.

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Alvera Noviyani : Variation of Tuberculosis Prevalence across Diagnostic Approaches and Geographical Areas of Indonesia. Advisor: Asst. Prof. KRIT PONGPIRUL, , MD, MPH, PhD.

Background: Tuberculosis (TB) has contributed a significant disease burden and economic loss worldwide. Given no gold standard for diagnosis, early identification of TB infection has been challenging. This study aimed to comparatively investigate the prevalence of TB across diagnostic approaches (sputum AFB, sputum culture, sputum genetic test, and chest x-ray) and geographical areas in Indonesia.

Methods: Participant demographic variables and TB screening test results were obtained from the Tuberculosis Unit, Health Research and Development Agency, Ministry of Health (HRDA-MoH). Variations across geographical areas and diagnostic approaches are expressed as prevalence rate and 95%CI.

Results: A total of 67,944 records were reviewed. Based on bacteriological evidence, the prevalence of TB in Indonesia was 759 (95%CI 589.7- 960.8) with variations across areas: 913 (95%CI 696.7-1,176.7; Sumatra), 593 (95%CI 447.2-770.6; Java-Bali), and 842 (95%CI 634.7- 1,091.8; others). Also, the prevalence of TB varied across diagnostic approaches, from 262 (sputum AFB) to 895 (sputum genetic test). Based on sputum AFB, the TB prevalence varied from 216.6 (95%CI 146.5-286.8; Java-Bali) to 307.4 (95%CI 208.3-406.5; Sumatra). Based on sputum culture, the TB

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CHAPTER ONE
INTRODUCTION

1.1 Research Background

Tuberculosis (TB) is one of the top diseases which causes death worldwide. According to the World Health Organization (World Health Organization, 2019) report in 2019, Tuberculosis (TB) caused 1.5 million deaths in 2018, including 251 thousand people of HIV/AIDS deaths globally. In that year, 10.4 million people fell ill with TB, with an estimated 1.1 million children became ill with TB and 251 thousand children died of TB (including children with HIV associated TB) and mostly it was induced by poverty and vulnerability of the community (World Health Organization, 2019).

The WHO estimates that 3.6 million people with TB are missed by health systems every year and do not receive adequate care (WHO, 2015). This is primarily because patients with TB may present with mild or no symptoms, particularly early on. Many affected people arrive at clinics too late with advanced disease or multi-drug resistant TB (MDR-TB), which is difficult to treat and more likely to cause death. TB occurs in every part of the world. In 2018, the largest number of new TB cases occurred in the South-East Asia region, with 44% of new cases, followed by the African region, with 24% of new cases and the Western Pacific with 18% (World Health Organization, 2019).

In 2018, 87% of new TB cases occurred 1in the 30 high TB burden countries. Eight countries accounted for two-thirds of the new TB cases: India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa (World Health Organization, 2019). Based on the Center for Disease Control and Prevention 2016, Tuberculosis can be found through testing and diagnosis. TB bacteria in the body can be identified using two kinds of test, which are the TB skin test (TST) and TB blood tests, but the result of both tests only tell that a person has been infected with TB bacteria. Other tests, such as a chest x-ray and a sample of sputum, are needed to be conducted whether the person has latent TB infection or TB disease (CDC (Center for Disease Control and Prevention), 2016).

The Republic of Indonesia is the largest island country in the world which has 17,508 islands in total (Fig 1.1). Geographically, Indonesia consists of five major islands, namely Sumatera, Java, Sulawesi, Kalimantan, and Irian Jaya Papua. Indonesia is a nation with a multilingual, multicultural, and multi-ethnic society (Stone et al., 2016).

An important aspect of knowing the prevalence of TB is following the importance of TB screening. That is inevitable, true positive predictive value and true negative predictive value will be influenced by prevalence. As such, this research can help provide data about priority areas. The area with a higher prevalence should be the priority and several areas can be postponed. Due to limited resources, we cannot do everything simultaneously.

Each method has pros and cons because there is no gold standard for the Tb detection process. Therefore, the prevalence of each method must be known. The method is important, but this is not a reliable number because there is more than one method to confirm. That is why we need to know the range. It means we need to know the reliability of the overall prevalence rate. I want to compare across different method, so I can know the range and can have a reliability level. By looking at several levels of prevalence, we can think of how reliable they are. because we will know this number can be between ranges. Then we will compare whether the prevalence variation is influenced in large part by geography or method.

1.2 Research problem

TB is one of 10 causes of death and the main cause of infectious agents. In 2017, TB caused around 1.3 million deaths (range, 1.2-1.4 million) among people with HIV negative and there were around 300,000 deaths due to TB (range, 266,000-335,000) among people with HIV positive. It is estimated that there are 10 million cases of pulmonary TB (range, 9-11 million) equivalent to 133 cases (range, 120-148) per 100,000 population (Erawati and Andriany, 2020).

Globally, the incidence of TB per 100,000 population has fallen by around 2% per year. The regions that experienced the fastest decline in 2013-2017 were the European WHO region (5% per year) and the WHO African region (4% per year). In that year, a significant decrease (4-8% per year) occurred in South Africa such as

Eswatini, Lesotho, Namibia, South Africa, Zambia, Zimbabwe), and the expansion of TB and HIV prevention and care, and in Russia (5% per year) through intensive efforts to reduce the burden of TB.

At the global level, in 2017 there were around 558,000 new cases (range, 483,000-639,000) resistant rifampicin TB where almost half were in three countries namely India (24%), China (13%), and Russia (10%). Among RR TB cases, it is estimated that 82% of these cases are MDR TB. Globally, 3.6% of TB cases (new cases) and 17% of TB cases (re-treatment) were MDR / RR TB cases. The absolute number of deaths due to TB among HIV negative is estimated to have fallen to 29% since 2000 (from 1.8 million in 2000 to 1.3 million in 2017) and down by 5% since 2015. Meanwhile, the number of TB deaths in HIV positive has decreased by 44% since 2000 (from 534,000 in 2000 to 300,000 in 2017) and has dropped to 20% since 2015 (Fig 1.2) (Ministry of Health, 2019).

In 2017, the best estimate of the proportion of TB patients who died due to disease (case fatality rate / CFR) was 16%, down from 23% in 2000. The CFR must decrease by 10% by 2020 to reach the first stage of the End TB Strategy. There is considerable variation in CFR outcomes, ranging from less than 5% in some countries to more than 20% in most countries in the WHO Africa region. This shows the inequality between countries in accessing TB diagnosis and treatment.

WHO estimates that the 2017 incidence will be 842,000 or 319 per 100,000 population while TB-HIV will be 36,000 cases per year or 14 per 100,000 population (Lakoh et al., 2020). Deaths due to TB are estimated at 107,000 or 40 per 100,000 population, and TB-HIV deaths are 9,400 or 3.6 per 100,000 population. With an incidence of 842,000 cases per year and notification of TB cases amounting to 569,899 cases, there are still around 32% of which have not been verified either unreached, undetected, or not reported. From this incident rate, the TB burden is calculated in each province and district/city. For the calculation of TB burden at the district/city level, the Directorate General of P2P has published a Guidebook for Determining the Load and Targets for Covering Discovery and Treatment of Tuberculosis in Indonesia 2019-2024 (fig 1.3). WHO estimates there are 23,000 MDR / RR cases in Indonesia (fig 1.4). In 2017 there were 442,000 TB cases recorded in the program, of which there were an estimated 8,600-15,000 MDR / RR TB, (estimated

2.4% of new cases and 13% of TB patients treated previously), but coverage of newly treated was around 27.36%.

One of the key strategies for tackling TB is an early diagnosis. Unfortunately, sputum testing is only 50% accurate and frequently misses the disease in its early stages (WHO, 2015). According to the World Health Organization (WHO) systematic screening strategy to ensure early and correct diagnosis for all people with TB, Chest X-ray (CXR) is one of the primary tools for screening (WHO, 2016). There are several methods to diagnose TB disease, although it can lead to a missed diagnosis. Thus, important research to compare the Prevalence of TB in geographical and diagnostic aspect is necessary needed.

TB situation in Indonesia

(Source: Sub TB, Ministry of Health)

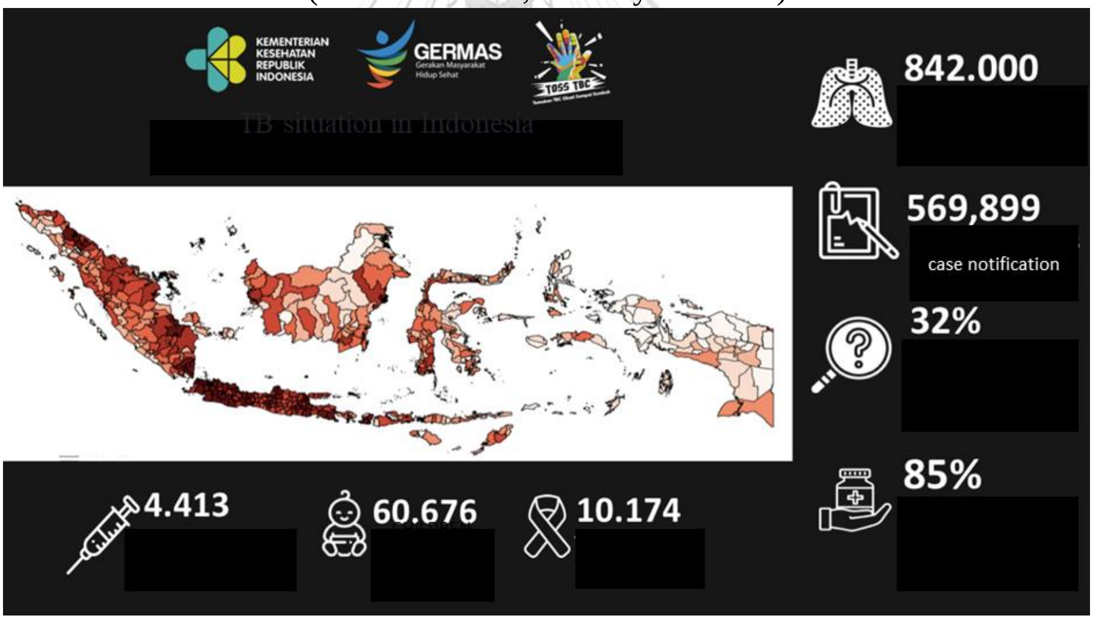


Fig 1.1 The situation of TB in Indonesia in 2018 (data as of May 1, 2019).

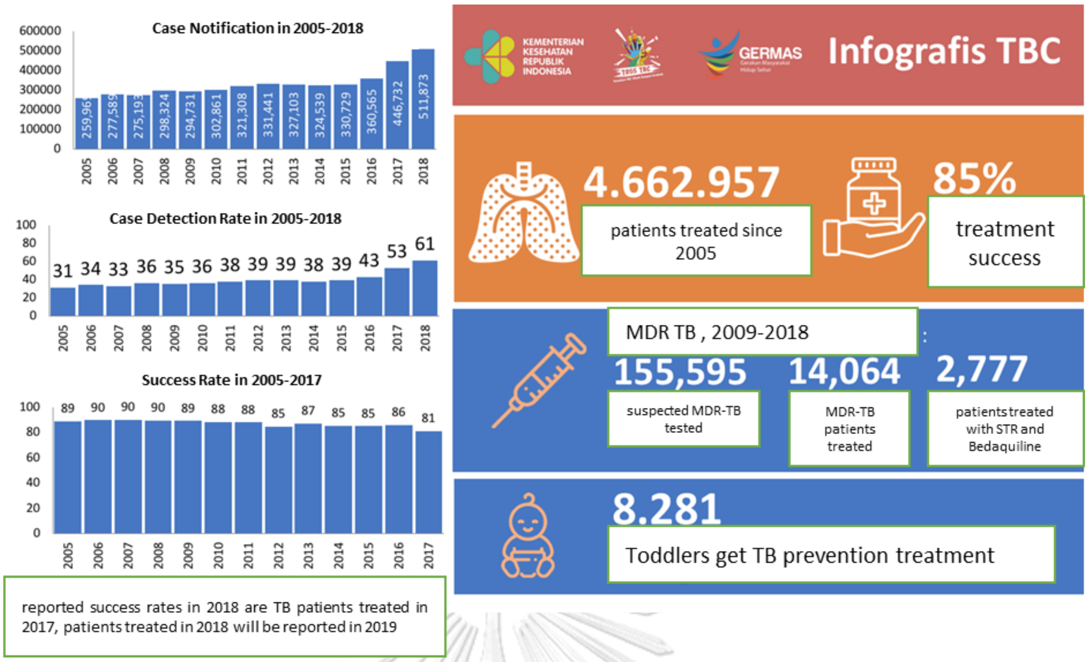
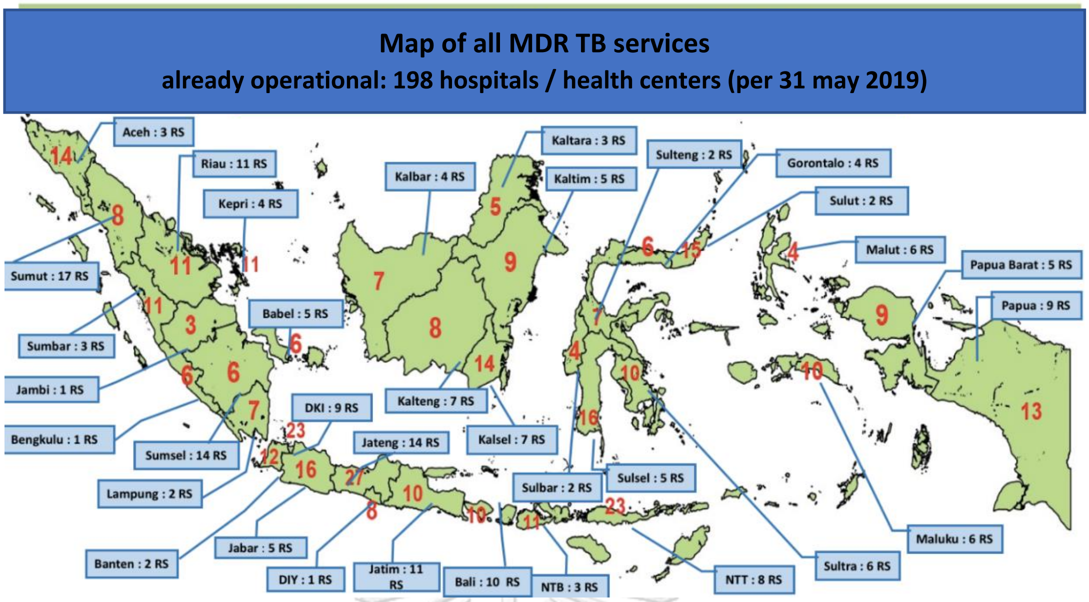


Fig 1.2. Conclusion of TB disease in 2005-2018

Fig 1.3. Health Facilities that Provide TB Services in Indonesia



Note :

RS = Hospital

Fig 1.4. Map of all MDR TB services

1.3 Research questions

I. What is the prevalence of Tuberculosis (TB) in Indonesia?

II. What is the prevalence of Tuberculosis (TB) in Indonesia across geographical areas?

III. What is the variation of Tuberculosis (TB) prevalence base on diagnostic approaches?

IV. How does the variation of TB Prevalence in Indonesia across diagnostic approaches and geographical areas?

1.4 Objective of the Research

1.4.1 General Objective

Knowing the prevalence of tuberculosis in populations aged 15 years and over in Indonesia.

1.4.2 Specific Objectives

I. To describe the variation of TB Prevalence geographically

II. To describe the variation in TB Prevalence across diagnostic approaches

III. To describe TB Prevalence both geographical and diagnostic variation

1.5.1 Benefits

1.5.1 For the Faculty of Medicine and related institutions

The results of the study are expected to be reference material related to variations in the prevalence of tuberculosis and can be used by academics as information on further research.

1.5.2 For the Government

The results of the research can be utilized by the Ministry of Health of the Republic of Indonesia as one of the supporting data in making a policy aimed at increasing the prevention and control of tuberculosis (TB). It also supports making a policy to plan strategies to increase case finding by improving diagnostic quality and innovating in various ways.

1.5.3 For the Community

The public can use this research as public awareness of the importance of increasing knowledge about Tuberculosis and the proper behaviour that can be done related to Tuberculosis.

1.5.4 For Researchers

As a means of implementing the epidemiological science that has been obtained during lectures, adding insight to researchers, providing an experience for researchers, as well as the requirements to obtain a Master of Science degree.

1.6 The scope of research

This study will be conducted to determine variations in prevalence in Indonesia in the age group of 15 years and over. This study will use a research instrument in the form of the Data set, This data set contains screening results of

Indonesian people using Chest X-ray and lab tests. This data set was obtained from the Health Research and Development Agency of the Tuberculosis Unit, Indonesian Ministry of Health. This data set represents Indonesia in 34 provinces covering 136 districts/cities in Indonesia consisting of Aceh, North Sumatra, West Sumatra, Riau, Jambi, South Sumatra, Bengkulu, Lampung, Bangka Belitung, Islands Riau, Jakarta, West Java, Central Java, Yogyakarta, East Java, Banten, Bali, West Nusa Tenggara, East Nusa Tenggara, West Kalimantan, Central Kalimantan, South Kalimantan, East Kalimantan, North Sulawesi, Central Sulawesi, South Sulawesi, Southeast Sulawesi, Gorontalo, West Sulawesi, Maluku, North Maluku, West Papua, Papua. The collected data will be analyzed descriptively and analytically according to the purpose of this study.

CHAPTER TWO
LITERATURE REVIEW

2.1 Overview of Indonesian country profile

The Republic of Indonesia is the largest island country in the world which has 17,508 islands in total. Indonesia is a republic country, located in Southeast Asia, between the Pacific and Indian oceans (Central Intelligence Agency, 2018). According to the Central Intelligence Agency report in 2018, the populations is 260,580,739 with 95% population growth rate per year. Geographically, Indonesia consists of five major islands, namely Sumatera, Java, Sulawesi, Kalimantan, and Irian Jaya Papua. Indonesia is a nation with multilingual, multicultural, and multi-ethnic society, these were influenced by the cultural history of Indonesia, which was mixed up by Mainland China, the Indian subcontinent, Europe, the Middle East, and the Austronesia culture (Stone et al., 2016).

2.2 Health Care System in Indonesia

Indonesia is engaged in the process of ensuring effective decentralization, which is implemented since 2001 at the district level. Decentralization is the process of delegating authority from the central government to the local government. The type of decentralization is the implementation of regional autonomy, which is widely given to the local government of a regency and a city. Through decentralization, it is expected that government can improve health services as well as the welfare of the community as is stated in Law No. 32 of 2004 on Regional Government of Indonesia (WHO, 2017). There are three levels of the health care system in Indonesia include a primary level of health care, secondary, and tertiary level. Primary health care is often called a community health care centre (*Puskesmas*) and village health posts (*pustu*) are found in the villages, where most facilities are community-based and provide primary health care and prevention programs. In each sub-district, at least one health centre is supposed to be headed by a doctor, supported by two or three sub-centres of which the majority, are headed by nurses. Health centres focus on health promotion, sanitation, mother and child health and family planning, community nutrition, disease prevention, and minor emergencies (Ministry of Health, 2016).

In Indonesia, there are 1,572 public hospitals (Ministry of Health, 2018a), providing secondary and tertiary care, are of four types: 1) Type D hospital (less than 50 beds with four specialists: an internist, an ob-gyn, a surgeon, and a paediatrician) provide basic secondary care at the district level, 2) Type C hospital (50-100 beds with more than four types of specialists) serve secondary and tertiary care for a larger district; 3) Type B hospital (between 100-400 beds with a variety of specialists) providing more advanced referral care at the provincial level, and 4) Type-A hospital (up to 1,500 beds) designed to provide top (national) referral care. Users of public health care facilities are charged based on the number of services they received (subsidized fees for services system). The user charges at health centres and third classroom of public hospitals are heavily subsidized (about 50-80% of the user fees are subsidized indirectly through publicly set fees).

2.3 Definition of Tuberculosis:

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* bacteria. Most of the tuberculosis germs attack the lungs but can also attack other organs (Department of Health, 2008). *M. tuberculosis* and seven very closely related mycobacterial species (*M. bovis, M. africanum, M. microti, M. caprae, M. pinnipedii, M. canetti and M. mungi*) together comprise what is known as the *M. tuberculosis* complex. Most, but not all, of these species have been found to cause disease in humans (CDC, 2013). There are two forms of tuberculosis namely pulmonary tuberculosis, which is the infectious form that accounted for 80% of all cases of tuberculosis, and extra-pulmonary tuberculosis, non-infectious, which can affect any part of the human body other than the lungs (lymph nodes, spine, pericardium, pleura, joints, genital urinary tract and abdomen) (Ait-Khalid N, et al., 2010 and Ministry of Health and Social Welfare; 2013).

2.4 Signs and symptoms:

Based on the Department of Health (Tuberculosis fact sheet Indonesia in 2017), Tuberculosis rarely begins with striking initial signs or symptoms. This disease will develop for weeks or even months before showing signs or symptoms; however, it might appear:

a. a cough that lasts for more than 2-3 weeks
b. phlegm production (cough with phlegm)
c. coughing up blood
d. fever
e. sweating at night
f. weight continues to decrease
g. lack of appetite
h. easily tired
i. hoarseness
j. chest always or sometimes hurts
k. swollen lymph nodes, especially in the neck

2.5 Treatment:

2.5.1 Active TB:

TB is treated with anti-tuberculosis drugs that are prescribed for at least 6 months, but in some cases, treatment may be prescribed for a longer period. Sometimes this treatment is referred to as TB chemotherapy (and is different from chemotherapy used for other conditions). The following medicines are generally used together to treat TB; Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide. Other drugs are sometimes used if TB bacterial strains are resistant to antibiotics or if one or more of the above drugs are not tolerated. Ensuring treatment and prevention makes the disease does not recur is important, and to prevent this, treatment must be carried out as prescribed according to instructions from the treating doctor for the right period without pauses, even though the patient feels his condition has improved (Department of Health, 2017).

2.5.2 Latent TB:

Treatment is usually done by giving one drug for 6-9 months. Isoniazid is the most commonly used type of drug, which is accompanied by vitamin B6. Vitamin B6 (pyridoxine) is given to prevent isoniazid side effects. Children should be given a shorter treatment time, but with two drugs at the same time (Department of Health, 2017).

2.6 Transmission:

Lung TB is transmitted by inhalation of liquid droplets released directly from the lungs of patients who contain TB bacteria when they cough while sneezing, laughing, and talking (Ait-Khalid N, et al., 2010). Depending on the environment, these tiny particles can remain suspended in the air for several hours. *M. tuberculosis* is transmitted through the air, not by surface contact. Transmission occurs when a person inhales a droplet nucleus containing *M. tuberculosis*, and the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs (CDC, 2013).

Infection occurs when a person inhales a droplet nucleus containing TB bacteria that reach the alveoli of the lungs. These bacteria are ingested by alveolar macrophages; the majority of these bacteria are destroyed or inhibited, but a small number may multiply intracellularly and are released when the macrophages die. If alive, these tubercle bacilli may spread by way of lymphatic channels or through the bloodstream to other organs (regional lymph nodes, the apex of the lung, kidneys, brain, and bone). This process of dissemination primes the immune system for a systemic response (CDC, 2013).

2.7 Testing and Diagnosis of Tuberculosis Infection and Disease:

Tuberculosis testing is used to identify, evaluate, and treat persons who are at high risk for latent tuberculosis infection (LTBI) or at high risk for developing TB disease when infected with Tuberculosis bacteria (*M. tuberculosis*). Selection of the suitable test for the detection of *M. tuberculosis* infection should be based on the reasons and the context for testing, test availability, and overall cost-effectiveness of testing (CDC, 2013). Currently, according to the Ministry of Health in Indonesia (2017), there are methods available for the detection of *M. tuberculosis* infection in Indonesia. The tests and diagnosis are:

TB diagnosis is done by:

1. See medical history
2. Physical examination

Specific tests include:

1. Chest x-ray
2. Sputum test (this test is taken to a specialized laboratory: the initial results will be returned in one or two days, but the final result might take several weeks).
3. medical biopsy, for example; lymph nodes.

Tests for diagnosing latent tuberculosis (hiding), including:

1. Tuberculin skin test (Mantoux test)
2. Test TB "QuantiFERON" - a blood test that can replace a skin test
3. Sometimes repeated tests have to be done to see if TB exposure has caused an infection

2.8 Screening for TB:

According to the Ministry of Health in Indonesia (2017) (Fig 2.1), the Screening process is needed when someone feels they have been exposed to someone with active TB, they should contact their local general practice doctor or the nearest TB service. Once a person is diagnosed with active TB, the person must follow a process to identify and contact people who have contact with him, for example, family or people from the same house, close friends, and colleagues.

People who are usually screened because they have the highest risk of having active TB are:

1. People who have just made contact with people who are diagnosed with active TB
2. Immigrants from countries where there are many people with TB
3. People whose immune systems are weak
4. People who work in the health sector
5. People who have visited many countries with TB and have lived there for 3 months or more

2.9 Prevention:

Referring to the Ministry of Health fact sheet in 2017, the main action to prevent TB in Indonesia is to reduce the source of bacteria by diagnosing people who have TB and make sure they are completely healed. By reducing the number of people infected with TB in the community, the likelihood of being exposed to TB is reduced. People who show suggestive symptoms should immediately conduct a medical examination to see an earlier diagnosis. Regarding the explanation above one of the ways to prevent TB infection and disease is the health education to the community is carried out by health workers who have the closest reach to the destination. There is also preventive medicine for TB, vaccines for TB (BCG vaccine) have been available for years, but only partially effective. This vaccine works most effectively in children. This vaccine is also recommended for young children who go to countries with high TB rates for 3 months or more (Ministry of Health, 2017).

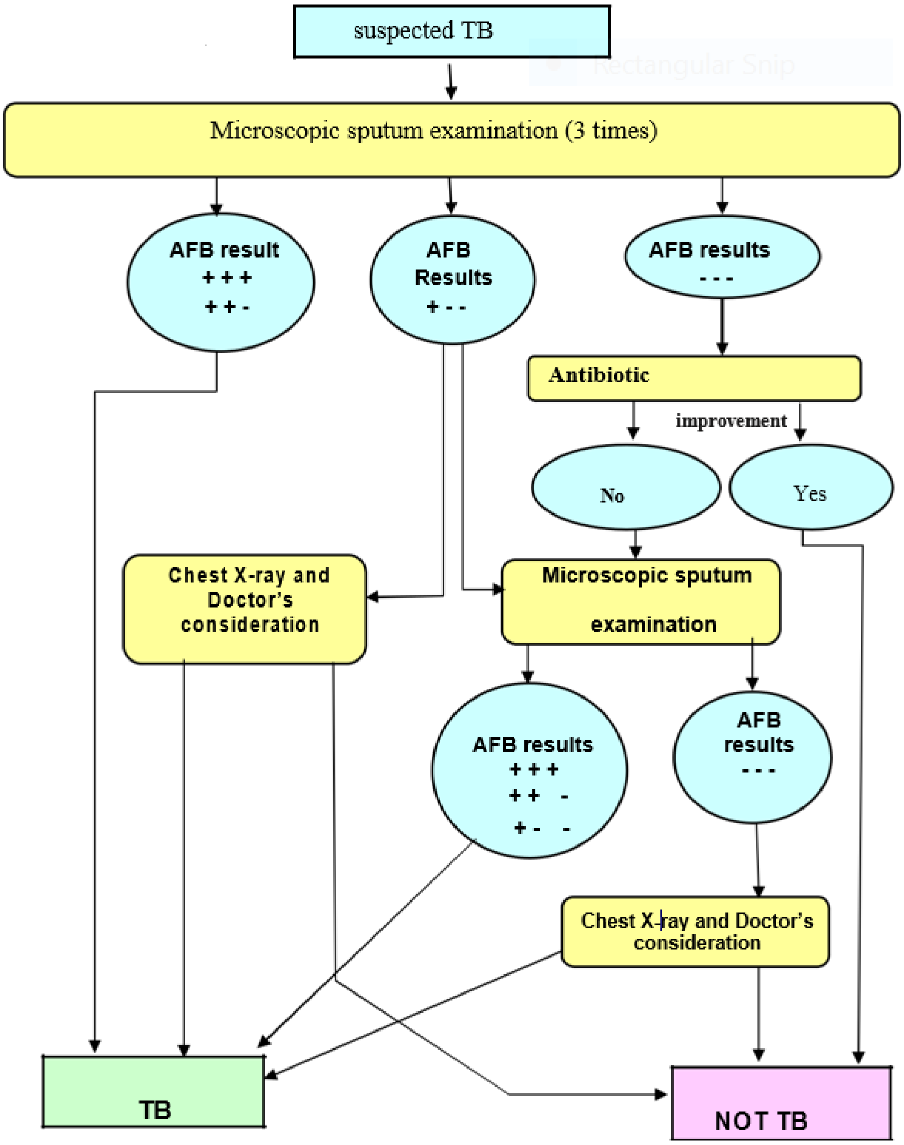


Fig 2.1 TB Diagnostic process.

CHAPTER THREE
CONCEPTUAL FRAMEWORK AND OPERATIONAL DEFINITION

3.1 Conceptual Framework

The conceptual framework in this study can be seen in (fig 3.1). It is divided into two main aspects which are demography and diagnostic methods.

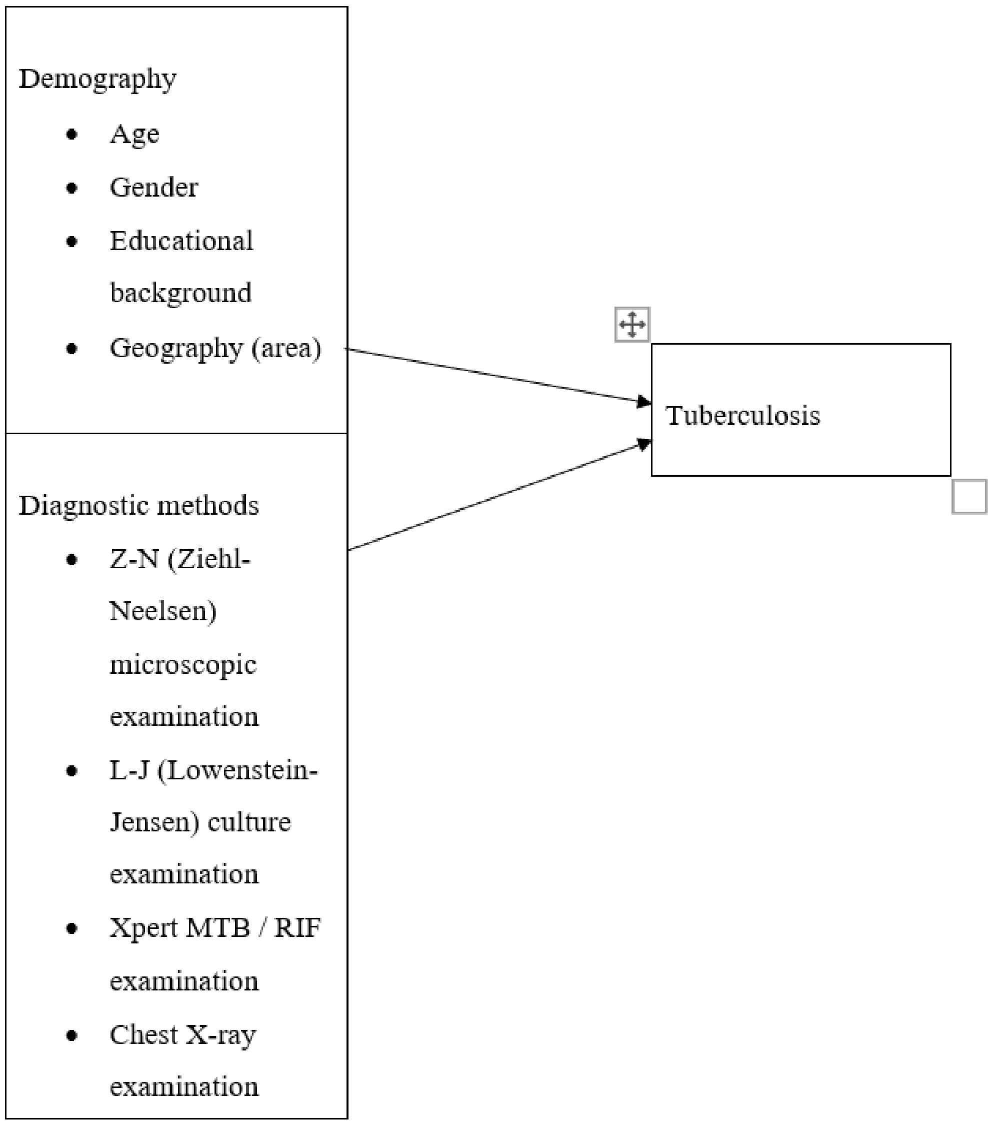


Figure 3.1 Conceptual framework of factors related to the prevalence of tuberculosis in Indonesia

Based on the conceptual framework, it is known that the independent variables used in this study are demographic factors (age, and place/area), and the diagnostic method used (ZN microscopic examination, LJ culture examination, Xpert MTB / RIF examination, and Chest X-ray examination) and Tuberculosis Prevalence is a dependent variable in this study.

3.2 Operational Definition

Operational definitions are definitions based on the properties of the variables to be observed and analyzed (Suryabrata, 2013). The operational definitions of the independent and dependent variables that will be observed in this study are as follows (Table 3.1)

Table 3.1 Operational Definition

Variable	Definition	Measuring Method	Measuring Instrument	Measurement Results	Measuring Scale
Dependent Variable					
Tuberculosis	Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* (Ministry of health, 2016).	Based on secondary data	Health ministry team examination results	Tuberculosis cases and not Tuberculosis cases	Nominal
Independent Variable					
Age	The number of years a life sample has passed based on the last birthday	Based on secondary data	Inspection cards filled out by the Ministry of Health team	≥ 15 years old`	Scale
Gender	Gender status of the respondent that can be known from the Resident Identity Card (KTP)	Based on secondary data	Inspection cards filled out by the Ministry of Health team	1. Male 2. Female	Nominal
Geographical Area	Research sample residence	Based on secondary data	Inspection cards filled out by the Ministry of Health team	Area : • Aceh (11) • North Sumatera (12) • West Sumatera (13) • Riau (14) • Jambi (15)	Nominal

				• South Sumatera (16) • Bengkulu (17) • Lampung (18) • Bangka Belitung (19) • Riau Island (21) • Jakarta (31) • West Java (32) • Central Java (33) • Yogyakarta (34) • East Java (35) • Banten (36) • Bali (51) • West Nusa Tenggara (52) • East Nusa Tenggara (53) • West Kalimantan (61) • Central Kalimantan (62) • South Kalimantan (63) • East Kalimantan (64) • North Sulawesi	

				(71) • Central Sulawesi (72) • South Sulawesi (73) • Southeast Sulawesi (74) • Gorontalo (75) • West Sulawesi (76) • Maluku (81) • North Maluku (82) • West Papua (91) • Papua (94)	
Z-N (Ziehl-Neelsen) microscopic examination	Diagnosis of TB by identifying acid-fast bacilli (AFB) in sputum that is not concentrated (direct smear) with Ziehl-Neelsen (ZN) staining (Dye C, Watt CJ, Bleed DM, Hosseini SM, and Raviglione MC, 2005).	Based on secondary data	lab examination results by the Ministry of Health team	Positive and Negative	Nominal
L-J	TB diagnosis uses	Based on	lab examination results by	Positive and Negative	Nominal

(Lowenstein-Jensen) culture examination	selective media for the cultivation and isolation of *Mycobacterium* species. Lowenstein-Jensen (LJ) medium is most widely used for tuberculosis culture (WHO,1998)	secondary data	the Ministry of Health team		
Xpert MTB / RIF examination	The Xpert MTB/RIF assay is an automated, cartridge-based nucleic acid amplification test that uses the multi-disease GeneXpert platform (WHO, 2016)	Based on secondary data	lab examination results by the Ministry of Health team	Positive and Negative	Nominal
Chest X-ray examination	CXR is an essential tool for early detection of tuberculosis (TB), and therefore fundamental to achieving the targets set out in WHO's End TB Strategy. CXR has high sensitivity, but limited specificity for detecting pulmonary TB. It is therefore especially suitable for TB screening and triaging. (WHO,	Based on secondary data	results of chest x-ray readings by the Ministry of Health team	Positive and Negative	Nominal

	2016)				

CHAPTER FOUR
RESEARCH METHODS

4.1 Study design

This study analysed the screening results of Indonesian people using various diagnostic approaches (sputum AFB, sputum culture, sputum genetic test, and chest x-ray) in the data set obtained from the Health Research and Development Agency of the Tuberculosis Unit, Indonesian Ministry of Health (HRDA-MoH). The primary study was carried out using a cross-sectional design which was carried out utilizing interviews, measurements, and chest X-ray examination, and sputum examination for all samples. Training and pilot tests, as well as cleaning, validation, and data analysis, had been completed.

4.2 Study setting

The data set represented Indonesia in all of the 34 provinces, which were classified into 3 large islands in Indonesia, Sumatra island, Java-Bali island, and other islands (eastern part of Indonesia). Indonesia as the largest archipelagic country in the world had two-thirds of its territory in the form of Indonesian oceans, namely 6.32 million square kilometres, 17,504 islands, and was one of the countries that had the longest coastline in the world after Canada. So, it was necessary to divide the time into 3 zones time in Indonesia, WIB (Western Indonesian Time), WITA (Central Indonesian Time), and WIT (Eastern Indonesian Time). There could be a time difference of up to 8 hours from one island to another. Besides, geographically, Indonesia was located between two continents (Asian Continent and Australian Continent) and two oceans (the Indian Ocean and the Pacific Ocean) which were the most dynamic regions, both economically and politically.

4.3 Study population

The population is a generalization area that consists of objects/subjects that have certain qualities and characteristics determined by researchers to be examined and then drawn conclusions (Sulistyaningsih, 2011). The population is an aggregate of individuals studied and can be formed as a sample frame to determine the target group (Ministry of Health, 2015). The population in this study is the population aged 15 years and over. The selection of participants followed the criteria below:

Inclusion criteria:

1. Individuals aged 15 years and over
2. Stay in the selected cluster for at least one month

Exclusion Criteria:

Individuals living in military barracks, diplomatic mission houses, hospitals, hotels, dormitories, temporary residences.

4.3.1 Sample size for research

Calculating the sample size with a certain level of accuracy requires several parameters, namely: estimation of TB prevalence (p), design effect (deff), the estimated number of people aged 15 years and above per cluster (M), the desired level of impression/inaccuracy (d), and estimated response (r). The estimated TB prevalence based on the 2004 National Tuberculosis Survey is 104 per 100,000 population (Ministry of Health, 2015 in Soemantri et al, 2005). Screening based on symptoms without chest X-ray may produce estimates below the actual prevalence at the time. Based on reports from ASEAN countries that have conducted surveys based on WHO-recommended methods (Cambodia (2002), Myanmar (2009), Philippines (2007) and Vietnam (2007)), the prevalence of positive smears observed from the survey turned out to be almost double or more than the TB notification rate in the survey year (Ministry of Health, 2015).

Referring to the geographical similarities and low HIV prevalence, the notification rate which is a conservative estimate of the positive smear prevalence is doubled. Notification in 2010 was 78 per 100,000 population so it was assumed a prevalence of 156 per 100,000 population. Parameters used to determine the number of samples :

- Prevalence (p) : 156 per 100.000 population,
- Proportion of population 15 years and over (a) : 71,1%,
- Confidence interval level 95% or α : 5%,
- Relative precision (d): 20% based on WHO recommendations,
- Minimum participation rate (r): 85% based on WHO recommendations,
- Cluster size (M): 500 considers the weekly operating cycle and WHO recommendations (400-800),

- Design effect (deff) : 1,5 (k> 0.6 estimated high cluster variations based on 2004 experience).

Calculation of the number of samples using the formulas below:

$$n_0 = \frac{1{,}96^2(1-p)}{d^2 p} \times deff \rightarrow n_0 = \frac{1{,}96^2(1-0{,}00156)}{0{,}2^2 \times 0{,}00156} \times 1,5 = 92.202,09$$

Because the study only includes adults as eligible populations, the number of samples is calculated as follows:

$$n_a = n_0 \times a \rightarrow n_a = 92.202,09 \times 0,711 = 65.555,69$$

An expected participation rate of 85%, the number of samples adjusted for the participation rate is calculated as follows:

$$n = \frac{n_a}{r} \rightarrow n = \frac{65.555,69}{0,85} = 77.124,34 \approx 78.000$$

Calculation of the number of clusters needed:

$$c = \frac{n}{M} \rightarrow c = \frac{78.000}{500} = 156$$

The number of samples is allocated to each region. The allocation method is a compromise of equal and proportional allocation with an allocation coefficient (γ) of 0.3

$$n_h^{(\gamma)} = n_h^{(E)}(1-\gamma) + n_h^{(P)}\gamma$$

The estimated number of participants aged 15 years and over based on the 2010 census (Central Statistics Agency 2010) was 82,155 in 156 clusters so that an estimated 527 participants per cluster were selected.

4.4 Types and Data Collection Methods

4.4.1 Types of data

The type of data in this study is secondary data obtained from the Health Research and Development Agency of the Tuberculosis Unit, Indonesian Ministry of Health. This data set represents Indonesia in 34 provinces. The data will be obtained from interviews using an integrated questionnaire, physical examination, and lab tests. The variables studied using the secondary data are demographic factors (age, and place/area), and the diagnostic method used (ZN microscopic examination, LJ culture examination, Xpert MTB / RIF examination, and Chest X-ray examination) as independent variables and Tuberculosis Prevalence is a dependent variable in this study.

4.4.2 Data collection method

Data collection in this research is by sending a complete proposal (background, objectives, theoretical framework, conceptual framework, operational definitions, methodology and a list of variables needed) to the Head of Health Research and Development Agency of the Ministry of Health of the Republic of Indonesia on Percetakan Negara Road No. 29, Central Jakarta and follow the next steps according to the data request flow.

4.4.3 Data collection instrument

Data collection tool from this study was by interviewing research samples using intergrated questionnaire and taking chest X-ray and sputum samples in 34 provinces covering 136 districts / cities in Indonesia consisting of Aceh, North Sumatra, West Sumatra, Riau, Jambi, South Sumatra, Bengkulu, Lampung, Bangka Belitung, Islands Riau, Jakarta, West Java, Central Java, Yogyakarta, East Java, Banten, Bali, West Nusa Taenggara, East Nusa Tenggara, West Kalimantan, Central Kalimantan, South Kalimantan, East Kalimantan, North Sulawesi, Central Sulawesi, South Sulawesi, Southeast Sulawesi , Gorontalo, West Sulawesi, Maluku, North Maluku, West Papua, Papua. This data set will be obtained from the Health Research and Development Agency, Ministry of Health of Indonesia, which will be studied and observed variables related to the scope of the study.

4.5 Data processing

Considering that not all variables from the data set will be used in this study, a selection of variables related to the title of this research will be conducted, the variables selected along with the use of the variables and their categorization will be elaborated, among others:

a. Age

   The number of years a life sample has passed based on the last birthday, In this study, the age range of the sample used will be 15 years and over.

b. Geographical area

   Where the research sample resides with a minimum stay is one month or more in the sampling area. This research will be conducted in 34 provinces in Indonesia.

c. ZN microscopic examination

   Diagnosis of TB by identifying acid-fast bacilli (AFB) in sputum that is not concentrated (direct smear) with Ziehl-Neelsen (ZN) staining (Dye C, Watt CJ, Bleed DM, Hosseini SM, and Raviglione MC, 2005). At this stage when positive results are obtained it will be followed by Xpert MTB / RIF examination to determine *Mycobacterium tuberculosis* (MTB) and resistance to rifampicin.

d. LJ culture examination

   TB diagnosis uses selective media for the cultivation and isolation of *Mycobacterium* species. Lowenstein-Jensen (LJ) medium is most widely used for tuberculosis culture (WHO,1998). Growing culture results will be examined with MPT64 to confirm bacterial species. if the MPT64 result is negative, then species confirmation is continued with niacin. Culture with MPT64 and Niacin negative will be determined as non-tuberculous mycobacteria (NTM).

e. Xpert MTB / RIF examination

The Xpert MTB/RIF assay is an automated, cartridge-based nucleic acid amplification test that uses the multi-disease GeneXpert platform (WHO, 2016). All sputum specimens will be examined microscopically, Xpert MTB / RIF, and culture.

f. Chest X-ray examination

All participants were asked to take a chest X-ray examination in the field, the results would indicate normal and abnormal lung or pleural parenchyma. The results of the reading are reread in the afternoon, if not normal, participants will be asked for sputum samples. The results of reading the chest thoracic photo are used to decide the participants who will have their sputum taken. The results of the central reading are used to decide the case definition.

This research uses secondary data, so the data processing is tabulating and checking missing data with the help of appropriate statistical computer software. The stages of editing, coding, and processing have been carried out by the Ministry of Health team. The researcher modifies the compute data by creating new variables to combine several existing variables, then recording certain variables that are in accordance with the operational research definition plan. The data cleaning stage is to see whether an error occurs or not by looking at the frequency distribution of each variable used in the study whether there is an empty section. If there is a missing value, then the data is not included in the data analysis.

4.6 Data Analysis and Presentation

4.6.1 Data analysis

Validated and merged data were transformed with SPSS version 22 and Stata software version 15.0. Categorical data were presented with counts and percentages. The prevalence of pulmonary TB in populations aged 15 years and over was calculated using TB cases as a numerator and populations aged 15 years and over as a denominator which is consistent with the WHO's global tuberculosis guidance (WHO, 2019). Variations across geographical areas and diagnostic approaches were expressed as prevalence with a 95% confidence interval (CI) using Clopper-Pearson Exact method.

4.6.2 Data presentation

The data that has been processed and analyzed in this study will be presented in the form of text, tables, pictures or graphs that are in accordance with existing data.

4.7 Ethical Consideration

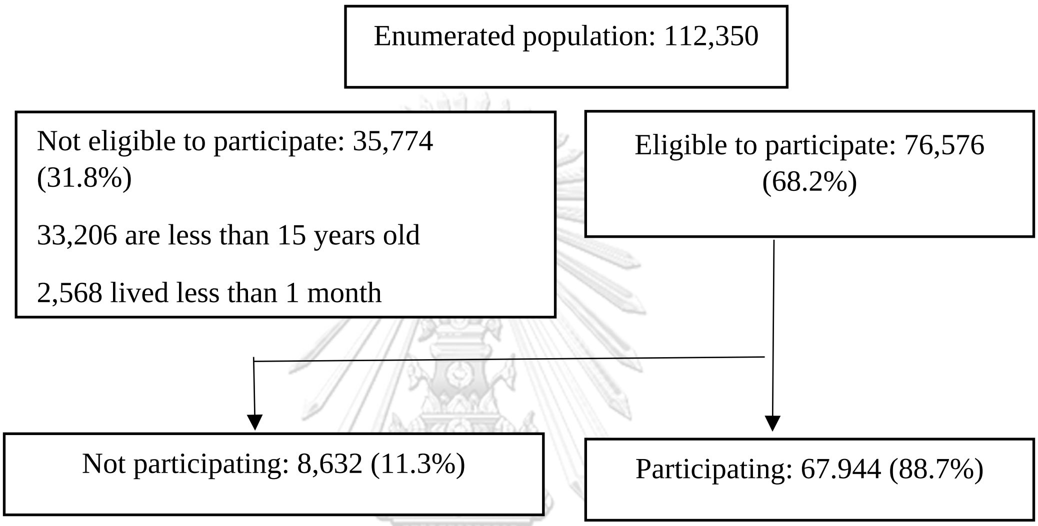
This was approved by the Health Research Ethics Committee of Faculty of Public Health Sriwijaya University (Ethical Approval No:301/UN9.1.10/KKE/2020) and Institutional Review Board of Chulalongkorn University (COA No. 1316/2020). This research using the ethical principles and guidelines for research involving human subjects (Belmont Report). Three core principles are identified and fulfilled: respect for persons (the participants' confidentiality is protected and treated with courtesy and respect and allowed for informed consent), beneficence (the research is undertaken by meant to contribute to the society and science with concern on securing the wellbeing of participants), and justice (this research treated the participants equally and fairly).

CHAPTER FIVE
RESEARCH RESULTS AND RESEARCH ANALYSIS

5.1 Research results

5.1.1 Population, eligible population and participants

The results of surveying along with the number of individuals participating in each stage can be seen in Figure 5.1



5.1.2 General demographic description

Located between the Indian and Pacific seas, Indonesia is the largest archipelago in the world. Indonesia consists of 17,491 islands, Indonesia has 34 provinces (province), including the Special Capital Region Jakarta. Province consists of districts (district) and municipality (city); districts and the city is further divided into districts, which are then divided into administrative villages (Ministry of Internal Affairs, 2019). The population of Indonesia is very diverse ethnically, culturally and linguistically. With a variety of different languages or dialects and ethnicities, the following is the presentation of population distribution that is eligible as participants according to demographic characteristics (Table 5.1).

Table 5.1 Distribution of eligible populations as participants according to demographic characteristics.

Characteristics	**Eligible**		**Non Eligible**		**Total**
	n	%	n	%	
Age group (years)					
0-4	0	0,0	10,063	100	10,063
5-9	0	0,0	11,294	100	11,294
10-14	0	0,0	11,846	100	11,846
15-24	16,982	95.0	903	5.0	17,885
25-34	17,760	96.3	692	3.7	18,452
35-44	16,107	97.0	501	3.0	16,608

45-54	12,677	97.8	291	2.2	12,968
55-64	7,410	98.3	128	1.7	7,538
65+	5,640	99.1	53	0.9	5,693
Gender					
Male	36,759	66.1	18,880	33.9	55,639
Female	39,817	70.2	16,894	29.8	56,711
Area classification					
Urban areas	37,865	69.6	16,532	30.4	54,398
Rural areas	38,711	66.8	19,242	33.2	57,952
Regions					
Sumatera	22,700	66.3	11,517	33.7	34,217
Java-Bali	31,049	71.6	12,292	28.4	43,341
others	22,827	65.6	11,965	34.4	34,792
Total	76,576	68.2	35,774	31.8	112,350

The proportion of the population that is eligible is more for female than for a male. In the Java-Bali region, there is a proportion of the eligible population more than other regions (Table 5.1). While the distribution of eligible populations and participants according to demographic characteristics is shown in table 5.2.

Table 5.2 Distribution of eligible populations and participants according to demographic characteristics.

Characteristics	**Eligible**	**Participants**		**Non-participants**	
	n	**n**	**%**	**n**	**%**
Age group (years)					
15-24	16,982	14,505	85.4	2,477	14.6
25-34	17,760	15,192	85.5	2,568	14.5
35-44	16,107	14,386	89.3	1,721	10.7
45-44	12,677	11,643	91.8	1,034	8.2
55-64	7,410	6,870	92.7	540	7.3
65+	5,640	5,348	94.8	292	5.2
Gender					
Male	36,759	31,632	86.1	5,127	13.9
Female	39,817	36,312	91.2	3,505	8.8
Area classification					
Urban areas	37,865	31,871	84.2	5,994	15.8
Rural areas	38,711	36,073	93.2	2,638	6.8
Regions					
Sumatera	22,700	19,739	87.0	2,961	13.0
Java-Bali	31,049	28,150	90.7	2,899	9.3
Others	22,827	20,055	87.9	2,772	12.1
Total	76,576	67,944	88.7	8,632	11.3

Table 5.2 shows that female population participation is higher than the male population. Participation increases with age. Based on the regional classification, population participation in rural areas is higher than in urban areas. The proportions of male and female participants did not differ according to age group, regional classification and region. The highest level of education in participants was elementary school graduates. The proportion of female participants who have never

attended school is higher than male, the proportion of male participants completing high school is higher than female (Table 5.3).

Table 5.3 Distribution of participants according to demographic characteristics.

Characteristics	Male		Female		Total	
	n	%	n	%	n	%
Age group (years)						
15-24	6,939	21.9	7,566	20.8	14,505	21.3
25-34	6,841	21.6	8,351	23.0	15,192	22.4
35-44	6,523	20.6	7,863	21.7	14,386	21.2
45-44	5,496	17.4	6,147	16.9	11,643	17.1
55-64	3,403	10.8	3,467	9.6	6,870	10.1
65+	2,430	7.7	2,918	8.0	5,348	7.9
Education						
Never attend school	1,595	5.0	3,560	9.8	5,155	7.6
Not / did not finish elementary school	3,632	11.5	4,678	12.9	8,310	12.2
Finished elementary school	8,375	26.5	9,618	26.5	17,993	26.5
Finished junior high school	7,024	22.2	7,544	20.8	14,568	21.5
Finished senior high school	8,858	28.0	8,210	22.6	17,068	25.1
Universities	2,148	6.8	2,702	7.4	4,850	7.1
Area classification						
Urban areas	14,810	46.8	17,061	47.0	31,871	46.9
Rural areas	16,822	53.2	19,251	53.0	36,073	53.1
Regions						
Sumatera	9,171	29.0	10,568	29.1	19,739	29.1
Java-Bali	13,034	41.2	15,116	41.6	28,150	41.4
Others	9,427	29.8	10,628	29.3	20,055	29.5
Total	31,632	100	36,312	100	67,944	100

5.2 Tuberculosis cases

There were 426 cases of tuberculosis in this study. Table 5.4 shows the breakdown of cases.

Table 5.4 TB cases based on team decisions with a distribution of examination results

	Tuberculosis cases	n	%
A	Smear positive		
	Positive culture and positive Xpert MTB/RIF	134	31.5
	Positive culture and negative Xpert MTB/RIF	7	1.6
	Culture not TB and positive Xpert MTB/RIF	24	5.6
	Total	165	38.7
B	Smear negative		
	Positive culture	188	44.1
	Positive culture not significant*, negative Xpert MTB/RIF and TB image on chest X-ray	55	12.9

Culture not TB, positive Xpert MTB/RIF, and TB image on Chest X-ray	17	4.0
Contamination culture, positive Xpert MTB/RIF, no chest X-ray (pregnant)	1	0.2
Total	261	61.3
TB cases total (A+B)	426	100

There was 1 case with a negative smear, contamination culture, positive Xpert MTB / RIF from pregnant women without a chest X-ray. Because of the contamination culture results and chest X-ray, the Xpert MTB / RIF results were the basis for these participants being included in TB cases.

5.3 Tuberculosis prevalence

The prevalence of pulmonary TB in populations aged 15 years and over is calculated using TB cases as a numerator and populations aged 15 years and over as a denominator. Prevalence is calculated per 100,000 population aged 15 years and over. Data were expressed as Prevalence rate and 95% CI. The estimated prevalence of TB cases is calculated per 100,000 population aged 15 years and over. The prevalence of TB can be seen in table 5.5.

Table 5.5 Estimated TB prevalence per 100,000 population aged 15 years and over.

Characteristics	**Estimation**	**SE**	**95%CI**	**RSE(%)**
Age group (years)				
15-24	360.8	61.5	254.3-494.7	17.0
25-34	753.4	110.3	561.8-995.0	14.6
35-44	713.8	105.5	527.4-941.0	14.8
45-54	835.5	127.9	608.9-1,108.3	15.3
55-64	1,029.5	169.7	734.1-1,398.5	16.5
65+	1,581.7	263.3	1,122,7-2,153.7	16.6
Total	**759.1**	**95.1**	**589.7-960.8**	**12.5**

The prevalence of tuberculosis is 759.1 (95% CI 589.7-960.8) per 100,000 population aged 15 years and over. Based on table 5.5, it can be seen that the prevalence of TB increases with age.

5.4 Tuberculosis prevalence according to demographic region

The islands of Indonesia are also known as the Indonesian Archipelago, this can refer to the islands that comprise the Indonesian state or to the geographical groups which include these islands. Indonesia is the largest archipelago in the world. Indonesia consists of 17,491 islands (Ministry of Internal Affairs, 2019). This research was conducted in 34 provinces in Indonesia. then, researchers will classify the results of the research into 3 large islands in Indonesia. The distribution of participants according to demographic characteristics can be seen in table 5.6.

Table 5.6 Distribution of participants according to demographic characteristics

Characteristics	Participant	
	n	**%**
Age group (years)		
15-24	14,505	85.4
25-34	15,192	85.5
35-44	14,386	89.3
45-54	11,643	91.8
55-64	6,870	92.7
65+	5,348	94.8
Gender		
Male	31,632	86.1
Female	36,312	91.2
Islands		
Sumatera	19,739	87.0
Java-Bali	28,150	90.7
Others	20,055	87.9
Total	**67,944**	**88.7**

Table 5.6 shows that female participate more highly than male, based on regional classification, population participation in Java-Bali is higher than in other islands.

Table 5.7 Distribution of participants according to gender among the regional classifications.

Characteristics	Male		Female		Total	
	n	%	n	%	n	%
Age group (years)						
15-24	6,939	21.9	7,566	20.8	14,505	21.3
25-34	6,841	21.6	8,351	23.0	15,192	22.4
35-44	6,523	20.6	7,863	21.7	14,386	21.2
45-54	5,496	17.4	6,147	16.9	11,643	17.1
55-64	3,403	10.8	3,467	9.6	6,870	10.1
65+	2,430	7.7	2,918	8.0	5,348	7.9
Islands						
Sumatera	9,171	29.0	10,568	29.1	19,739	29.1
Java-Bali	13,034	41.2	15,116	41.6	28,150	41.4
Others	9,427	29.8	10,628	29.3	20,055	29.5
Total	**31,632**	**100**	**36,312**	**100**	**67,944**	**100**

The table shows that the proportions of male and female participants did not differ according to age group, classification area and region. The prevalence of tuberculosis is 759.1 per 100,000 population. Based on table 5.8 it appears that the prevalence in urban areas is higher than in rural areas. The prevalence of positive TB is higher in Sumatra than in other regions with 913.1 (95%CI 696.7-1,176.7).

Table 5.8 Estimated TB prevalence per 100,000 population aged 15 years and over according to demographic characteristics

Characteristics	Estimated	SE	95% Cl	RSE (%)
Area classification				
Urban areas	845.8	94.4	678.2-1,047.7	11.2
Rural areas	674.2	92.2	511.9-873.6	13.7
Region				
Sumatra	913.1	122.7	696.7-1,176.7	13.4
Java-Bali	593.1	82.8	447.2-770.6	14.0
Others	842.1	116.4	634.7-1,091.8	13.8
Total	**759.1**	**95.1**	**589.7-960.8**	**12.5**

Tuberculosis prevalence in Indonesia is higher in urban areas than rural areas, and the Sumatra region is the highest prevalence of TB with 913.1 (95%CI 696.7-1,176.7).

5.5 Tuberculosis prevalence according to diagnostics methods

5.5.1 Chest X-ray examination

Table 5.9 Distribution of participants who took a chest X-ray

Characteristics	Participants	Chest X-ray	
	n	n	%
Age group (years)			
15-24	14,505	13,654	94.1
25-34	15,192	14,099	92.8
35-44	14,386	13,851	96.3
45-54	11,643	11,354	97.5
55-64	6,870	6,639	96.6
65+	5,348	4,739	88.6
Total	**67,944**	**64,336**	**94.4**

The proportion of participants aged 65 years and over who were photographed thorax is lower than other age groups. The proportion of male who is photographed thorax is higher than female.

Table 5.10 Distribution of participants according to screening results and gender

Screening	Male		Female		Total	
	n	%	n	%	n	%
Coughing ≥ 14 days or coughing up blood						
Yes	5,064	16.0	4,488	9.6	8,552	12.6
No	26,568	84.0	32,824	90.4	59,392	87.4
Chest X-ray						
Abnormal	6,353	20.1	4,849	13.4	11,202	16.5
Normal	24,331	76.9	28,805	79.3	53,136	78.2

No chest X-ray	948	3.0	2,658	7.3	3,606	5.3
Total	**31,632**	**100**	**36,312**	**100**	**67,944**	**100**

Table 5.11 Distribution of positive screened participants

Coughing ≥ 14 days or coughing up blood		**Chest X-ray result**	
		N	%
Yes	Normal	3,844	24.9
Yes	Abnormal	4,459	28.9
No	Abnormal	6,743	43.6
Yes	No chest X-ray	249	1.6
others		151	1.0
Total		15,446	100

Among participants who were screened positive, 44% had no symptoms of cough 14 days or more or coughing up blood. Tuberculosis prevalence according to Chest X-ray examination is 725.2 (95%CI 718.1-732.2) per 100,000 population.

5.5.2 Laboratorium results

5.5.2.1 Z-N (Ziehl-Neelsen) microscopic examination

Microscopic examination is used for diagnosis, monitoring, and defining the cure rate of treatment. Three sputum specimens must be collected and examined in two consecutive days (**spot-early morning-spot**) (Keflie and Ameni, 2014). Results of the microscopic examination in detail can be seen in table 5.12.

Table 5.12 Results of sputum microscopy for AFB

Sputum test results		**Early morning**						
		Negative	**Scanty**	**1+**	**2+**	**3+**	**NA**	**Total**
Spot	**Negative**	14,169	60	28	5	4	550	14,816
	Scanty	46	11	9	7	3	2	78
	1+	26	5	17	15	2	4	69
	2+	6	2	3	14	5	0	30
	3+	2	0	2	2	8	1	15
	NA	117	1	0	1	0	0	119
	Total	**14,366**	**79**	**59**	**44**	**22**	**557**	**15,127**

The proportion of non-availability of smears in the morning sputum is higher than the spot sputum. no visible difference in the proportion of high positive smears (1+, 2+, 3+) between early morning and spot sputum.

Table 5.13 Results of sputum smear examination

Sputum examination	Spot sputum		Morning sputum		Combination (spot sputum and morning sputum)	
	n	%	N	%	n	%
Sputum collected	15,126	100	14,619	100	15,141	100
Sputum checked	15,008	99.2	14,570	99.7	15,127	99.9
Positive	192	1.3	204	1.4		
2 positive	-	-	-	-	105	0.7
1 positive 1 negative	-	-	-	-	177	1.2
1 positive 1 NA	-	-	-	-	9	0.1
Negative	14,816	98.7	14,336	98.6		
2 negative	-	-	-	-	14,169	93.7
1 negative only	-	-	-	-	667	4.3
NA	118	0.8	49	0.3	14	0.1

Table 5.13 shows that there is no difference in smear results between spot sputum and morning sputum. Tuberculosis prevalence according to sputum smear examination is 256.5 (95%CI 210.1-302.9) per 100,000 population.

5.5.2.2 L-J (Lowenstein-Jensen) culture examination

The Löwenstein-Jensen media, better known as the LJ media, is a growth medium specifically used for the culture of *Mycobacterium* species, especially *Mycobacterium tuberculosis* (Elbir H, Abdel-Muhsin AM, Babiker A, 2008). Culture examination results in the spot sputum and morning sputum can be seen in table 5.14.

Table 5.14 Results of L-J culture examination (spot and early morning sputum).

Culture	Spot sputum		Morning sputum		Total	
	n	%	n	%	n	%
Sputum collected	4,534	100	14,619	100	15,141	100
Sputum checked	4,433	97.8	14,569	99.7	15,109	99.8
Research results						
MTB	133	3.0	358	2.5	400	2.7
NTM	79	1.8	334	2.3	405	2.7

Contamination	47	1.1	431	3.0	339	2.2
Negative	4,174	94.1	13,441	92.2	13,965	92.4
NA	101	2.2	50	0.4	32	0.2

This table shows the results of spot sputum culture examination for contamination by 1.1% while the results of morning sputum culture examination for contamination by 3%.

Table 5.15 Compliance of sputum culture examination results (spot and morning sputum)

	Culture	**Morning sputum**					
		Negative	**MTB**	**NTM**	**Contamination**	**NA**	**Total**
Spot sputum	**Negative**	3,772	41	104	87	170	4,174
	MTB	39	89	0	3	2	133
	NTM	59	0	14	5	1	79
	Contamination	34	2	1	8	2	47
	NA	85	1	3	3	13	105
	Total	3,989	133	122	106	188	4,538

From 106 participants with contaminated sputum culture results, 95 (89.6%) had spot sputum results and from 47 participants with contaminated spot sputum culture, 37 (78.7%) had results on sputum morning. Among negative culture results, there were 41 with MTB positive from morning culture and of the negative morning cultures, there were 39 with a positive spot culture of MTB.

Table 5.16 Estimation of TB prevalence according to culture examination

Culture examination results	**Estimation**	**95% CI**
Positive	545	509.5-583
Negative	945.5	941.7-949

Tuberculosis prevalence according to culture examination is 545 (95%CI 509.5-583) per 100,000 population.

5.5.2.3 Xpert MTB / RIF examination

Xpert MTB/RIF for detecting TB is highly specific (99%), and results are false positives possibly related to detection by Xpert MTB / RIF of the dead *M. tuberculosis* bacillus will not be detected by culture. The specificity of Xpert MTB / RIF in detecting rifampicin resistance is very high (98%) (World Health Organization (WHO), 2014). The Xpert MTB/RIF examination result can be seen in table 5.17 and 5.18.

Table 5.17 The results of Xpert MTB

Examination results	Xpert MTB
Positive	213
Negative	407
Not detected	22
Error/invalid	4
Total	646

Table 5.18 The results of Xpert RIF

Examination results	Xpert RIF
Sensitive	184
Resistance	19
Negative	1
Not detected	1
Indeterminate	10
Total	215

According to table 5.17 and 5.18, X-pert MTB/RIF result indicates that there was 213 *M. tuberculosis* (MTB) detected, 184 MTB was detected and was not resistant to rifampicin (that is, it is rifampicin susceptible), and 19 MTB was detected, and it was resistant to rifampicin. A small proportion of tests may result in an error or invalid result; these tests need to be repeated. TB prevalence according to Xpert TB examination is 894.9 (95%CI 848.7-928.2) per 100,000.

5.5.3 Compatibility between smear results and culture results

Table 5.19 Smear and culture results in spot sputum

Spot sputum		Culture					
		Negative	MTB(+)	NTM	Contamination	NA	Total
Sme	Negative	4,148	96	78	46	0	4,368

Scanty	21	9	0	0	0	30
1+	5	19	1	0	0	25
2+	0	8	0	0	0	8
3+	0	1	0	1	0	2
NA	0	0	0	0	101	101
Total	**4,174**	**133**	**79**	**47**	**101**	**4,534**

Microscopic examination of spot sputum obtained 65 (1.4%) positive, including 35 positive non-scanty smears (1+, 2+, 3+). There were 28 (83%) positive culture of MTB in participants with positive smears that were not scanty. From the negative smear results, there were 2.2% positive cultures of MTB. The proportion of negative smears among participants of positive culture MTB was 72.2%.

Table 5.20 Smear and culture results in morning sputum

Morning sputum		**Culture**					
		Negative	**MTB(+)**	**NTM**	**Contamination**	**NA**	**Total**
Smear	**Negative**	13,367	247	330	421	1	14,366
	Scanty	54	17	6	2	0	79
	1+	15	35	3	6	0	59
	2+	3	39	0	2	0	44
	3+	2	20	0	0	0	22
	NA	0	0	0	0	49	49
	Total	**13,411**	**358**	**339**	**431**	**50**	**14,619**

Microscopic examination of morning sputum obtained 65 (1.4%) positive, including 35 positive non-scanty smears. From 125 positive non-scanty smears, there were 92 (73.6%) with a positive culture of MTB. A negative smear result obtained 1.7% of a positive culture of MTB. The proportion of negative smears among MTB positive culture participants was 69.0%.

5.5.4 Comparison of smear, Xpert MTB / RIF, and culture results

Table 5.21 Examination results of smear, Xpert MTB/RIF, and Culture

Examination results			**Culture**					
			Negative	**MTB**	**NTM**	**Contamination**	**NA**	**Total**
Smear	**Positive**	**Xpert MTB/RIF**						
		Positive	18	133	1	5	0	**157**
		Negative	105	5	13	1	0	**124**
		NA	6	3	0	9	1	**10**
		Total	129	141	14	6	1	**291**
	Negative	**Xpert MTB/RIF**						
		Positive			10	13		**23**
		Negative			370	299		**669**
		NA	13,836	259	11	21	17	**14,144**
		Total	**13,836**	**259**	**391**	**333**	**17**	**14,836**

A total of 291 participants with positive smears, including 105 (36%) results with Xpert MTB / RIF and negative cultures. Of the 291 participants with positive smear laboratory results, the presence of MTB was not proven by culture or Xpert MTB / RIF in 126 (43.3%) participants.

5.5.5 Comparison of screening and laboratory results

Table 5.22 shows the distribution of TB cases based on the results of symptom screening and chest X-ray. The "symptoms" in this table are coughing for 14 days or more or coughing up blood. "Abnormal chest X-ray" is the finding of pulmonary or pleural parenchymal abnormalities.

Table 5.22 Number of TB cases based on screening results and laboratory results

Screening	Positive smear	Negative smear with positive bacteriology	Positive bacteriology
Symptoms (yes) and normal chest X-ray	5	16	21
Symptoms (yes) and abnormal chest X-ray	109	111	220
Symptoms (no) and abnormal chest X-ray	49	132	181
Symptoms (yes) and no chest X-ray	2	1	3
Others	0	1	1
Total	**165**	**261**	**426**

There was an abnormal chest X-ray in 29.7% positive smears and 42.5% positive bacteriology.

5.6 Tuberculosis prevalence according to the demographic region and diagnostics methods

Table 5.23 Distribution of TB cases according to demographic characteristics

Characteristics	Positive smear		Negative smear with positive bacteriology		Negative		NA		Total	
	n	%	n	%	n	%	n	%	n	%
Age group (year)										
15-24	19	11.5	25	9.6	14,413	21.5	48	14.3	14,505	21.3
25-34	34	20.6	58	22.2	15,052	22.4	48	14.3	15,192	22.4
35-44	35	21.2	47	18.0	14,259	21.2	45	13.4	14,386	21.2
45-54	30	18.2	52	19.9	11,509	17.1	52	15.5	11,643	17.1
55-64	21	12.7	37	14.2	6,766	10.1	46	13.8	6,870	10.1
65+	26	15.8	42	16.1	5,184	7.7	96	28.7	5,348	7.9
Gender										
Male	120	72.7	169	64.7	31,194	46.4	149	44.5	31,632	46.6
Female	45	27.3	92	35.3	35,989	53.6	186	55.5	36,312	53.4
Area classification										
Urban areas	88	53.3	140	53.6	31,497	46.9	146	43.6	31,871	46.9
Rural areas	77	46.7	121	46.4	35,686	53.1	189	56.4	36,073	53.1
Region										
Sumatra	55	33.3	88	33.7	19,381	28.9	215	64.2	19,739	28.1

Java-Bali	59	35.8	81	31.0	27,920	41.5	90	26.9	28,150	41.4
others	51	30.9	92	35.3	19,882	29.6	30	9.0	20,055	29.5
Total	**165**	**100**	**261**	**100**	**67,183**	**100**	**335**	**100**	**67,944**	**100**

5.6.1 Tuberculosis prevalence according to the demographic region and Chest Xray examination

Table 5.24 shows that the prevalence of TB with positive Chest Xray is higher at the age of 15-24 years, higher in male than female, and higher in rural areas. The prevalence is higher in the eastern region in Indonesia than in Sumatra and Java-Bali.

Table 5.24 Estimation of TB prevalence on positive Chest X-Ray results per 100,000 population aged 15 years and over according to demographic characteristics

Characteristics	Estimation	95%CI
Age group (years)		
15-24	783.8	741.2-828.7
25-34	109.1	104.3-114.2
35-44	142.9	137.3-148.7
45-54	205.7	198.5-213.2
55-64	284.7	274.2-295.5
65+	373.7	360.9-386.8
Gender		
Male	200.8	196.4-205.3
Female	133.5	130.1-137.1
Area classification		
Urban areas	150.1	146.2-154
Rural areas	177.9	174-181.9
Region		
Sumatra	159.2	154.1-164.3
Java-Bali	152.1	147.9-156.3
Others	864	809-921.4

5.6.2 Tuberculosis prevalence according to the demographic region and Smear examination

Table 5.25 shows that the prevalence of TB with a positive smear is higher in male than female. The prevalence increases with age, urban areas are higher than rural areas, and Sumatra is higher than in other regions.

Table 5.25 Estimation of TB prevalence on positive Smear results per 100,000 population aged 15 years and over according to demographic characteristics

Characteristics	Estimation	95%CI
Age group (years)		
15-24	137.5	77.3-197.8
25-34	239.9	155.5-324.4
35-44	265.1	170.7-359.4
45-54	271.5	166.3-376.7
55-64	318.6	174.1-463.1

65+	527.6	292.0-763.2
Gender		
Male	392.5	314.5-470.5
Female	131.0	87.6-174.4
Area classification		
Urban areas	282.2	219.6-344.7
Rural areas	231.4	163.3-299.5
Region		
Sumatra	307.4	208.3-406.5
Java-Bali	216.6	146.5-286.8
Others	259.9	184.2-335.6

5.6.3 Tuberculosis prevalence according to the demographic region and Culture examination

Table 5.26, shows that the prevalence of TB with positive Culture is higher in male than female, and higher in urban areas. The prevalence is higher in the eastern region in Indonesia than in Sumatra and Java-Bali.

Table 5.26 Estimation of TB prevalence on positive Culture results per 100,000 population aged 15 years and over according to demographic characteristics

Characteristics	**Estimation**	**95%CI**
Age group (years)		
15-24	414.5	330.7-518.3
25-34	561.4	477-659.7
35-44	584.7	503.8-677.5
45-54	479.7	408.9-561.8
55-64	529.6	446.5-627.2
65+	678.9	583.6-788.6
Gender		
Male	607.9	558.6-661.2
Female	463	414.2-517.3
Area classification		
Urban areas	736.6	673.8-804.7
Rural areas	408.8	369-452.7
Region		
Sumatra	635.9	564.9-715.1
Java-Bali	487.9	433.6-548.6
Others	2,129.8	1,664-2,735.6

5.6.4 Tuberculosis prevalence according to the demographic region and Xpert TB examination

Table 5.27 shows that the prevalence of TB with positive Xpert TB is higher in male than the female with a slight difference, and higher in urban areas. The prevalence is higher in the eastern region in Indonesia than in Sumatra and Java-Bali

Table 5.27 Estimation of TB prevalence on positive Xpert TB results per 100,000 population aged 15 years and over according to demographic characteristics

Characteristics	Estimation	95%CI
Age group (years)		
15-24	851.8	659.6-944.6
25-34	893.6	766.1-955.6
35-44	933.3	809.7-978.7
45-54	891.3	761.4-954.6
55-64	909.1	748.6-971.1
65+	875	729.5-947.8
Gender		
Male	896.9	839.9-935.2
Female	890.4	794.4-944.7
Area classification		
Urban areas	912	847.3-950.8
Rural areas	876.1	800.7-925.6
Region		
Sumatra	875	775.4-934.2
Java-Bali	838.7	748.4-900.8
Others	941.2	663.6-992.3

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CHAPTER SIX
DISCUSSION

6.1 Population, eligible population and participants

The target population in this study is the population aged 15 years and over. The eligible population is people aged 15 years and over who have lived continuously at the study site for at least one month. The target population and the eligible population are not statistically different and therefore no weighing is required.

The participation rate in this study (88.7%) shows that the results of the study can be generalized to represent the national (Indonesia) and regional (Sumatra, Java-Bali, others) levels (Ministry of Health of Indonesia, 2015). The participation rate of the productive age group (15-44 years) is lower than the older age group. This condition is in accordance with the prevalence results in Myanmar (Ministry of Health of Myanmar., 2010) and Cambodia (Mao et al., 2014). It is assumed that the young age group has higher mobility. The participation rate of male is lower than female, especially at a young age. This may be because more male work outside their residence area. Participation in rural areas is higher than in urban areas, possibly because members of the community in urban areas have higher mobility, especially in the productive age group.

6.2 Demographic characteristics

Indonesia as the largest archipelagic country in the world has two-thirds of its territory in the form of Indonesian oceans, namely 6.32 million square kilometres, 17,504 islands and is one of the countries that has the second-longest coastline in the world after Canada which is 99,093 square kilometres (Pudjiastuti., 2016). so it is necessary to divide the time into 3 zones time in Indonesia, WIB (Western Indonesian Time), WITA (Central Indonesian Time) and WIT (Eastern Indonesian Time). There can be a time difference of up to 8 hours from one island to another. In addition, geographically, Indonesia is located between two continents (Asian Continent and Australian Continent) and two oceans (the Indian Ocean and the Pacific Ocean) which are the most dynamic regions, both economically and politically. This strategic geographical location makes Indonesia both superior and highly dependent on the marine (Soemarmi et al., 2019).

Apart from the comparative advantage based on geographical location, the potential of human resources needs to be considered. Due to limited transportation facilities caused by the location between islands which are quite far from one another, the limited number of health workers, health facilities, and medical equipment can be a significant problem for Indonesia. The 3 major islands in this study (Sumatra, Java-Bali, and others) showed that the participation of female was higher than male. This may be because male prefer to work more. Based on the region classification, community participation in the Java-Bali island region is higher than in other islands. This may be due to the large number of people living on the island of Java-Bali compared to the population living in the eastern part of Indonesia.

Tuberculosis prevalence in Indonesia is higher in urban areas than rural areas, and the Sumatra region is the highest prevalence of TB with 913.1 (95%CI 696.7-1,176.7). This can occur because there is more access to health services in the islands of Sumatra and Java, but is slightly different for island areas in central and eastern Indonesia. This happened because the two islands were still underdeveloped areas.

6.3 Chest X-ray examination

The proportion of participants aged 65 years and over who underwent chest X-ray was lower than younger ages. Most of the reason is that they are unable to visit the study sites because of illness, disability, or unable to walk. The proportion of female participants who underwent chest X-rays was lower than the male because some pregnant women did not have chest X-rays.

There were 26.1% of participants who went to health personnel of all participants who showed positive screening symptoms. TB cases obtained from positive screening were 245 (57.5%). Symptom-based case finding has not been optimal. The passive TB case detection that has been carried out so far may also have contributed to the delay in TB diagnosis and treatment. The limitations of case finding or symptom detection tools and access to health services need to be improved.

Among participants who were screened positive, 44% had no symptoms of cough 14 days or more or coughing up blood. Tuberculosis prevalence according to Chest X-ray examination is 725.2 (95%CI 718.1-732.2) per 100,000 population. The use of chest X-ray increased the number of asymptomatic TB cases by 181 (73.9% of symptomatic cases). If the Chest X-ray was not used in screening, this study would have lost 42.5% of cases. This means that the use of chest X-rays can improve case finding. Intensive case finding needs to be supported by all levels of society, including communities and community organizations that care about TB.

6.4 Laboratory examination

Contamination in morning sputum (3%) was higher than spot sputum (1.1%). This difference is suspected because when removing the sputum spots, the participants were accompanied by laboratory staff, while the issuance of morning sputum in their respective homes was unaccompanied.

Comparison of the results of microscopic examination and culture examination showed high specimens with positive smears but negative cultures. On the spot sputum, there were 65 specimens with positive smears, 26 (40%) of them with negative cultures. In the morning sputum, there were 204 specimens with positive smears, 74 (36%) of them with negative cultures. When combined with the Xpert MTB / RIF results on specimens with positive smears, 36% were cultured and Xpert MTB / RIF negative. *Mycobacterium tuberculosis* was identified only in 165 (57%) of the 291 participants with a positive smear. The high number of positive smears that are not TB can be caused by NTM infection or NTM contamination.

The accuracy of TB diagnosis is reduced when only microscopic examination is used. Other additional accurate examinations are needed to enhance the quality of the microscopic examination. Xpert MTB / RIF examination is proven to reduce false-positive results. Since this study was conducted in a community, further research to see this trend in routine health services is needed to update the TB diagnostic algorithm. Tuberculosis prevalence according to sputum smear examination, culture examination and Xpert MTB/RIF examination are 256.5 (95%CI 210.1-302.9), 545.0 (95%CI 509.5-583.0) and 894.9 (95%CI 848.7-928.2) per 100,000 population respectively.

6.5 Tuberculosis prevalence

The prevalence of TB in the population aged 15 years and over is 759.1 per 100,000. The prevalence of TB was higher in the male group (prevalence of positive TB smear 393 per 100,000 and TB with bacteriological confirmation 1,082 per 100,000) than female (prevalence of positive TB smear 131 per 100,000 and TB with bacteriological confirmation 461 per 100,000). This result is consistent with other countries that show a higher prevalence in male than female (Kebede et al., 2014; Ministry of Health of Myanmar 2010; Mao et al., 2014). This is probably because a male is more exposed to TB risk factors.

The highest TB prevalence rate is in the old age group (55 years and over). When viewed from the absolute burden of TB, the rate is still very high among the productive age groups, this shows that TB transmission is still very high in the community. The prevalence of TB with positive Chest Xray is higher at the age of 15-24 years, higher in male than female, and higher in rural areas. The prevalence is higher in the eastern region in Indonesia than in Sumatra and Java-Bali. Apart from the possibility that the participants in these areas are more frequently exposed to TB germs and TB risk factors, this may be because the area is still underdeveloped so that lack of education can be one of the determining factors.

The prevalence of TB with a positive smear is higher in male than female. The prevalence increases with age, urban areas are higher than rural areas, and Sumatra is higher than in other regions. Generally in urban areas, the participation rate is relatively low although the TB prevalence in urban areas is not lower than in rural areas, the low participation rate can make the estimation of the interval from urban prevalence to be wide. The high prevalence rate of TB in the island of Sumatra could be caused by the density and a large number of cities and districts on the island, which resulted in more people being directly exposed to TB germs and TB sufferers. This could also be caused by the rural geographical location, making it difficult to send samples.

The prevalence of TB with positive culture is higher in male than female, and higher in urban areas. The prevalence is higher in the eastern region in Indonesia than in Sumatra and Java-Bali. This is because the central and eastern regions of Indonesia are still remote and underdeveloped areas, so there may be many TB risk factors and the lack of availability of access to health services that affect the handling and prevention of TB in these areas. The high number of non-TB positive smears shows that a more accurate but simple method of diagnosis such as Xpert MTB / RIF is needed to reduce false-positive rates and unnecessary treatment. The prevalence of TB with positive Xpert TB is higher in male than the female with a slight difference, and higher in urban areas. The prevalence is higher in the eastern region in Indonesia than in Sumatra and Java-Bali.

CHAPTER SEVEN
CONCLUSIONS AND RECOMMENDATIONS

7.1 Conclusions

The prevalence of pulmonary TB in Indonesia with bacteriological confirmation is 759.1 (95%CI 589.7-960.8) per 100,000 population aged 15 years and over. TB prevalence on positive Chest X-Ray results is 725.2 (95%CI 718.1-732.2) per 100,000 population aged 15 years, The prevalence of pulmonary TB with smear examination is 256.5 (95%CI 210.1-302.9) per 100,000 population aged 15 years and over, the prevalence of pulmonary TB with culture examination is 545.0 (95%CI 509.5-583.0) per 100,000 population aged 15 years and over, and the prevalence of pulmonary TB with Xpert MTB / RIF examination is 894.9 (95%CI 848.7-928.2) per 100,000 population aged 15 years and over.

Tuberculosis prevalence in Indonesia is higher in urban areas than rural areas, and the Sumatra region is the highest prevalence of TB with 913.1 (95%CI 696.7-1,176.7) per 100,000 population aged 15 years and over, while Java-Bali and other areas are 593.1 (95%CI 447.2-770.6) and 842.1 (95%CI 634.7-1,091.8) per 100,000 population respectively. The prevalence of pulmonary TB based on Chest X-ray results in the island of Sumatra, Java-Bali, and other areas are 159.2 (95%CI 154.1-164.3), 152.1 (95%CI 147.9-156.3) and 864.0 (95%CI 809.0-921.4) per 100,000 population aged 15 years and over. The prevalence of positive smear pulmonary TB in the island of Sumatra, Java-Bali, and other island area is 307.4 (95%CI 208.3-406.5), 216.6 (95%CI 146.5-286.8), and 259.9 (95%CI 184.2-335.6) per 100,000 population aged 15 years and over. The prevalence of pulmonary tuberculosis based on culture examination in the island of Sumatra, Java-Bali, and other island areas is 635.9 (95%CI 564.9-715.1), 487.9 (95%CI 433.6-548.6), and 2,129.8 (95%CI 1,664.0-2,735.6) per 100,000 population aged 15 years and over. The prevalence of pulmonary TB based on Xpert MTB / RIF examinations in the island of Sumatra, Java-Bali and other island areas is 875.0 (95%CI 775.4-934.2), 838.7 (95%CI 748.4-900.8), and 941.2 (95%CI 663.6-992.3) per 100,000 population aged 15 years and over.

7.2 Recommendations

1. TB control should be a national priority because of the high burden it causes.
2. Improve TB case management in reducing transmission and effectiveness of treatment through:

   a. Early detection of TB case detection with a more accurate method

   b. Improve the quality and quantity of health services and human resources for TB services
3. The use of the Chest X-ray machine has been shown to contribute to significant case finding of those who do not show the main symptoms of TB. The use of Chest X-rays as a screening tool is important. It is necessary to allocate medical devices that are evenly distributed to every region in Indonesia.
4. TB treatment coverage is still low, so innovative efforts are needed to increase access to health services.

To reduce geographic problems, the number of standardized laboratories must be increased so that they can be reached by the public.

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