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DEVELOPING VSEIR MODEL WITH THE VACCINATION TO REDUCE THE SPREAD OF TUBERCULOSIS DISEASE IN NORTH SUMATERA

(PENGEMBANGAN MODEL VSEIR DENGAN PENGARUH VAKSINASI UNTUK MENGURANGI PENYEBARAN PENYAKIT TB DI SUMATERA UTARA)

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ABSTRACT

This study aims to build a new model of the spread of pulmonary tuberculosis (TB) in order to reduce the level of distribution, with the added effect of vaccination models susceptible exposed to infection and recovery (VSIR) who had previously built up to be a model VSEIR. To test the validity of this model will be proven stability analysis. Analysis of both models is conducted using linearization method by studying the nature of equilibrium points. Simulation for models using derive parameter values in an attempt to study the spread of dengue viruses in North Sumatera. The research also aims to find out the value of Reproductive number R_0 over the total of the Tuberculosis cases reporting in North Sumatera. Furthermore, a comparison between the real data and the numerical solution using the fourth order Runge-Kutta method (RK4). To overcome the spread will be tested in the analysis of optimal singular control over this VSIR and Susceptible Exposed Infected and Recovery (SEIR) models of Tuberculosis, finally, we also proof the optimal singular control for Vaccination Susceptible Exposed Infected and Recovery (VSEIR) model.

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Praise the presence of Almighty God, the final report of the research competing with the title: The modified of Vaccination Susceptible Exposed Infected Recovery model with vaccination influence to reduce the spread of Tuberculosis disease in North Sumatra can be resolved with the cooperation of the chairman and two members of the State University of Medan (UNIMED)..

The contents of this progress report, among others, talked about models of development schemes Vaccination, Susceptible, Exposed, Infected, and Recovery (VSEIR) for Tuberculosis. It also analysing the stability of the equilibrium point and the determining eigenvalues, reproductive Numbers. For control the vaccination and treatment schedules in analysis, we proof the optimal of singular control of vaccination, susceptible, infected, and Recovery (VSIR), susceptible, exposed, infected, and Recovery (SEIR) as well VSEIR, respectively. Outcomes-outcomes are also shown to support this research. We also write a future plan for this research.

With the writing of this report, is expected to enhance the readers' insight and exploratory research of this competition. We need to convey to the readers of this research has been funded by the Higher Education with No. No. 062/UN33.8/LL/2014 for a period of two years. We always provide the best for the nation and the readers.

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CHAPTER I
INTRODUCTION

1.1 Background

Tuberculosis (TB) is a bacterial disease acquired through air bone infection. Mycobacterium tuberculosis (MTB) is the causative agent of tuberculosis. TB disease can affect anyone (old, young, men, women, poor, or rich) and anywhere. TB disease is usually transmitted through contaminated air with Mycobacterium tuberculosis bacteria that are released during coughing TB patients, and in children the source of infection is generally derived from adult TB patients. These bacteria often enter and when accumulated in the lungs will breed a lot (especially in people with a low immune system), and can spread through the blood vessels or lymph nodes. That is why TB infection can infect virtually all body organs such as the lungs, brain, kidneys, gastrointestinal tract, bone, lymph nodes, etc., although the organs most commonly affected are the lungs [1]. Each year, Indonesia increased by a quarter of a million new TB cases and approximately 140,000 deaths occur each year due to tuberculosis. In fact, Indonesia is the third largest country with the problem of tuberculosis in the world [1]. According to the World Health Organization, one –third the world's population is infected, either latently or actively with tuberculosis [2].

During the year 2010, around 73.8 percent of TB patients are in North Sumatra. Based on a survey of these, Medan city is the largest number of sufferers. In general, the detection rate of TB case increased in North Sumatra. According to the North Sumatra Department of Health in 2005, we estimated that at 15,517 cases of TB sufferers and in 2010 as many as 15,614 TB-positive people in North Sumatra, while based on the estimated, it amount to 21 148 people. Based on data from the Department of Health in 2010 there are six districts/ cities in North Sumatra in 2010 with the highest number of patients based on the population in Medan around 2,397 patients, Siantar around 288 patients, Binjai around 260 patients, Tanjung Balai around 150 patients, Tebing Tinggi around 145 patients and Deli Serdang around 1,554 patients [3].

Immunization is considered important because it has some benefits for toddlers, such as preventing the spread of Tuberculosis. BCG immunization was given 1 month of age giving one the benefit prevent transmission of tuberculosis (TB) are heavy. "If the baby is not complete immunized under the age of one year as BCG has not given, it must be done if the test maontoux baby five months of age or older. This test is to determine whether the baby is negatively affected by TB. If the test result is negative, it can only be given BCG immunization [1].

Despite some successes associated with the use of BCG vaccine and some TB treatment therapies, this pandemic has continued to increase and has led to a growing consensus that new control strategies will be needed for disease eradication. The optimal control has a long history of being analysed to problems in epidemiology problems. Bowong [4] control a tuberculosis model indicating how a control term on the chemoprophylaxis should be introduced in the population to reduce the number of individuals with active TB. Yang et al. [5] focus primarily on controlling the disease using an objective function based on a combination of minimizing the number of TB infections and minimizing the cost of control strategies. In this work, main emphasis is on a complete analysis of the optimally properties corresponding to trajectories. There controls are natural candidates for optimally and are widely used in medical treatment were a maximum dose of treatment is given repeatedly with breaks in between. We develop simple and easily verifiable conditions which allow us to determine the locally of bang-bang control. In this paper, we investigate the optimality singular controls of SEIR models of tuberculosis with vaccination and treatment theoretically. These are controls correspond to time-vary the vaccination and treatment schedules.

The mathematical model for tuberculosis found that compartmental dynamics such as Susceptible, Infected, Removed with vaccination (VSIR) [4]. Since the disease can remain latent, become active, or it can progress from laten TB to active TB either by endogenous reactivation or exogenous reinfection [5]. Based on previous statement, we modify [4] and adopts the class Exposed (E) to VSIR model. Thus, this paper will discuss about formulation of model, analysis and simulation using the fourth order Runge Kutta (KR4).

Many researchers have researched about this TB, for example, Nyabadza and Kgosimore (2012) have formulated a model for the TB compartment with two age classes, namely: children and adults. Qualitative analysis was conducted to determine the stability of the model equilibrium models in terms of the model reproduction number $\boldsymbol{R_0}$. Numerical simulations are also performed to investigate the role played by several key epidemiological parameters in the dynamics of the disease. Ozcaglar et al (2012) have created a model that simulates the dynamics of tuberculosis transmission, treatment, drug resistance, control strategies to improve adherence to treatment, HIV/ TB co-infection, and patient groups. Abdulkarim (2007), examines the dynamics of age-structured models of the transmission of TB transmission along the lines of classical McKendrick-Foerster, age-structured population models are based on several assumptions which contradicts the assumption castillo-chaves depending on the age and age-dependent mortality rate of contact, vaccination and treatment,

will be removed and quarantine infected to non-disease caused death. Tome and Oliveira (2011), a model susceptible-Infected-Recovery (SIR) and susceptible-exposed-infected (SEI), studied on the Cayley tree of coordination number $\boldsymbol{k}$. The spread of the disease in the formation was found to occur when a greater chance of infection b $\boldsymbol{bc} = \boldsymbol{k} / (2\,(k-1))$, which is equivalent to a dynamic site percolation models, the spread of infection occurs when opportunities $\boldsymbol{p}$ greater than $\boldsymbol{pc} = \boldsymbol{1} / ((k - \boldsymbol{1}))$.

CHAPTER II
LITERATURE REVIEW

In a study of the spread of epidemic dengue fever, and SIR and SEIR models approach has been used. These model are expected to be able to know the number of hosts infected with the epidemic, the number of hosts recovered, the number of hosts recovered, the number of mosquitoes that become suspect, the number of hosts infected with the virus show symptoms denggi and the number of people potentially infected with dengue virus.

2.1. Susceptible Infected Recovery **(SIR)**

Susceptible Infected Recovery (SIR) was first introduced by Kermack and Kendrick in 1927. At the SIR model, the human population is divided into three groups, namely susceptible or vulnerable to the symbols S, infected or infected symbolized by the I and recovery or recovered symbolized by R. Total number of such groups is $N = SIR$. Here, S or SIR modelling is susceptible to uninfected individuals but groups can be infected with the disease. Therefore, this group also has the possibility to be infected (I). I or an infected individual can spread the disease in susceptible individuals. The time required by patients with infectious disease is called the period of the disease, after a period of illness then individually moved and become individuals who recovered or recovered. Meanwhile, recovery individuals R have been recovered or immune from the disease.

SIR model is written in the form of ordinary differential equations (GDP), which is one part of a deterministic model, with continuous time. The analogy is similar to the reaction kinetics, which can be assumed to be infected and susceptible individuals change occurs at a rate proportional to the population size. The rate of change of new infected individuals defined as $\boldsymbol{\alpha SI} - \beta I$, with $\boldsymbol{\alpha}$ a transmission value while the value of $\boldsymbol{\beta}$ is the rate of healing. Infected individuals are assumed to be recovered with a constant probability all the time. Which then changes constantly with the rate of healing per capita is denoted as $\boldsymbol{\beta}$ and symbolized as $\boldsymbol{\beta I}$ entirety. Based on this assumption, then we can form a model scheme as follows.

Figure 1. Schematic of the SIR model

The diagram can be constructed in the following differential equation:

$$\frac{dS}{dt} = -\alpha SI \tag{1}$$

$$\frac{dI}{dt} = \alpha SI - \beta I \tag{2}$$

$$\frac{dR}{dt} = \beta I \tag{3}$$

These equations describe the individual transitions from S to I and then to R. By adding these three equations this equation can easily be shown that the total population is constant.

2.2. Susceptible Exposed Infected Recovery **(SEIR)**

SIR model discussed above is by simply taking into account the types of diseases that can infect other people after they are infected. Many diseases have a latent or open phase, wherein said individual is infected but not contagious. For example measles, there is a period of about seven to eight days that a person is exposed, while the virus multiplies. After this period, the individual will experience a cough and mild fever. At this point the individual is said to be infected and contagious. In such cases it is necessary to describe the different models of the situation, ie, with the addition of individuals exposed or latent. In this section SEIR models including birth and death will be explained along with the exploration of differential equations that describe the flow from one class to another. The flow of this model can be considered in the diagram below.

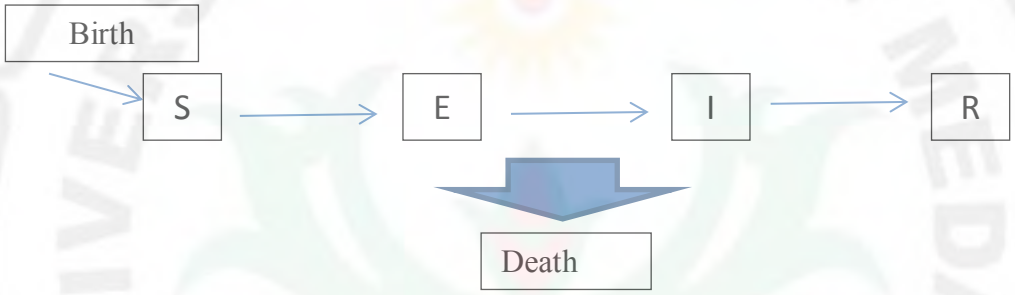


Figure 2. Scheme of SEIR Model

In this model the population (N) is divided into four classes: susceptible, exposed, infectious,and recovered, the number of individuals in the class, or their density is represented by each $S\ (t), E\ (t), I\ (t), R\ (t)$, we have:

$$N = S(t) + E(t) + I(t) + R(t) \tag{4}$$

Prior to directly explore the dynamics equations considered susceptible class (S (t)). Initially, S(t) is considered the entire population (N). In such cases the population S (t) increases with the birth rate (b), but decreased with the death of one person. The degree to which individuals die at the rate of mortality (μ) times the number of susceptible individuals. Upon contact with an infectious individual, a small fraction of S (t) moves from class to class vulnerable open.

$$\frac{dS}{dt} = \alpha - \beta SI - \mu S \tag{5}$$

The next three differential equations can be viewed in the same way, with people entering the class/ compartment from the previous, and left the compartment to move on to the next compartment, or die.

$$\frac{dE}{dt} = \beta SI - (\delta + \mu)E \tag{6}$$

$$\frac{dI}{dt} = \delta E - (\gamma + \mu)I \tag{7}$$

$$\frac{dR}{dt} = \gamma I - \mu R \tag{8}$$

where $t > 0, S(0) = S_0 > 0, E(0) = E_0 > 0, I(0) = I_0 > 0.$

2.3.Vaccination Susceptible Infected Recovery (VSIR)

Models for the spread of tuberculosis by Vaccination susceptible Infected Recovery (VSIR) was created by Momoh et al (2012). The model has been divided into four classes, namely population: The infantry passively immune, susceptible, Infected, Recovery. The model is described as follows:

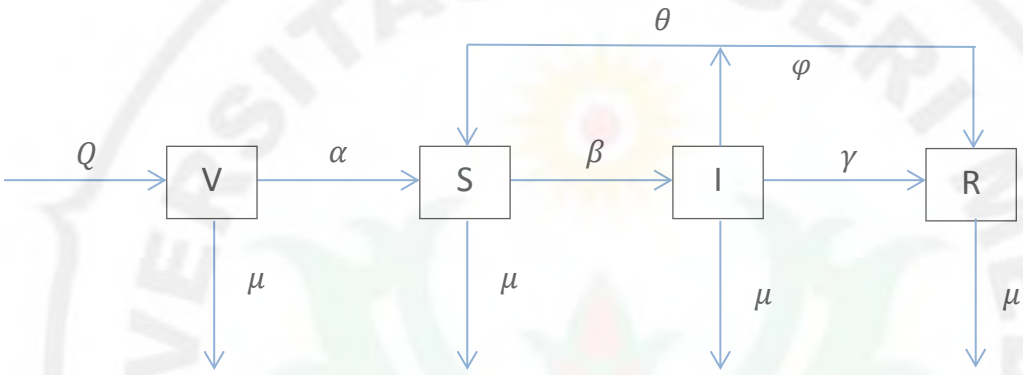


Figure 3. VSIR Model

Individuals who put in classes V through a natural birth at a rate Q through passive vaccination, V population declined because of natural mortality at rate μ and the individual moves to S as a result of the use of passive vaccination rate α. S population increased due to the arrival of individuals from classes V and R at rate α and θ. S-class population decline due to the movement of individuals into classes that are infected at rate β and the natural death rate μ. Population I declined because treatment for TB at rate γ and the natural death rate μ and deaths from TB infection rate φ. A population increase due to the movement of individuals at rate γ of I and decreases due to the movement of individuals to θ and S in the rate of natural mortality at rate μ. The model described above then become ordinary differential equation as follows:

$$\frac{dV}{dS} = Q - (\mu + \alpha)V$$

$$\frac{dS}{dS} = \alpha V - (\mu + \beta I)S + \theta S$$

$$\frac{dI}{dS} = \beta SI - (\mu + \varphi + \gamma)I$$

$$\frac{dR}{dS} = \gamma I - (\mu + \theta)R$$

where

$Q =$ Natural birth rate

$V =$ passive immunity infants at time $\boldsymbol{t}$

$S =$ Susceptible class when the time $\boldsymbol{t}$

$I =$ Infected class at time $\boldsymbol{t}$

$R =$ Recovery class at time $\boldsymbol{t}$

$\mu =$ Natural mortality rate

$\alpha =$ Rate efficiency duration of vaccine

$\beta =$ TB contact rate

$\varphi =$ Deaths from TB infection

$\gamma =$ Rate of duration of vaccine efficiency

$\theta =$ Rate in which the individual becomes vulnerable

2.4.Maximum Principle

Theorem 1. () (Pontryagin Maximum principle (PMP) for linear time optimal problem) *Assume the domain of control* Ω *to bea compact, convect subset of* $\mathbb{R}^m$. *An admissible control* $u(.)$ *and its corresponding trajectories* $x(.)$ *both defined on* $[t_0, t_1]$ *extermal if only if ther are exist non zero absolutely continuous vector* $p(.)$ *solution of adjoint equation*

$$\dot{p}(t) = -p(t)A(t) \quad a.e.\ on\ [t_0, t_1] \tag{9}$$

Such that

$$p(t)B(t)u(t) = \max_{u\in\Omega} p(t)B(t)u \tag{10}$$

Such vector is called a an adjoint vector.

Proof. Assume $x(.)$ to be the extermal trajectories corresponding to the extremal control $u(.)$ both defined on $[t_0, t_1]$. By definition we have $x(t_1) \in \partial A_\Omega(t_1)$ where $x(.)$ is written as

$$x(t) = \Phi(t)\left(x_0 + \int_{t_0}^{t} \Phi^{-1}(s)B(s)u(s)ds\right) \tag{11}$$

The accessibility set $\partial A_\Omega(t_1)$ is compact and convex and since $x(t_1) \in \partial A_\Omega(t_1)$, there are exists a support hyperline $\prod$ to $A_\Omega(t_1)$ at $x(t_1)$. Let $\bar{p}$ be a non zero normal row vector to $\prod$ at $x(t_1)$ outward with respect to $A_\Omega(t_1)$. Let $p(t)$ be defined for $t_0 < t < t_1$ by $p(t) = p_0^{\Phi^{-1}}(t)$, $p(t_1) = \bar{p}$. We have

$$p(t)x(t) = p_0x_0 + \int_{t_0}^{t} p(s)B(s)u(s)ds. \tag{12}$$

Le us assume that there exits a subset of $[t_0, t_1]$ of non zero measure such that for all t in this subset we have

$$p(t)B(t)u(t) < \max_{u\in\Omega} p(t)B(t)u \tag{13}$$

Using Filippov selection Theorem, we can define a measurable control $\hat{u}(.)$ satisfying a.e. on $t_0 < t < t_1$

$$p(t)B(t)\hat{u}(t) = \max_{u\in\Omega} p(t)B(t)u \tag{14}$$

Let $\hat{x}(.)$ be the trajectories associated to $\hat{u}(.)$. We have

$$p(t)\hat{x}(t) = p_0x_0 + \int_{t_0}^{t} p(s)B(s)\hat{u}(s)ds. \tag{15}$$

Moreover, by construction of $\hat{u}(.)$ and from (12) the following inequality holds:

$$\int_{t_0}^{t} p(s)B(s)u(s)ds < p(s)B(s)\hat{u}(s)ds. \tag{16}$$

Hence we deduce that

$$p(t_1)x(t_1) < p(t_1)\hat{x}(t_1) \tag{17}$$

This contradicts the fact that $x(t_1) \in \partial A_\Omega(t_1)$ and that $p(t_1)$ is outward normal to $\prod$ at $x(t_1)$. Therefore we must have a.e.

$$p(t)B(t)u(t) = \max_{u\in\Omega} p(t)B(t)u \tag{18}$$

Conversely, if $u(.)$ satisfies a.e. the equality

$$p(t)B(t)u(t) = \max_{u\in\Omega} p(t)B(t)u\,(t) \tag{19}$$

We show that $x(t_1) \in \partial A_\Omega(t_1)$. Indeed assume that $x(t_1) \in \partial Int\, A_\Omega(t_1)$. Therefore there exists $\hat{x}_1 \in \partial A_\Omega(t_1)$ such that

$$p(t_1)x(t_1) < p(t_1)\hat{x}_1 \tag{20}$$

Let $u(.)$ Be a control defined on $[t_0, t_1]$ steering x_0 to $\hat{x}_1$ and $\hat{x}(.)$ the corresponding trajectory. It follows that

$$p(t_1)B(t)\hat{u}(t_1) \le p(t_1)B(t)u(t_1) \text{ a.e.} \tag{21}$$

Hence, by computing we get

$$p(t_1)\hat{x}(t_1) < p(t_1)\hat{x}_1 \le p(t_1)x(t_1) \tag{22}$$

Which contradicts to the inequality (19).

2.5.Determination singular extremal

Let (z,u), $z=(x,p)$ be a singular extremal defined on $[0.T]$. By definition it is a solution a.e. on $[0.T]$ of the following equations:

$$\dot{x}(t)=X\big(x(t)\big)+u(t)Y(t),\qquad \dot{p}(t)=-p(t)\left(\frac{\partial X}{\partial x}\big(x(t)\big)+u(t)\frac{\partial Y}{\partial x}\big(x(t)\big)\right) \tag{23}$$

And it is contained for each t in the set

$$\Sigma_1:\{(x,p),\langle p,Y(x)\rangle=0\} \tag{24}$$

Since $t\to z(t)$ is an absolutly continuous in curve Σ_1, differentiating $t\to\langle p(t),Y(x(t))\rangle=0$, one gets

$$\langle p(t),[X,Y](x(t))\rangle=0, \tag{25}$$

a.e. on $[0.T]$, where the Lie bracket is computed with the convention

$$[Z_1,Z_2](x)=\frac{\partial Z_1}{\partial x}(x)Z_2(x)-\frac{\partial Z_2}{\partial x}(x)Z_1(x). \tag{26}$$

Since $t\to(x(t),p(t))$ is continuous, the curve $t\to z(t)$ is contained for each $t\in[0.T]$ in the set

$$\Sigma_2:\{(x,p)\in\Sigma_1,\langle p(x(t),[Y,X](x(t))\rangle=0\}. \tag{27}$$

Hence, differentiating $t\to\langle p(x(t),[Y,X](x(t))\rangle=0$, we get the relation

$$\langle p(t),\big[[Y,X],X\big](x(t))\rangle+u(t)\langle p(t),\big[[Y,X],X\big](x(t))\rangle=0. \tag{28}$$

For almost every $t\in[0,T]$.

This last relation allow us to compute $u(.)$ in many cases and justifies the following definition.

Definition 2. () *For any singular extremal (z,u)defined on $[0,T]$, $\mathcal{R}(z,u)$ will denote the set $\{0\le t\le T;\ \langle p(t),\big[[Y,X],Y\big](x(t))\rangle\}\neq 0$. The set $\mathcal{R}(z,u)$possibly empty is always an open subset of $[0,T]$.*

Proposition 3. *Let (z,u)be singular extremal defined on $[0,T]$ and assume that $\mathcal{R}(z,u)$ not empty. Then*

1. *For a.e. $t\in\mathcal{R}(z,u)$,*

$$u(t)=\hat{u}\big(z(t)\big)=-\frac{\langle p(t),\big[[Y,X],X\big](x(t))\rangle}{\langle p(t),\big[[Y,X],Y\big](x(t))\rangle} \tag{29}$$

2. *z restricted to $\mathcal{R}(z,u)$ is smooth and is solution for every t of the equations:*

$$\dot{x}(t)=X\big(x(t)\big)+\dot{\hat{u}}(t)(z(t))Y(z(t)) \tag{30}$$

$$\dot{p}(t)=-p(t)\left(\frac{\partial X}{\partial x}\big(x(t)\big)+\hat{u}(z(t))\frac{\partial Y}{\partial x}x(t)\right) \tag{31}$$

Proposition 4. *Let* $(x,(u,v))$*be a controlled trajectory of the system and let* λ *be a solution to the corresponding adjoint equations. Given a continuously differentiable vector field h, define*

$$\psi(t) = \langle \lambda(t), h\big(x(t)\big)\rangle \tag{32}$$

Then the derivative of ψ *is given by*

$$\dot{\psi}(t) = \langle \lambda(t), [f + g_1 u + g_2 v, h]\big(x(t)\big)\rangle \tag{33}$$

CHAPTER III
OBJECTIVE OF THE RESEARCH

3.1. Objective of the Research

The general objective of this research is to create a new model of the spread of TB disease in the exposed class which is considered in VSIR, in order to reduce the diffusion rate. While the particular purpose is:

1. Make epidemiological models VSEIR
2. Proving the stability of the model VSEIR
3. Implementing Model VSEIR to obtain the amount of spread of disease.
4. Calculating the spread of disease from the model optimization VSEIR

3.2. Urgency

As the background that TB disease is still a disease that is a health issue and the attention of the world and an increase in TB cases in North Sumatra, this study should be implemented to avoid casualties died and many more of course to reduce treatment costs to be borne by the government and society.

3.3.Innovation Finding

Pada penelitian kali ini, model baru diperoleh dari pengembangan model yang dikemukakan oleh Momoh et al. (2012) yaitu Vaccination Susceptible Infected Recovery (VSEIR), disamping itu juga akan diuji stabilitas dari model akan diperoleh optimasi dari jumlah penyebaran penyakit Tuberculosis tersebut.

CHAPTER IV
METODOLOGY

In previous studies, mathematical modeling of the spread of tuberculosis and vaccine effect using a model Vaccination Susceptible Infected Recovery (VSIR) has been introduced by Momoh et al in 2012. They have to model the case of TB with multiple steps:

1. First Step

The simplest model to build a model of the dynamics of the spread of tuberculosis is susceptible-Infected-Removed (SIR). In 1927,Kermack and McKendrick make them consider a model where fixed by simply dividing the population into three components, namely susceptible $S(t)$, infected $I(t)$, and removed the $R(t)$. In this study, the SIR model will be reviewed again as the basic theory of the formation of a new model.

2. Second Step

For the second step, the model VSIR reviews back as the theoretical basis for the model to be created. For VSIR, the population of TB population is divided into four classes, namely: passively immune infant (V), susceptible (S), Infected (I), Recovery (R). The model is described as follows:

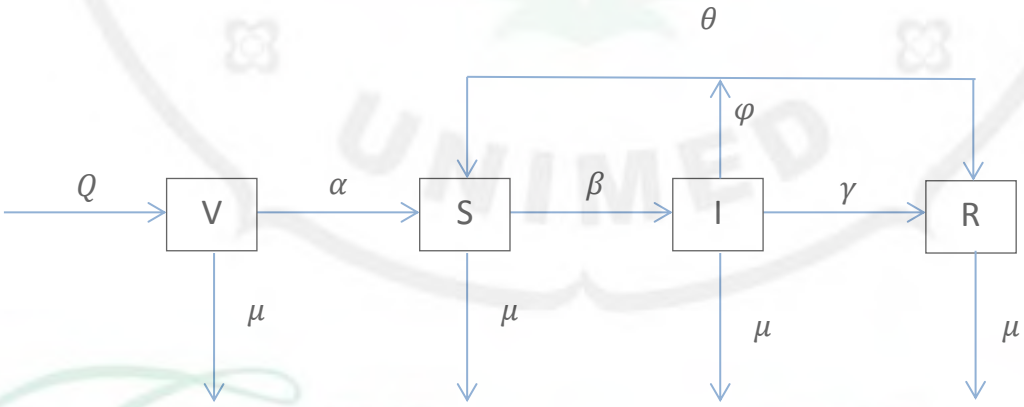


Figure 4. VSIR Model

Individuals who put in classes V through a natural birth at a rate Q through passive vaccination, V population declined because of natural mortality at rate μ and the movement of individuals into S as a result of the use of passive vaccination rate α. S population increased due to the arrival of individuals from classes V and R at rate α and θ. S-class population decline due to the movement of individuals into classes that are infected at rate β and the natural death rate μ. Population I declined because treatment for TB at rate γ and the

natural death rate μ and deaths from TB infection rate φ. A population increase due to the movement of individuals at rate γ of I and decreases due to the movement of individuals to θ and S in the rate of natural mortality at rate μ.

Here, Q is the rate of natural birth, V passive immunity infants at time t, S is a susceptible class at time t, I is the class Infected at time t, R is the class recovery at time t, the natural death in rate μ. Rate α is efficient duration of vaccine TB contact rate β Deaths from TB infected in rate φ. Rate γ is the duration of vaccine efficiency, θ is rate which individuals become susceptible. The model described above then becomes the following ordinary differential equation:

$$\frac{dV}{dS} = Q - (\mu + \alpha)V,$$

$$\frac{dS}{dS} = \alpha V - (\mu + \beta I)S + \theta S,$$

$$\frac{dI}{dS} = \beta SI - (\mu + \varphi + \gamma)I,$$

$$\frac{dR}{dS} = \gamma I - (\mu + \theta)R,$$

3. Third Step

In the model of SEIR, the population is divided into four subclasses, namely the class of vulnerable populations (susceptible (S)), class infected population (Exposed (E)), the class population is infected (Infected (I)), and a class of population recovery (Recovery (R)). Then S states the proportion of susceptible individuals at time t, E states the proportion of individuals infected at time t, I states the proportion of individuals infected at time t, the proportion of individuals R declared cured at the time t, and N denotes the total proportion of individuals.

The parameter used is b declare the birth rate, death rate μ naturally stated, the contact rate β states, states healing rate γ, and δ expressed individual rate class to class E, the value of $b, \mu, \beta, \gamma, \delta > 0$. The number of individuals in the class of susceptible (S) decreased by the transmission of the disease, $\beta\ S\ 1\ /\ N$ and natural mortality, $\mu\ S$ and increases due to births, βN. Number of Individuals Exposed to the class (E) decreased by natural death $\mu\ E$, and class E goes to classes Infected (I), and increased as a result of disease transmission $\beta\ S\ 1\ /\ N$ number of individuals in class Infected (I) have declined with natural mortality, $\mu\ I$ and individuals who recovered, $\gamma\ I$ and increased as a result of individuals coming from class E.

the number of individuals in the class R. μR decreases due to natural mortality, and increases as the individual has recovered, $\gamma\ I$. Based on the above, made transfer diagram as follows:

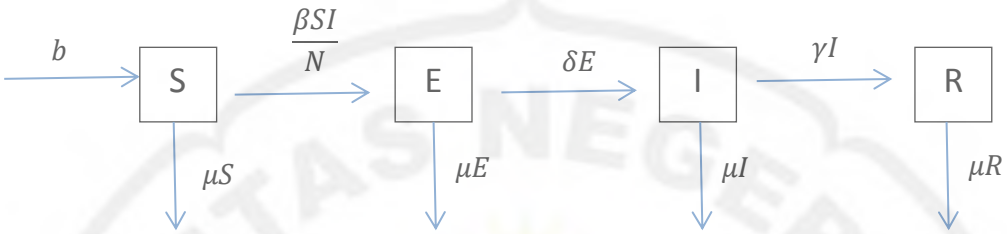


Figure 5. SEIR Model

Mathematical model based on the transfer diagram above as follows:

$$\frac{dS}{dt} = b - \mu S - \frac{\beta}{N} SI$$

$$\frac{dI}{dt} = \frac{\beta}{N} SI - (\mu + \delta)E$$

$$\frac{dI}{dt} = \delta E - (\mu + \gamma)I$$

$$\frac{dR}{dt} = \gamma I - \mu R$$

where: $t > 0, S(0) = S_0 > 0, E(0) = E_0 > 0, I(0) = I_0 > 0,$ and $R(0) = R_0 > 0$.

4. Fourth Step

Formation of a new model taking into account the exposed class (E) on the previous models Vaccination Susceptible Infected Recovery (VSIR) introduced by Momoh et al. (2012). Momoh et al. (2012) have incorporated individuals into classes V through the natural birth rate Q through passive vaccination, V population decline due to natural mortality at rate μ and the movement of individuals into S as a result of the use of passive vaccination rate α. The parameters used are b declare the birth rate, death rate μ naturally stated, the contact rate β states, states healing rate γ, and δ expressed individual rate class to class E, the value of $b, \mu, \beta, \gamma, \delta > 0$.

The number of individuals in the class of susceptible (S) decreased by the transmission of the disease, $\beta\ S\ 1\ /\ N$ and natural mortality, $\mu\ S$ and increases due to births, βN. Number of Individuals Exposed to the class (E) decreased by natural death $\mu\ E$, and E class goes to classes Infected (I), and increased as a result of disease transmission $\beta\ S\ 1\ /\ N$ number of individuals in Infected class (I) have declined with natural mortality, $\mu\ I$ and

individuals who recovered, γI and increased as a result of individuals coming from class. The number of individuals in class μR decline due to natural mortality, and increases as the individual has recovered, γI. Based on the above, the following transfers were made diagrams:

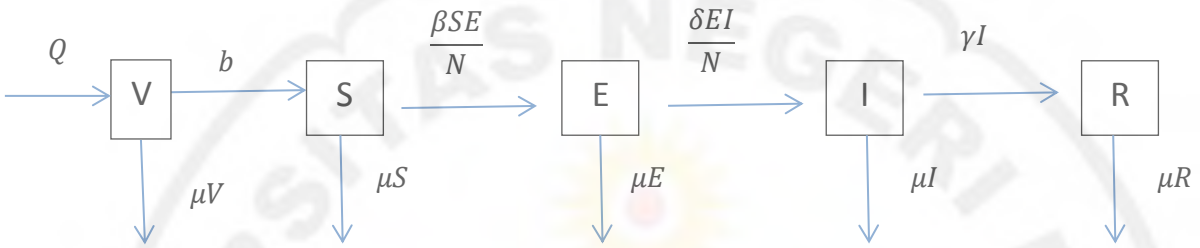


Figure 6. VSEIR Model

5. Fifth Step

Determination Equilibrium point, eigenvalues and reproductive numbers by using the definition.

6. Sixth Step

Stability proving using theorem 2.1 and theorem 2.2

7. Seventh Step

Determining control optimization using geometric optimal control theory methods to analyse the relationship between the vaccination and the optimal treatment schedule applied. Overall, this study measures fishbone is written using the following:

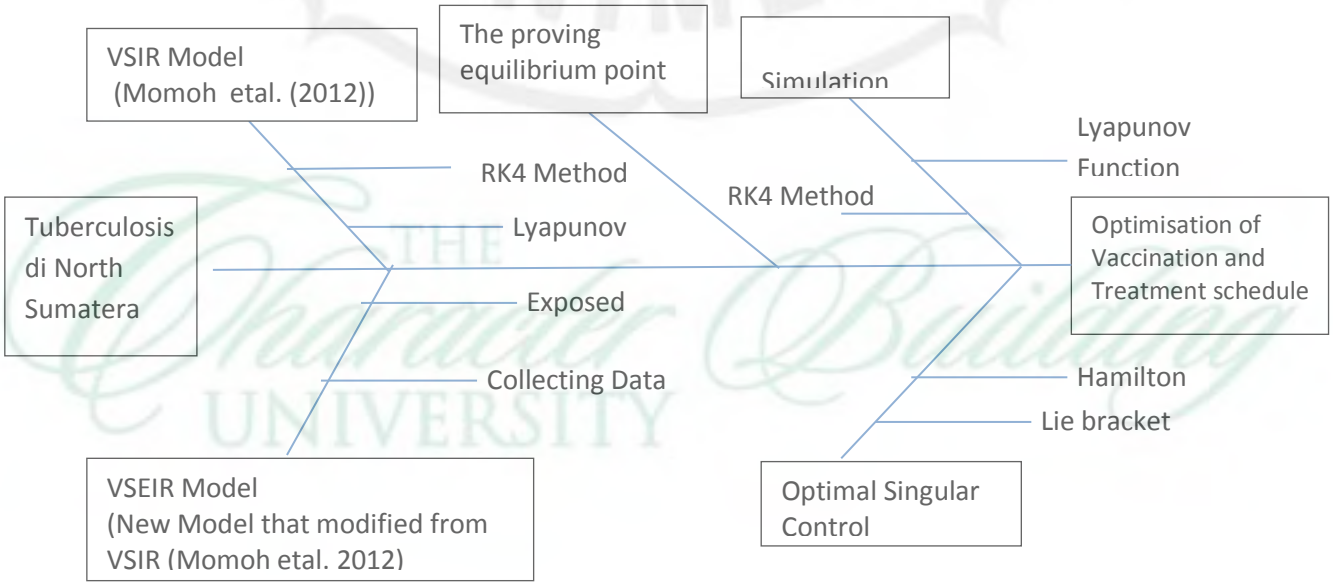


Figure 7. Fishbone Diagram

CHAPTER IV
RESULT AND DISCUSSION

4.1. Formulation of Model

The total population size $N(t)$ is divided into four distinct epidemiological subclasses of individuals which are vaccination, susceptible, infectious, and recovered, with sizes denoted by $V(t), S(t)$, $I(t)$, and $R(t)$, respectively. Thus, $N(t)$ can be written as $N(t) = V(t) + S(t) + I(t) + R(t)$. The VSIR model [4] having vaccination, infected and recovered period is described by the following system of differential equations:

$$\frac{dV}{dt} = q - (\mu_1 + \delta_1)V, \tag{34}$$

$$\frac{dS}{dt} = \delta_1 V - (\mu_2 + \delta_2 I)S + \theta S, \tag{35}$$

$$\frac{dI}{dt} = \delta_2 IS - (\mu_4 + \mu_{TB} + \delta_4)I, \tag{36}$$

$$\frac{dR}{dt} = \delta_4 I - (\mu_5 + \theta)R, \tag{37}$$

where human birth in natural through passive vaccination ($V(t)$) at rate p, non negative parameters $\mu_1, \mu_1, \mu_3, \mu_2, \mu_5$ denote as natural death of population of the V, the S, the I and the R, respectively. Population of infected Tuberculosis died in rate μ_{TB}. The susceptible population decreased due to coming individual from the V in rate δ_1. δ_2 denotes the transfer rate from susceptible to infected population. Infected population increases due to movement of individuals from infected individuals I in rate δ_4 dan decreased due to movement of individuals in to the S at rate θ. In this paper, we assume that human recovering is fully recovered. In flow of mathematical model, we assume that each compartment occurs interaction between classes. Hence, Eqs (1)-(4) can be written as

$$\frac{dV}{dt} = qN - \mu_1 V - \delta_1 VS, \tag{38}$$

$$\frac{dS}{dt} = \delta_1 VS - \mu_2 S - \delta_2 IS, \tag{39}$$

$$\frac{dI}{dt} = \delta_2 SI - (\mu_4 + \mu_m + \delta_4)I, \tag{40}$$

$$\frac{dR}{dt} = \delta_4 I - \mu_5 R. \tag{41}$$

Here, we assume that all new birth got BCG vaccination. Using a compartmental approach, one may assume that a susceptible individual first goes through a latent period (and is said to become exposed or in class $E(t)$). The exposed individual increases from susceptible individuals in at rate α and decreases in rate ρ and μ_3 couse of death. Then, any interaction between exposed and infected in rate ρ. The exposed population The VSEIR model having

infectious force, infected and recovered period is described by the following system of differential equations:

$$\frac{dV}{dt} = qN - \mu_1 V - \delta_1 VS, \tag{42}$$

$$\frac{dS}{dt} = \delta_1 VS - \mu_2 S - \alpha ES, \tag{43}$$

$$\frac{dE}{dt} = (\alpha S - \mu_3 - \rho I)E, \tag{44}$$

$$\frac{dI}{dt} = \rho EI - (\mu_4 + \mu_{TB} + \delta_4)I, \tag{45}$$

$$\frac{dR}{dt} = \delta_4 I - \mu_5 R, \tag{46}$$

with conditions

$$N = V + S + E + I + R \rightarrow R = N - V - S - I, \tag{47}$$

where the positive parameters $\mu_1, \mu_2, \mu_3, \mu_4, \mu_5$ and μ_5 are the rate of natural death of vaccitaion individual $(V(t))$, susceptible individual $(S(t))$, exposed individual $(E(t))$, Infected individual $(I(t))$ and recovery individual $(R(t))$, respectively. q denote the rate of natural birth through passive vaccination. The model can be simplified by assuming the following fractions [6]

$$u = \frac{V}{N}, \quad w = \frac{S}{N}, \quad x = \frac{E}{N}, \quad y = \frac{I}{N}, \text{ and } z = \frac{R}{N}. \tag{48}$$

Thus, the model for human populations can be simplified as follows

$$\frac{du}{dt} = q - (\mu_1 + \delta_1)u, \tag{49}$$

$$\frac{dw}{dt} = (\delta_1 u - \mu_2 - \alpha x)w, \tag{50}$$

$$\frac{dx}{dt} = (\alpha w - \mu_3 - \rho y)x, \tag{51}$$

$$\frac{dy}{dt} = \rho xy - \beta y, \tag{52}$$

$$\frac{dz}{dt} = \delta_4 y - \mu_5 z, \tag{53}$$

where $\beta = (\mu_4 + \mu_{TB} + \delta_4)$.

4.2. Stability Analysis

4.2.1. Disease Free Equilibrium (DFE)

Critcal point will occur while the value of

$$\frac{du}{dt} = \frac{dw}{dt} = \frac{dx}{dt} = \frac{dy}{dt} = \frac{dz}{dt} = 0. \tag{54}$$

Substitute (49)-(53) in to Eq. (54) as follows

$$q - (\mu_1 + \delta_1 w)u = 0, \tag{55}$$
$$\delta_1 uw - (\mu_2 + \alpha x)w = 0, \tag{56}$$
$$(\alpha w - \mu_3 - \rho y)x = 0, \tag{57}$$
$$\rho xy - \beta y = 0, \tag{58}$$
$$\delta_4 y - \mu_5 z = 0. \tag{59}$$

Inserting Eqs. (55)-(58) into Eq. (59) indicates the equilibrium point of the system are:

$F_1 = \left(\frac{q}{\mu_1}, 0, 0, 0, 0\right)$, and $F_2 = (u_0, w_0, x_0, y_0, z_0)$ with values

$$u_0 = \frac{\mu_2}{\delta_1}, \qquad w_0 = \frac{q\delta_1 - \mu_1\mu_2}{\delta_1\mu_2}, \quad x_0 = 0, \qquad y_0 = 0, \qquad z_0 = 0. \tag{60}$$

Linearization of Eqs. (49)-(53) on the equilibrium points $\left(\frac{q}{\mu_1}, 0, 0, 0, 0\right)$, yields the following equation

$$\begin{pmatrix} \frac{d\,u}{d\,t} \\ \frac{d\,w}{d\,t} \\ \frac{d\,x}{d\,t} \\ \frac{d\,y}{d\,t} \\ \frac{d\,z}{d\,t} \end{pmatrix} = \begin{pmatrix} -\mu_1 & \frac{q\alpha}{\mu_1} & 0 & 0 & 0 \\ 0 & \frac{q\delta_1}{\mu_1} - \mu_2 & 0 & 0 & 0 \\ 0 & 0 & -\mu_3 & 0 & 0 \\ 0 & 0 & 0 & -\beta & 0 \\ 0 & 0 & 0 & \delta_4 & -\mu_5 \end{pmatrix} \begin{pmatrix} u \\ w \\ x \\ y \\ z \end{pmatrix}. \tag{61}$$

Using MAPLE, Eq (61) leads to five eigenvalues equations as follows:

$$-\lambda^5+\left(\frac{q\delta_1}{\mu_1}-\beta-\mu_1-\mu_2-\mu_3-\mu_5\right)\lambda^4 + \left[\left(\frac{q\delta_1(\beta+\mu_3+\mu_5)}{\mu_1}\right) + (q\delta_1-(\mu_1+\mu_5+\mu_2+\mu_3)\beta-\mu_3(\mu_1+\mu_2)-(\mu_5+\mu_1)\mu_2)\right]\lambda^3 + \left[\frac{q\delta_1(\mu_3\beta+\beta\mu_5+\mu_5\mu_3)}{\mu_1}\right]\lambda^2 + \left[\frac{q\delta_1\beta(\mu_5-\mu_3)}{\mu_1}+q\delta_1(\mu_5+\mu_3+\beta)-\mu_1\mu_2(\beta+\mu_5+\mu_3) - \mu_1\mu_5(\beta+\mu_3)-\mu_3\mu_5(\beta+\mu_2)-\mu_2\mu_5(\beta+\mu_3)-\mu_2\mu_3(\beta + \mu_5)\right]\lambda-\mu_1\mu_2\mu_3\mu_5\beta+q\delta_1\mu_3\mu_5\beta=0, \quad (62)$$

with eigenvalues

$$\lambda_1 = -\mu_1, \quad \lambda_2 = -\frac{\mu_1\mu_2-q\delta_1}{\mu_1}, \quad \lambda_3=-\mu_3, \quad \lambda_4=-\beta, \quad \lambda_5=-\mu_5. \quad (63)$$

4.2.2. Epidemic Equilibrium State

Linearization of Eqs (49)-(53) on the equilibrium point $(u_0, w_0, x_0, y_0, z_0)$ yields the following equation:

$$\begin{pmatrix} \frac{du}{dt} \\ \frac{dw}{dt} \\ \frac{dx}{dt} \\ \frac{dy}{dt} \\ \frac{dz}{dt} \end{pmatrix} = \begin{pmatrix} -\frac{q\delta_1-\mu_1\mu_2}{\mu_2}-\mu_1 & -\mu_2 & 0 & 0 & 0 \\ \frac{q\delta_1-\mu_1\mu_2}{\mu_2} & 0 & -\frac{\delta_2(q\delta_1-\mu_1\mu_2)}{\delta_1\mu_2} & 0 & 0 \\ 0 & 0 & \frac{\alpha(q\delta_1-\mu_1\mu_2)}{\delta_1\mu_2}-\mu_3 & 0 & 0 \\ 0 & 0 & 0 & -\beta & 0 \\ 0 & 0 & 0 & \delta_4 & -\mu_5 \end{pmatrix} \begin{pmatrix} u \\ w \\ x \\ y \\ z \end{pmatrix}. \quad (64)$$

Using MAPLE, Eq (64) leads to five eigenvalue equations as follows

$$
\begin{aligned}
-\lambda^5 + \left[-\beta - \mu_3 - \mu_5 - \frac{q(\alpha-\delta_1)}{\mu_2} - \frac{\mu_1\alpha}{\delta_1}\right]\lambda^4 \\
+ \left[-(\mu_5+\mu_3)\beta - q\delta_1 + \mu_1\mu_2 - \mu_3\mu_5 - \frac{\alpha\mu_1\beta}{\delta_1} + \frac{q\alpha\beta}{\mu_2} - \frac{q\delta_1\mu_5}{\mu_2}\right. \\
\left. + \frac{\alpha q^2\delta_1}{\mu_2^2} - \frac{q\delta_1\mu_3}{\mu_2} + \frac{q\alpha\mu_5}{\mu_2} - \frac{q\alpha\mu_1}{\mu_2}\right]\lambda^3 \\
+ \left[\frac{\delta_1 q^2\alpha}{\mu_2} + \frac{\mu_2\alpha\mu_1^2}{\delta_1} + \frac{\delta_1 q^2\alpha\beta}{\mu_2^2} + \frac{\delta_1 q^2\alpha\mu_5}{\mu_2^2} - \frac{q\delta_1\beta(\mu_3+\mu_5)}{\mu_2}\right. \\
- \frac{q\alpha\beta(\mu_1+\mu_5)}{\mu_2} - \frac{\alpha\mu_1\mu_5\beta}{\delta_1} - \delta_1 q(\mu_5-\mu_3) + \mu_2\mu_1(\mu_5+\mu_3) \\
\left. - \delta_1 q\beta + (\mu_2\mu_1 - \mu_3\mu_5)\beta - 2q\alpha\mu_1\right]\lambda^2 \\
+ \left[\frac{\delta_1\alpha q^2\beta}{\mu_2} + \frac{\delta_1\alpha q^2\mu_5}{\mu_2} + \frac{\delta_1\alpha q^2\beta\mu_5}{{\mu_2}^2} + \frac{\mu_2\alpha{\mu_1}^2\beta}{\delta_1} + \frac{\mu_2\alpha{\mu_1}^2\mu_5}{\delta_1}\right. \\
- \frac{\delta_1 q\beta\mu_5(\mu_1+\mu_3)}{\mu_2} - \delta_1 q\beta(\mu_3+\mu_5) - \delta_1 q\mu_3\mu_5 + \mu_2\mu_1\beta(\mu_3+\mu_5) \\
\left. + \mu_2\mu_1\mu_3\mu_5 - 2q\alpha\mu_1(\beta-\mu_5)\right]\lambda \\
+ \left[\frac{\delta_1 q^2\alpha\mu_5\beta}{\mu_2} + \frac{\mu_2\alpha\mu_1^2\beta\mu_5}{\delta_1} - \delta_1 q\beta\mu_3\mu_5 + \beta\mu_1\mu_2\mu_3\mu_5 - 2q\alpha\beta\mu_1\mu_5\right] \\
= 0
\end{aligned}
\tag{65}
$$

with eigenvalues

$$
\begin{aligned}
\lambda_1 = -\frac{q\delta_1 - \sqrt{q^2\delta_1^2 - 4q\delta_1\mu_2^2 + 4\mu_1\mu_2^3}}{2\mu_2}, \quad \lambda_2 \\
= -\frac{q\delta_1 + \sqrt{q^2\delta_1^2 - 4q\delta_1\mu_2^2 + 4\mu_1\mu_2^3}}{2\mu_2}, \\
\lambda_3 = -\frac{\delta_1\mu_2\mu_3 - q\delta_1\alpha + \alpha\mu_1\mu_2}{\mu_2\delta_1}, \quad \lambda_4 = -\beta, \quad \lambda_5 = -\mu_5.
\end{aligned}
\tag{66}
$$

Since $R_e(\lambda_1) < 0,\ R_e(\lambda_2) < 0, R_e(\lambda_3) < 0, R_e(\lambda_4) < 0,\ R_e(\lambda_5) < 0$, then it is asymptomatically stable.

4.2.3. Equilibrium point of VSEIR model for North Sumatera Indonesia

Parameters of this model are variously determined. Some parameters are taken from annually Health fact [1] and supplement data from previous study by Momoh et al. [4]. The parameter is known as $q = 0.11, \mu_1 = 0.1, \mu_2 = 0.133, \mu_3 = 0.14, \mu_5 = 0.133, \delta_1 = 0.675, \delta_2 = 0.544, \delta_3 = 0.644, \delta_4 = 0.7$ and $\mu_{TB} = 0.05$. The equilibrium points were determined using VSEIR model with set parameters for the state of north Sumatera.

$$
\frac{du}{dt} = 0.15 - 0.1u - 0.675uw, \tag{67}
$$

$$\frac{dw}{dt} = 0.675\,uw - 0.03w - 0.544wx, \tag{68}$$

$$\frac{dx}{dt} = 0.544wx - 0.04x - 0.644xy \tag{69}$$

$$\frac{dy}{dt} = 0.644xy - 0.904y, \tag{70}$$

$$\frac{dz}{dt} = 0.7y - 0.133z. \tag{71}$$

Then to obtain the critical point, Eqs. (67) to (71) are equal to zero, as below

$$0.15 - 0.1u - 0.675uw = 0, \tag{72}$$

$$0.675\,uw - 0.03w - 0.544wx = 0, \tag{73}$$

$$0.544wx - 0.04x - 0.644xy = 0, \tag{74}$$

$$0.644xy - 0.904y = 0. \tag{75}$$

$$0.7y - 0.133z = 0. \tag{76}$$

The equilibrium points of VSEIR model are

$$(u, w, x, y, z) = (V, S, E, I, R) = (1.11,0,0,0,0) \tag{77}$$

and

$$(u, w, x, y, z) = (0.197037037, 0.686438318, 0, 0\ ,0). \tag{78}$$

The second equilibrium points are $(0.197037037, 0.686438318, 0, 0\ ,0)$, whereas, other points are not logic for equilibrium points because any negative point indeed. By using MAPLE, the eigenvalue (λ) are investigated; as follow: at equilibrium point $(1.11,0,0,0,0)$, eigen values $\lambda_1 = 0.61625, \lambda_2 = -0.904, \lambda_3 = -0.1, \lambda_4 = -0.14$ and $\lambda_5 = -0.133$. At equilibrium point $(0.197037037, 0.686438318, 0, 0\ ,0)$ has eigen value, such as $\lambda_1 = 0.233422445, \lambda_2 = -0.1329999996, \lambda_3 = -0.1485765736, \lambda_4 = -0.4147692913$ and $\lambda_5 = -0.9040000006$.

4.2.4. VSEIR model for stability analysis in North Sumatera Indonesia

Result of VSEIR model in searching the equilibrium point and eigenvalues are discussed in Table 1. Based on the table, the equilibrium points of VSEIR model in North Sumatera is saddle points. It indicates that no occurrence of infected Tuberculosis since there are no infected human when 1.11 human are suspected of TB. Every human in the population are health and there aren't human that infected by virus.

Table (1). Equilibrium points and Stability Analysis

Equilibrium points (V, S, E, I, R)	Eigen values	Stability analysis
$(1.11,0,0,0,0)$	Real and opposite sign	Saddle point
$(0.197037037, 0.686438318, 0, 0\ ,0)$	Real and opposite sign	Saddle point

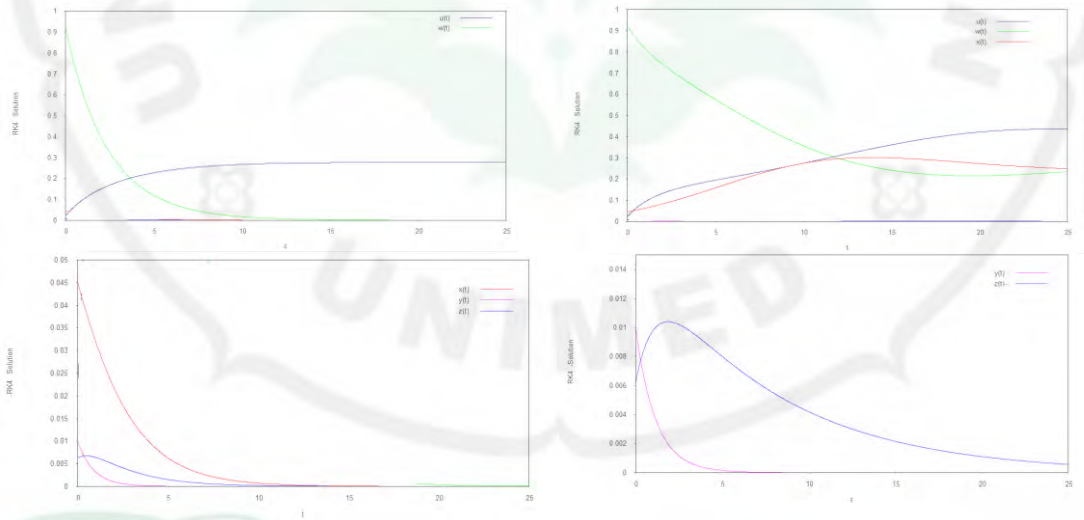
4.2.5. VSEIR Model of tuberculosis in North Sumatera

Several investigations have done for VSEIR model of Tuberculosis in this paper. This model is suitable for the state of North Sumatera. Some parameters are taken from annually Health fact [1] and supplement data from previous study by Momoh et al. [4]. The parameter is

known as $q = 0.11, \mu_1 = 0.1, \mu_2 = 0.133, \mu_3 = 0.14, \mu_5 = 0.133, \delta_1 = 0.675, \alpha = 0.544, \rho = 0.644, \delta_4 = 0.7$ and $\mu_{TB} = 0.05$. The initial polulation is reported by health department of North Sumatera [3]. Table 1 show the stability analysis looking from equilibrium and eigenvalues. From table, all equilibrium points were saddle point. Determining a breeding rate on VSEIR is important in Epidemiology problem since this rate shows the infected population will occur in main state. The determination of R_0 was proposed by [7]. $R_0 > 1$ implies that endemic steady state is stable and the infection for a population. $R_0 \leq 1$ implies that the uninfected steady state is stable. The other hand, the tuberculosis infects an individual, if $R_0 > 1$, otherwise.

$$R_0 = \frac{q\delta_1\beta - \mu_1\mu_2\mu_4}{\mu_1\mu_2(\delta_4 + \mu_{TB})} \tag{79}$$

A simulation carried out using MAPLE. Stability analysis tended to asymptotically stable. Illustration of the dynamics of each epidemic giving in Figure 1(a) and 1(b). Figure 1a shows the probability of vaccination, susceptible, exposed, infected and recovery individuals that have $R_0 \leq 1$. It shows that North Sumatra is free disease area of TB. Otherwise, in Figure 1 (b), $R_0 > 1$, it indicates North Sumatera is epidemic area of TB.



(a) dynamic system for $R_0 \leq 1$ (b) dynamic system for $R_0 > 1$

Figure 8. Transmission of Tuberculosis with initial condition

4.3. Formulation As An Optimal Control Problem of SEIR Model

The epidemiology model is of type SEIR [4] which has four classes. The class, *S* represents the susceptible who do not have the disease, *E* represents the exposed who are infected but are yet to show any sign of symptoms, *I* represents the infective who have the disease and can transmit it to others, *R*, denotes the recovered class of those who went through infection and emerge with permanent or temporary infection-acquired immunity. In this paper, we only

consider an SIER model [1]. We assume that the treatment in rate s, the recruitment due to immigration in rate γ, the slow and fast progression in rate ϑ, ρ , respectively was omitted. The immunity in the class R may not be permanent and the class R should be followed by the class S of individuals who regain their susceptibility when temporary immunity ends.

Let $S(t)$ represent the number of susceptible individuals, $E(t)$ represent exposed individuals, $I(t)$ the number of infective ones and $R(t)$ the number of recovered ones, all at time. We also denote the total number of individuals by $N, N = S + E + I + R$, and in [4] assume that all new births enter the susceptible class S. Therefore we consider the following dynamics:

$$\dot{S} = \pi - \beta IS - \mu S \tag{80}$$

$$\dot{E} = \beta IS - \mu E, \tag{81}$$

$$\dot{I} = DIS + DE - (\mu + \mu_T)I, \tag{82}$$

$$\dot{R} = \varepsilon I - sI - \beta IR - \mu R, \tag{83}$$

Thus, the controlled mathematical model is written as follow

$$\dot{S} = \pi - \beta IS - \mu S - Su, \tag{84}$$

$$\dot{E} = \beta IS - \mu E - Eu, \tag{85}$$

$$\dot{I} = DIS + DE - (\mu + \mu_T)I - Iv, \tag{86}$$

where π, represents the rate of recruitment of susceptible individuals, βIS, represents the loss of the number of susceptible individuals that are being infected by individuals from class I with the parameter β standing for the average number of adequate contacts (i.e., contacts sufficient for transmission) of a person per unit of time.

The last term of equation (84), Su represents the effect of vaccination, and it is assumed that vaccination removes the fraction Su of individuals from the class S and makes them resistent. In equation (85), the E decreased by natural death of the Eu, and individual class E to class is infectious (I) and increased as a result of disease transmission βIS, the last term Eu, represents the effect of vaccination of E. The variabel u is a control that represents the rate at which susceptible individuals are vaccinated. It takes values in a compact interval, $0 \leq u \leq u_{max}$. In the I, Eq. (86), D, represents detection rate of TB . The additional outflow Iv is related to the cure of infected individuals due to treatment and v represents the rate at which infectious individuals are treated at each time period, the second control in the model with values in the interval $0 \leq v \leq\leq v_{max}$.

Thus there are two possible mechanisms as controls: immunization of the susceptible and exposed individuals and treatment of the infected ones. These actions are modelled by the two controls u dan v that for mathematical reasons are taken as Lebesque-measurable

functions. The action of both controls enriches the class R of the recovered individuals by removing them from the class of susceptible and infected ones, respectively. The class R is defined as $R = N - I - S - E$. For the model to be realistic, we need to make sure that all the variables including R remain positive. The initial numbers of individuals in each of the populations are positive numbers denoted by

$$N(0) = N_0, S(0) = S_0\ , E(0) = E_0\ \text{ and }\ I(0) = I_0. \tag{87}$$

Note that if there are no infected individuals initially, $I_0 = 0$, I remains identically zero. The model, thus don't represent the on the set of infection, but only its course. From biological considerations, a closed set

$$Q = \{(S, E, I, R): 0 < S, 0 < E, 0 < I, S + E + I + R < N\},$$

where $\mathbb{R}^4$, denote the non-negative cone and its lower dimensional faces. It can be verified that Q is posively invariant with respect to (1-4). We denote by ∂Q and $\dot{Q}$ the boundary and the interior of Q.

Let the population sizes of all there classes, S_0, E_0, I_0 and R_0 are given, find the best strategy in terms of combined efforts of vaccination and treatment that would minimize the number of people who die from the infection while at the same time also minimizing the cost vaccination and treatment of the population.

In this paper, we consider the following objective for a fixed terminal time T:

$$J(u, v) \int_0^T aE(t) + bI(t) + cu(t) + dv(t)dt \tag{88}$$

The first term in the objective, $aE(t)$ represents the number of exposed who are infected but are yet to show any sign of symptoms at time t, $bI(t)$, represents the number of people who are exposed and infected at time t and are taken as b measure for the deaths associated with the outbreak. The terms, $cu(t)$ and $dv(t)$ represent the cost of vaccination and treatment, respectively, and are assumed to be proportional to the vaccination and treatment rates.

We shall apply methods of geometric optimal control theory to analyze the relations between optimal vaccination and treatment schedules. These techniques become more transparent if the problem is formulated as a Mayer –type optimal control problem : that is , one where we only minimize a penalty term at the terminal point. Such a structure can easily be achieved at the cost of one more dimension if the objective is adjoined as an extra variable. Defining

$$\dot{Z} = aE + bI + cu + dv, \qquad Z(0) = 0. \tag{89}$$

We therefore consider the following optimal control problem. For a fixed terminal time , minimize the value $Z(T)$ subject to the dynamics

$$\dot{Z}\ \dot{S} = aE + bI + cu + dv, \qquad Z(0) = 0, \tag{90}$$
$$\dot{S} = \pi - \beta IS - \mu S - Su \qquad S(0) = 0, \tag{91}$$
$$\dot{E} = \beta IS - \mu E - Eu, \qquad E(0) = 0, \tag{92}$$
$$\dot{I} = DIS + DE - (\mu + \mu_T)I - Iv, \qquad I(0) = 0, \tag{93}$$

Over all Lebesque measurable function

$$u: [O, T] \to [0, u_{max}] \quad \text{and} \quad v: [0, T] \to [0, v_{max}]$$

Introducing the state $\dot{x} = (Z, S, E, I)^T$, the dynamics of the system is a multiinput control-affine system of the form

$$\dot{x} = f(x) + g_1(x)u + g_2(x)v, \tag{94}$$

with drift vector field f given by

$$f(x) = \begin{pmatrix} aE + bI \\ \pi - \beta IS - \mu S \\ \beta IS - \mu E \\ DIS + DE - (\mu + \mu_T)I \end{pmatrix}, \tag{95}$$

and control vector fields g_1 and g_2 given by

$$g_1 = \begin{pmatrix} c \\ -S \\ -E \\ 0 \end{pmatrix} \quad \text{and} \quad g_2(x) = \begin{pmatrix} d \\ 0 \\ 0 \\ -I \end{pmatrix}. \tag{96}$$

We call an admissible control pair (u, v) with corresponding solution x a controlled trajectory of the system.

4.4. Necessary Conditions For Optimality of SEIR Model

First-order necessary conditions for optimality of a controlled trajectory by the *Pontryagin maximum principle* [4,15] : For a row-vector $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4) \epsilon (\mathbb{R}^4)$, we define the Hamiltonian $H = H(\lambda, x, u, v)$ as the dot product, $\langle ., . \rangle$ of the row vector λ with the column vector that defines the dynamics, that is

$$\begin{aligned} H &= \langle \lambda, f(x) + g_1(x)u + g_2(x)v \rangle \\ &= \lambda_1(aE + bI + cu + dv) + \lambda_2(\pi - \beta IS - \mu S - Su) + \lambda_3(\beta IS - \mu E - Eu) \\ &\quad + \lambda_4(DIS + DE - (\mu + \mu_t)I - Iv). \end{aligned} \tag{97}$$

Then, if (u_*, v_*) is an optimal control defined over the interval $[0, T]$ with corresponding trajectory $x_* = (Z_*, S_*, E_*, I_*)^T$, there exists an absolutely continuous co-vector, $\lambda: [0, T] \to (\mathbb{R}^4)^*$, such that following conditions hold [6]

(a) λ satisfies the adjoin equation (written as row vector and with D_f and D_{gi} denoting the Jacobian matrices of the partial derivatives)

$$\dot{\lambda} = -\lambda(Df(x_*) + Dg_1(x_*)u_* + Dg_2(x_*)v_*), \tag{98}$$

with terminal condition

$$\lambda(T) = \left(\frac{\pi}{\mu}, \quad 0, \quad 0, \quad 0\right) \tag{99}$$

(b) for almost every time $t\epsilon[0, T]$ the optimal controls $\big(u_*(t), v_*(t)\big)$ minimize the Hamiltonian along $\big(\lambda(t), x_*(t)\big)$ over the control set $[0, u_{max}] \times [0, v_{max}]$ and,

(c) the Hamiltonian is constant along the optimal solution.

We call a pair $\big(x,(u,v)\big)$ consisting of admissible controls (u,v) with corresponding trajectory x for wich there exist multipliers λ such that the conditions of the Maximum Principle are satisfied an *external* (pair) and the triple $(x,(u,v),\lambda)$ is an external lift. Note that the dynamics does not depend on the auxiliary variable Z and thus by the adjoint equation (6) the multiplier λ_1 is constant; by the terminal condition (20) , it is thus given by $\lambda_1(t) \equiv \frac{\pi}{\mu}$. In particular, the overall multiplier $\lambda(t)$ is never zero. For almost any time t, the optimal controls $\big(u_*(t),v_*(t)\big)$ minimize the Hamiltonian $H(\lambda(t),x_*(t),u,v)$ over the compact interval $[0,u_{max}]\times[0,v_{max}]$. Since H is linear in the controls, this minimization problem splits into separate one-dimensional problems that can easily be solved. Defining the so-called *switching functions* Φ_1 and Φ_2 as

$$\Phi_1(t) = \langle\lambda(t).\, g_1\big(x_*(t)\big)\rangle = c - \lambda_3(t)S_*(t) \tag{100}$$

and

$$\Phi_2(t) = \langle\lambda(t).\, g_2\big(x_*(t)\big)\rangle = d - \lambda_4(t)I_*(t) \tag{101}$$

It follows that the optimal controls satisfy

$$u_*(t) = \begin{cases} 0 & if \quad \Phi_1(t) > 0 \\ u_{max} & if \quad \Phi_1 < 0 \end{cases} \quad \text{and} \quad v_*(t) = \begin{cases} 0 & if \quad \Phi_2(t) > 0 \\ v_{max} & if \quad \Phi_2(t) < 0 \end{cases}$$

The minimum condition alone does determine the controls at times when $\Phi_1(t) = 0$ if $\Phi_1(\tau) = 0$, but $\Phi_1(\tau) \neq 0$, then the control switches between the value 0 and its maximum value depending on the sign of $\dot{\Phi}\iota(\tau)$. Controls with this property are called bang-bang controls and we refer to the constant controls with values in the endpoints of the control intervals as *bang* controls. The other extreme occurs when a switching function vanishes over an open interval. In this case also derivatives of $\Phi_1(t)$ must vanish and this typically allows to compute such a control. Controls of this kind are called *singular* [6]. While the name might give impression that these controls are less important, quite the contrary is true. Singular controls (if they exist) tend to be either that best (minimizing) or the worst (maximizing) strategies and in either case they are essential in determining the structure of optimal controls. This typically needs to be synthesized from bang and singular controls through an analysis of the switching function. Thus singular controls generally play a major role in a synthesis of optimal controlled trajectories and this paper we analyse their existence and local for the problem in Eqs. (90)-(93).

An essential tool in this analysis is the Lie bracket of vector fields which naturally arises in the formulas for the derivatives of the switching function. Give two differentiable vector fields f dan g defined on a common open subset of $\mathbb{R}^n$, their *Lie bracket* can be defined as

$$[f,g](x) = Dg(x)f(x) - Df(x)g(x) \tag{102}$$

The Lie-bracket is anti-commutative, i.e.,$[f,g] = -[g,f]$, and for arbitrary vector fields f,g and h it satisfies the Jacobi identity [5]

$$[f,[g,h]]+[g,[h,f]]+[h,[f,g]]\equiv 0 \tag{103}$$

The following result provides an elegant and important framework for efficient computations of the derivatives of the switching functions. It is easily verified by a direct computation.

4.5. The Structure Of Singular Controls of SEIR Model

We investigate the existence and local optimality of singular controls for the system in Eqs (90)-(93). By Propositions 4 in Eq. (32)-(33) the derivatives of the switching functions $\Phi_1(t)=\langle\lambda(t),g_1(x(t))\rangle$ and $\Phi_2(t)=\langle\lambda(t),g_2(x(t))\rangle$ are given by

$$\dot{\Phi}_1(t)=\langle\lambda(t),[f+\dot{g}_1u+g_2v,g_1]x(t)\rangle \tag{104}$$

$$\dot{\Phi}_2(t)=\langle\lambda(t),[f+\dot{g}_1u+g_2v,g_2]x(t)\rangle \tag{105}$$

By anti-commutative of the Lie bracket $[g_i,g_i]\equiv 0$ and a simple computation verifies that the control vector fields g_1 and g_2 commute, i.e., $[g_1,g_2]\equiv 0$ as well. We thus have that

$$\dot{\Phi}_1(t)=\langle\lambda(t),[f,g_1](x,(t))\rangle \quad \text{and} \quad \dot{\Phi}_2(t)=\langle\lambda(t),[f,g_2](x,(t))\rangle.$$

Elementary calculations verify that

$$[f,g_1](x)=\begin{pmatrix} aE \\ -\pi \\ 0 \\ DIS+DE \end{pmatrix} \quad \text{and} \quad [f,g_2](x)=\begin{pmatrix} bI \\ -\beta IS \\ \beta IS \\ -DE \end{pmatrix}.$$

We first analyse the control, i.e., vaccinations schedules. Applying Propositions 2 once more to $\dot{\Phi}_1$, it follows that

$$\ddot{\Phi}_1(t)=\langle\lambda(t),[f+g_1u+g_2v,[f,g_1]](x(t))\rangle \tag{106}$$

A direct calculation shows that g_2 and $[f,g_1]$ commute as well, $[g_2,[f,g_1]]\equiv\begin{pmatrix} 0 \\ 0 \\ 0 \\ ED \end{pmatrix}$, and that

$$[g_1,[f,g_1]](x)=\begin{pmatrix} -aE \\ -\pi \\ 0 \\ -DSI-DE \end{pmatrix}.$$

The relation

$$\dot{\Phi}_1\equiv-\lambda_1(t)aE(t)-\lambda_2(t)\pi(t)+\lambda_4(t)(DSI+DE)(t)\equiv 0 \tag{107}$$

Implies that

$$\langle\lambda(t),[g_1,[f,g_1]](x(t))\rangle=-2\lambda_4(t)(DSI+DE)(t)$$

And $\Phi_1(t)=c-\lambda_3(t)S(t)\equiv 0$ gives that $\lambda_3(t)$ must be positive along a singular are. Hence we have that

$$\langle\lambda(t),[g_1,[f,g_1]](x(t))\rangle=-2\lambda_4(t)(DSI+DE)(t)<0$$

Singular controls of this type, i.e., for which $\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle$ does not vanish, are said to be of order 1 and it is a second-order necessary condition for minimallity, the so-called *Legendre-Clebsh condition,* that this quantity be negative [9] . Thus for this model singular controls u are locally optimal. Furthermore, in this case, we taking into account that $[g_2, [f, g_1]] \equiv \begin{pmatrix} 0 \\ 0 \\ 0 \\ DE \end{pmatrix}$, we can compute the singular control as

$$u_{sin}(t) = -\frac{\langle \lambda(t), [f, [f, g_1]](x(t)) \rangle}{\langle \lambda(t), [g_1, [f, g_1](x(t))] \rangle} \tag{108}$$

Here,

$$[f, [f, g_1]](x) = \begin{pmatrix} a\beta IS - a\mu E - bDIS - bDE \\ -\pi\beta I - \pi\mu + \pi\beta S^2 DI + \pi\beta SDE \\ \pi\beta I - \beta S^2 DI - \beta SDE \\ 2DI\pi - DI^2\beta S - DI\mu S + D\beta IS + \mu_T \end{pmatrix} \tag{109}$$

Since $\langle \lambda(t), [f, g_1](x(t)) \rangle \equiv 0$, it follows from (31) that

$$\mu_{sin}(t) = -\frac{1}{2\lambda_2 \pi}\left[-\lambda_2(a\beta IS + bDIS + bDE) + \psi(t)(\lambda_2 - \lambda_3) - \mu - \frac{\lambda_4}{2\lambda_2}\left(\frac{\mu + \mu_T}{\pi}\right) DE\right], \tag{110}$$

where, $\psi(t) = \beta I\pi - \pi\beta S^2 DI - \pi\beta SDE$. Therefore, we obtain the following result

Proposition 5. *A singular control u is of order* 1 *and satisfies the Legendre-Clebsch condition for minimality. The singular control is given as a function depending both on the state and the multiplier in the form*

$$\mu_{sin}(t) = -\frac{1}{2\lambda_2 \pi}\left[-\lambda_2(a\beta IS + bDIS + bDE) + \psi(t)(\lambda_2 - \lambda_3) - \mu - \frac{\lambda_4}{2\lambda_2}\left(\frac{\mu + \mu_T}{\pi}\right) DE\right]$$

where $\psi(t) = \beta I\pi - \pi\beta S^2 DI - \pi\beta SDE$.

For treatment control, we define the switching function as

$$\Phi_2(t) = \langle \lambda(t), g_2(x(t)) \rangle \tag{111}$$

By using proposition 2, the first derivative of Eq. 34 we have

$$\dot{\Phi_2}(t) = (\lambda(t), [f, g_2](x)(t)) = \lambda_1 bI - \lambda_2 \beta IS + \lambda_3 \beta IS - \lambda_4 DE \tag{112}$$

As we know, to check the optimally Eq 111, Eq. 112 will be zero, we have

$$(\lambda(t), [f, g_2](x)(t)) = \lambda_1 bI - \lambda_2 \beta IS + \lambda_3 \beta IS - \lambda_4 DE = 0. \tag{113}$$

Hence, we have

$$\ddot{\Phi}_2 = (\lambda, f, [f, g_2]) = -\lambda_1(bI\mu - bDIS - 2bDE + a\beta IS) - \lambda_2(\beta S^2 DI + \beta SDE + \beta^2 I^2 S - \pi\beta SDE) + \lambda_3(\pi\beta I - \mu\beta IS + \beta S^2 DI + 2\beta SDE) - \lambda_4(2D\beta IS - DI^2\beta S - D^2 ES + 2DE\mu_T) < 0$$

It also shows a second-order necessary condition for minimallity, the so-called *Legendre-Clebsh condition,* that this quantity be negative [9] . Thus for this model singular controls u are locally optimal. Furthermore, in this case,and taking

$$v_{sin}(t) = -\frac{\langle \lambda(t), [f, [f, g_2]](x(t)) \rangle}{\langle \lambda(t), [g_2, [f, g_2]](x(t)) \rangle}. \quad (114)$$

Here, we have

$(\lambda, f, [f, g_2]) = -\lambda_1(bI\mu - bI\mu_T - bDIS - 2bDE + a\beta IS) - \lambda_2(\beta S^2 DI + \mu_T\beta IS + \beta SDE + \beta^2 I^2 S - \pi\beta SDE) + \lambda_3(\pi\beta I - \mu\beta IS + \beta S^2 DI - \mu_T\beta IS + 2\beta SDE) - \lambda_4(2D\beta IS - DI^2\beta S - D^2 ES - DE\mu_T)$ and $\left(\lambda\left(g_2(f, g_2)\right)\right) = -\lambda_1 bI - \lambda_4 DE$

we can compute the singular control as

$$v_{sin}(t) = \frac{1}{-(\lambda_1 bI + \lambda_4 DE)}(\lambda_1 bDIS + 2\lambda_1 bDE - \lambda_1 bI\mu - \lambda_1 bI\mu_T - \lambda_1 a\beta IS - \lambda_2\beta S^2 DI - \lambda_2\beta SDE + \lambda_2\beta SI\mu_T - \lambda_2\beta^2 I^2 S + \lambda_2\pi\beta SDE + \lambda_3\pi\beta I - \lambda_3\mu\beta IS + \lambda_3\beta S^2 DI + 2\lambda_3\beta SDE + \lambda_3\beta SI\mu_T - 2\lambda_4 D\beta IS + \lambda_4 DI^2\beta S + \lambda_4 D^2 ES - \lambda_4 DE\mu_T) \quad (115)$$

Therefore, we obtain the following result:

Proposition 6. *The control v is singular.*

4.6. FORMULATION AS AN OPTIMAL CONTROL PROBLEM OF VSIR MODEL

Our aim is to solve the following problem: firstly, we define the given initial population sizes of all four classes, V, S, I, and R. Find the best strategy in terms of combined efforts of vaccination and treatment that would minimize the number of people who die from the infection while at the same time, also minimizing the cost of vaccination and treatment of the population. For tuberculosis since the immunity is waning so the immunity is not permanent, and in this paper we splited the model of vaccinated control becomes c_1 and c_2, where c_1 and c_2 denote as cost for vaccinated child and adult ones, respectively for a fixed terminal time T, we consider the following objective:

$$J(u, v) = \int_0^T aV(t) + bI(t) + (c_1 + c_2)u(t) + dv(t)dt \quad (116)$$

The first term in the objective, *aV(t)*, represent infants individual with passive immunity at time t, $aI(t)$, represents the number of people who are infected at time t and is taken as a

measure for the deaths associated with the outbreak. The terms, $(c_1 + c_2)u(t)$ and $dv(t)$ represent the cost of vaccination and treatment, respectively. For a fixed terminal time T, minimize the value $Z(T)$subject to the dynamics, similar to [3].

$$\dot{Z} = aV + bI + (c_1 + c_2)u + dv \qquad Z(0) = 0 \qquad (117)$$
$$\dot{V} = Q - (\mu + \delta)V - Vu \qquad V(0) = 0 \qquad (118)$$
$$\dot{S} = \delta V - (\mu + \beta I)S + \theta S - Su \qquad S(0) = 0 \qquad (119)$$
$$\dot{I} = \beta SI - (\mu + \mu_m + \psi)I - Iv \qquad I(0) = 0 \qquad (120)$$

Over all Lebesgue measurable functions

$$u: [0, T] \to [0, u_{max}] \text{ and } v: [0, T] \to [0, v_{max}]$$

Introducing the state $x = (Z, V, S, I)^T$, the dynamics of the system is a multi input control-affine system of the form

$$\dot{x} = f(x) + g_1(x)u + g_2(x)v$$

With drift vector field f given by

$$f(x) = \begin{pmatrix} aV + bI \\ Q - (\mu + \delta)V \\ \delta V - (\mu + \beta I)S + \theta S \\ \beta IS - (\mu + \mu_m + \psi)I \end{pmatrix}$$

and control vector fields g_1 and g_2 given by

$$g_1(x) = \begin{pmatrix} c_1 + c_2 \\ -V \\ -S \\ 0 \end{pmatrix} \text{ and } g_2(x) = \begin{pmatrix} d \\ 0 \\ 0 \\ -I \end{pmatrix}.$$

We call an admisisible control pair (u, v) with corresponding solution x a *controlled trajectory* of the system.

4.7 NECESSARY CONDITIONS FOR OPTIMALITY OF VSIR MODEL

Let a first order necessary conditions for optimality of a controlled trajectory are given by *Pontryagin maximum* principle and let a row vector $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4)\epsilon(\mathbb{R}^4)^*$, we defined the Hamiltonian $H = H(\lambda, x, u, v)$ as the dot product, $\langle ., . \rangle$, of the row vector λ with the column vector that defines the dynamics, as necesssary conditions for optimality given by the *Pontryagin maximum principle* [2,6], that is

$$H = \langle \lambda, f(x) + g_1(x)u + g_2(x)v \rangle$$

$$= \lambda_1(aV + bI + (c_1 + c_2)u + dv) + \lambda_2(Q - (\mu + \delta)V - V_u) + \lambda_3(\delta V + \theta S - (\mu + \beta I)S - S_u) + \lambda_4(\beta IS) - (\mu + \mu_m + \psi)I - Iv)$$

Then, if (u_*, v_*) is an optimal control defined over the interval $[0, T]$ with corresponding trajectory $x_* = (Z_*, V_*, S_*, I_*)^T$, there exists an absolutely continuous co-vector, $\lambda: [0, T] \rightarrow (\mathbb{R}^4)^*$ such that the following conditions hold:

(a) λ satisfies the adjoint equations (written as a row vector and Df and Dg_i denoting the Jacobian matrices of the partial derivatives)

$$\dot{\lambda} = -\lambda\ (Df(x_*) + Dg_1(x_*)u_* + Dg_2(x_*)v_*) \tag{121}$$

With terminal condition

$$\lambda(T) = \left(\frac{Q}{\mu + \delta}, \frac{\delta Q}{(\mu + \delta)(\mu - \theta)}, 0, 0\right) \tag{122}$$

(b) for almost every time $t\epsilon[0, T]$ the optimal controls $(u_*(t), v_*(t))$ minimize the hamiltonian along $(\lambda(t), x_*, (t))$ over the control set $[0, u_{max}]x[0, v_{max}]$ and
(c) the Hamiltonian is constant along the optimal solution.

We call a pair $\big(x, (u, v)\big)$ consisting of admissible controls (u, v) with corresponding trajectory x for which there exist multipliers λ such that the conditions of the maximum Principle are satisfied an *extremal* (pair) and the triple $(x, (u, v), \lambda)$ is an extremal lift (to the cotangent bundle).

Note that the dynamics does not depend on the auxiliary variable Z and thus by the adjoint equation (9) the multiplier λ_1 is constant; by the terminal condition (10) it is thus given by $\lambda_1(t) \equiv \frac{Q}{\mu+\delta}$. In particular, the overall multiplier $\lambda(t)$ is never zero. For almost any time t, the optimal controls $(u_*(t), v_*(t))$ minimize the Hamiltonian $H(\lambda(t), x_*(t), u, v)$ over the compact interval $[0, u_{max}]x[0, v_{max}]$. Since H is linear in the controls, this minimization problem splits into two separate one-dimensional problems that can easily be solved. Defining the so-called *switching functions* Φ_1 and Φ_2 like in [7] as

$$\Phi_1(\mathrm{t}) = \langle \lambda(\mathrm{t}), \mathrm{g}_1(\mathrm{x}_*(\mathrm{t})) \rangle = (c_1 + c_2) - \lambda_2(t)V_*(t) - \lambda_3(\mathrm{t})\mathrm{S}_*(\mathrm{t})$$

and

$$\Phi_2(\mathrm{t}) = \langle \lambda(\mathrm{t}), \mathrm{g}_2(\mathrm{x}_*(\mathrm{t})) \rangle = d - \lambda_4(\mathrm{t})\mathrm{I}_*(\mathrm{t})$$

it follows that the optimal controls satisfy

$$u_*(t) = \begin{cases} 0 & if\ \Phi_1(t) > 0 \\ u_{max} & if\ \Phi_1(t) < 0 \end{cases} \text{ and } v_*(t) = \begin{cases} 0 & if\ \Phi_1(t) > 0 \\ v_{max} & if\ \Phi_1(t) < 0 \end{cases}.$$

The minimum condition alone does not determine the control at times when $\Phi_i(t) = 0$. If $\Phi_i(\tau) \neq 0$, then the control switches between the value 0 and its maximum value depending on the sign of $\dot{\Phi}_i(\tau)$. Controls with this property are called bang-bang controls and we refer to the constant controls with values in the andpoints of the control intervals as *bang* controls. The other extreme occurs when a switching function vanishes over an open interval. In this case all derivatives of $\dot{\Phi}_i(t)$ must vanish and this typically allows to compute such a control. Controls of this kind are called *singular* [9]. While the name (which has historical reasons) might give the impression that these controls are less important, quite the contrary is true. According Singular controls (if they exist) tend to be either the best (minimizing) or the worst (maximizing) strategies and in either case they are essential in determining the structure of optimal controls. These typically then need to be synthesized from bang and singular controls through an analysis of the switching function. Thus singular controls generally play a major role in a synthesis of optimal controlled trajectories and in this paper we analyze their existence and loocal optimality for the problem in (117) - (120).

An essential tool in this analysis is the Lie bracket of vector fields which naturally arises in the formulas for the derivatives of the switching function. Given two differentiable vector fields f and g defined on a common open subset of $\mathbb{R}^n$, their *Lie bracket* can be defined as

$$[f, g](x) = Dg(x)f(x) - Df(x)g(x)$$

The Lie-bracket is anti-commutative, i.e., $[f, g] = -[g, f]$, and for arbitary vector fields f, g and h it satisfies the Jacobi identity[8]

$$\big[f, [g, h]\big] + \big[g, [h, f]\big] + [h, [f, g]] \equiv 0 \tag{123}$$

The following result provides an important framework for efficient computations of the derivatives of the switching functions. It is easily verified by a direct *computation*.

4.8 THE STRUCTURE OF SINGULAR CONTROLS OF VSIR MODEL

Now, we start by investigating the existence and local optimality of singular controls for the system in (117) - (120). By proposition 4 the derivatives of the switching functions $\Phi_1(t) = \langle \lambda(t), g_1(x(t)) \rangle$ and $\Phi_2(t) = \langle \lambda(t), g_2(x(t)) \rangle$ are given by

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f + g_1 u + g_2 v, g_1](x(t)) \rangle$$
$$\dot{\Phi}_2(t) = \langle \lambda(t), [f + g_1 u + g_2 v, g_2](x(t)) \rangle$$

By anti-commutativity of the Lie bracket $[g_i, g_i] \equiv 0$ and a simple computation verifies that the control vector fields g_1 and g_2 commute, i.e., $[g_1, g_2] \equiv 0$ as well. We thus have that

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f, g_1](x(t)) \rangle \text{ and } \dot{\Phi}_2(t) = \langle \lambda(t), [f, g_2](x(t)) \rangle$$

Elementary calculations verify that

$$[f, g_1](x) = \begin{pmatrix} aV \\ -Q \\ 0 \\ \beta SI \end{pmatrix}$$

and

$$[f, g_2](x) = \begin{pmatrix} bI \\ 0 \\ -\beta SI \\ 0 \end{pmatrix}$$

We first analyze the control u, i.e., vaccination schedules. Applying Proposition 2 once more to $\ddot{\Phi}_1$, it follows that

$$\ddot{\Phi}_1(t) = \langle \lambda(t), \big[f + g_1 u + g_2 v, [f, g_1]\big](x(t)) \rangle \tag{124}$$

and

$$\big[g_1, [f, g_1]\big](x) = \begin{pmatrix} -aV \\ -Q \\ 0 \\ -\beta SI \end{pmatrix} \tag{125}$$

The switching function of (13) is

$$\dot{\Phi}_1(t) \equiv \lambda_1(t) aV(t) - \lambda_2(t) Q + \lambda_4(t) \beta S(t) I(t). \tag{126}$$

Implies that

$$\langle \lambda(t), \big[g_1, [f, g_1]\big](x(t)) \rangle = -(2\lambda_1(t) aV(t) + 2\lambda_4(t) \beta S(t) I(t)) \tag{127}$$

and $\Phi_1(\mathrm{t}) = (c_1 + c_2) - \lambda_2(t) V_*(t) - \lambda_3(\mathrm{t}) \mathrm{S}_*(\mathrm{t}) \equiv 0$ gives that $\lambda_2(t)$ and $\lambda_3(t)$ must be positive along a singular arc. Hence we have that

$$\langle \lambda(t), \big[g_1, [f, g_1]\big](x(t)) \rangle = -(2\lambda_1(t) aV(t) + 2\lambda_4(t) \beta S(t) I(t)) < 0.$$

Singular controls of this type , i.e., for which $\langle \lambda(t), \big[g_1, [f, g_1]\big](x(t)) \rangle$ does not vanish, are said to be of order 1 and it is a second-order necessary condition for minimality, the are so called *legendre-Clebsch condition*, that this quantity be negative [9]. Thus for this model singular controls u are locally optimal. Furthermore, we can compute the singular control as

$$u_{sin}(t) = -\frac{\langle \lambda(t), \big[f, [f, g_1]\big](x(t)) \rangle}{\langle \lambda(t), \big[g_1, [f, g_1]\big](x(t)) \rangle} \tag{128}$$

To evaluate the vector fields, this equation can be simplified. A direct, but some what lengthy computation shows

$$[f,[f,g_1]](x) = \begin{pmatrix} 2aQ - aV\mu - a\delta V - b\beta SI \\ -(\mu+\delta)Q \\ \delta Q + \beta^2 S^2 I \\ \beta I\delta V - \mu\beta IS + \theta\beta IS + \beta^2 I^2 S \end{pmatrix}$$

and

$$\begin{aligned} &\langle \lambda(t), [f,[f,g_1]](x(t))\rangle \\ &= \lambda_1(t)\Big((a(2Q - \mu V(t) - \delta V(t)) - b\beta S(t)I(t)\Big) - \lambda_2(t)(\mu+\delta)Q \\ &+ \lambda_3(t)(\delta Q + \beta^2 S^2(t)I(t)) + \lambda_4(\beta I(t)S(t)(\theta + \beta I(t)S(t) - \mu) \\ &+ \beta\delta I(t)V(t)) \end{aligned} \tag{129}$$

we can write

$$[f,[f,g_1]](x) = \mu[f,g_1](x) + \frac{\delta}{2}[g_1,[f,g_1]] + \omega(x),$$

where

$$\omega(x) = \lambda_1(2aQ - a\delta V - b\beta IS) + \lambda_3(\delta Q + \beta^2 S^2 I) + \lambda_4(\delta\beta IV - \beta^2 I^2 S + \beta IS\theta).$$

Since $\langle \lambda(t), [f,g_1](x(t))\rangle \equiv 0$, it follows from (16) that

$$u_{sin}(t) = -\frac{1}{2}\delta + \frac{1}{2}\frac{\omega(x)}{\lambda_1 aV + \lambda_4 \beta IS}$$

Once more using (14), we simplified the second term to $\frac{\omega(x)}{2\lambda_2 Q}$ and we obtain the following result:

Proposition 7. *A singular control u is of order 1 and satisfied the Legendre-Clebsch condition for minimality. The singular control is given as a function depending both on the state and the multiplier in the form*

$$u_{sin}(t) = \frac{1}{2}\left(\frac{\omega(x)}{\lambda_2 Q} - \delta\right).$$

Based on the structure of singular control we apply the same way to analysis treatment control (v). Let switching function Φ_2 give

$$\Phi_2(t) = \langle \lambda(t), g_2(x(t))\rangle$$

The first derivative of Φ_2 is

$$\dot{\Phi}_2(t) = \langle \lambda(t), [f + g_1 u + g_2 v, g_2](x(t))\rangle$$

and the second derivative is given by

$$\ddot{\Phi}_2(t) = \langle \lambda(t), [f, + g_1 u + g_2 v, [f,g_2]](x(t))\rangle.$$

Furthermore, a direct calculation verifies that

$$[g_2,[f,g_2]] = \begin{pmatrix} -bI \\ 0 \\ \beta IS \\ 0 \end{pmatrix} = -[f,g_2](x)$$

Since $g_2$and $[f,g_1`]$ commute, it follows from the Jacobi identity that $[g_1,[f,g_2]] = [g_2,[f,g_1]] \equiv 0$.
we found $\langle \lambda(t),[f,g_2](x(t))\rangle \equiv 0$ and thus also

$$\langle \lambda(t),[g_2,[f,g_2]](x(t))\rangle \equiv 0$$

and $[f,f,g_2]$ and $[g_2,[f,g_2]] \equiv 0$. Thus there is no singular on V, we obtain the following result

Proposition 8. *The control v cannot be singular.*

4.9 FORMULATION AS AN OPTIMAL CONTROL PROBLEM OF VSEIR MODEL

Let the population sizes of all there classes, S_0, E_0, I_0 and $R_0$are given, find the best strategy in terms of combined efforts of vaccination and treatment that would minimize the number of people who die from the infection while at the same time also minimizing the cost vaccination and treatment of the population.

In this paper, we consider the following objective for a fixed terminal time T:

$$J(u,v) = \int_0^T a_1 V + a_2 I(t) + (a_3 + c_3)u(t) + a_4 v(t)dt \qquad (130)$$

The first term in the objective, $aE(t)$ represents the number of exposed who are infected but are yet to show any sign of symptoms at time t, $bI(t)$, represents the number of people who are exposed and infected at time t and are taken as a_2 measure for the deaths associated with the outbreak. The terms, $(a_3 + c_3)u(t)$ and $a_4 v(t)$ represent the cost of vaccination and treatment, respectively, and are assumed to be proportional to the vaccination and treatment rates.

We shall apply methods of geometric optimal control theory to analyse the relations between optimal vaccination and treatment schedules. These techniques become more transparent if the problem is formulated as a Mayer –type optimal control problem : that is , one where we only minimize a penalty term at the terminal point. Such a structure can easily

be achieved at the cost of one more dimension if the objective is adjoined as an extra variable. Defining

$$\dot{Z} = a_1 V + a_2 I + (a_3 + c_3)u + a_4 v, \qquad Z(0) = 0. \tag{132}$$

We therefore consider the following optimal control problem. For a fixed terminal time, minimize the value $Z(T)$ subject to the dynamics

$$\dot{Z} = a_1 V + a_2 I + (a_3 + c_3)u + a_4 v, \qquad Z(0) = 0, \tag{133}$$

$$\dot{V} = qN - \mu_1 V - \delta_1 VS - Vu, \qquad V(0) = 0, \tag{134}$$

$$\dot{S} = \delta_1 VS - \mu_2 S - \delta_2 IS - Su, \qquad S(0) = 0, \tag{135}$$

$$\dot{E} = \alpha S - \mu_3 E - \rho I - Eu, \qquad E(0) = 0, \tag{136}$$

$$\dot{I} = \rho IE - \beta I - Iv, \qquad I(0) = 0, \tag{137}$$

where $\beta = \mu_4 + \mu_{TB} + \delta_4$. Over all Lebesque measurable function

$$u: [O, T] \to [0, u_{max}] \quad \text{and} \quad v: [0, T] \to [0, v_{max}]$$

Introducing the state $\dot{x} = (Z, V, S, E, I)^T$, the dynamics of the system is a multiinput control-affine system of the form

$$\dot{x} = f(x) + g_1(x)u + g_2(x)v, \tag{138}$$

with drift vector field f given by

$$f(x) = \begin{pmatrix} a_1 V + a_2 I \\ Nq - \mu_1 V - \delta_1 SV \\ -\mu_2 S + \delta_1 SV - \alpha SE \\ -\mu_3 E + \alpha SE - \rho IE \\ \rho IE - \beta I \end{pmatrix}, \tag{139}$$

and control vector fields g_1 and g_2 given by

$$g_1 = \begin{pmatrix} a_3 + c_3 \\ -V \\ -S \\ -E \\ 0 \end{pmatrix} \quad \text{and} \quad g_2(x) = \begin{pmatrix} a_4 \\ 0 \\ 0 \\ 0 \\ -I \end{pmatrix}. \tag{140}$$

We call an admissible control pair (u, v) with corresponding solution x a controlled trajectory of the system.

4.10 NECESSARY CONDITIONS FOR OPTIMALITY OF VSEIR MODEL

First-order necessary conditions for optimality of a controlled trajectory by the *Pontryagin maximum principle* [4,15] : For a row-vector $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4)\, \epsilon\, (\mathbb{R}^4)$, we define the Hamiltonian $H = H(\lambda, x, u, v)$ as the dot product, $\langle ., . \rangle$ of the row vector λ with the column vector that defines the dynamics, that is

$$H = \langle \lambda, f(x) + g_1(x)u + g_2(x)v \rangle$$
$$= \lambda_1(a_1 V + a_2 I + (a_3 + c_3)u + a_5 v) + \lambda_2(Nq - \mu_1 V - \delta_1 SV - V) +$$
$$\lambda_3(-\mu_2 S + \delta_1 SV - \alpha SE - S) + \lambda_4(-\mu_3 E + \alpha SE - \rho IE - E) + \lambda_5(\rho IE - \beta I - Iv). \quad (141)$$

Then, if (u_*, v_*) is an optimal control defined over the interval $[0, T]$ with corresponding trajectory $x_* = (Z_*, S_*, E_*, I_*)^T$, there exists an absolutely continuous co-vector, $\lambda: [0, T] \rightarrow (\mathbb{R}^4)^*$, such that following conditions hold [6]

(a) λ satisfies the adjoin equation (written as row vector and with D_f and D_{gi} denoting the Jacobian matrices of the partial derivatives)

$$\dot{\lambda} = -\lambda(Df(x_*) + Dg_1(x_*)u_* + Dg_2(x_*)v_*), \quad (142)$$

with terminal condition

$$\lambda(T) = \left(\frac{q}{\mu_1}, \quad 0, \quad 0, \quad 0\right) \quad (143)$$

(b) for almost every time $t\epsilon[0, T]$ the optimal controls $\big(u_*(t), v_*(t)\big)$ minimize the Hamiltonian along $\big(\lambda(t), x_*(t)\big)$ over the control set $[0, u_{max}] \times [0, v_{max}]$ and,

(c) the Hamiltonian is constant along the optimal solution.

We call a pair $\big(x, (u, v)\big)$ consisting of admissible controls (u, v) with corresponding trajectory x for wich there exist multipliers λ such that the conditions of the Maximum Principle are satisfied an *external* (pair) and the triple $(x, (u, v), \lambda)$ is an external lift. Note that the dynamics does not depend on the auxiliary variable Z and thus by the adjoint equation (6) the multiplier λ_1 is constant; by the terminal condition (20) , it is thus given by $\lambda_1(t) \equiv \frac{\pi}{\mu}$. In particular, the overall multiplier $\lambda(t)$ is never zero. For almost any time t, the optimal controls $\big(u_*(t), v_*(t)\big)$ minimize the Hamiltonian $H(\lambda(t), x_*(t), u, v)$ over the compact interval $[0, u_{max}] \times [0, v_{max}]$. Since H is linear in the controls, this minimization

problem splits into separate one-dimensional problems that can easily be solved. Defining the so-called *switching functions* Φ_1 and Φ_2 as

$$\Phi_1(t) = \langle \lambda(t).\, g_1\big(x_*(t)\big)\rangle = c - \lambda_3(t)S_*(t) \tag{144}$$

and

$$\Phi_2(t) = \langle \lambda(t).\, g_2\big(x_*(t)\big)\rangle = d - \lambda_4(t)I_*(t) \tag{145}$$

It follows that the optimal controls satisfy

$$u_*(t) = \begin{cases} 0 & if \quad \Phi_1(t) > 0 \\ u_{max} & if \quad \Phi_1 < 0 \end{cases} \qquad \text{and} \qquad v_*(t) = \begin{cases} 0 & if \quad \Phi_2(t) > 0 \\ v_{max} & if \quad \Phi_2(t) < 0 \end{cases}$$

The minimum condition alone does determine the controls at times when $\Phi_1(t) = 0$ if $\Phi_1(\tau) = 0$, but $\Phi_1(\tau) \neq 0$, then the control switches between the value 0 and its maximum value depending on the sign of $\dot{\Phi}\iota(\tau)$. Controls with this property are called bang-bang controls and we refer to the constant controls with values in the endpoints of the control intervals as *bang* controls. The other extreme occurs when a switching function vanishes over an open interval. In this case also derivatives of $\Phi_1(t)$ must vanish and this typically allows to compute such a control. Controls of this kind are called *singular* [6]. While the name might give impression that these controls are less important, quite the contrary is true. Singular controls (if they exist) tend to be either that best (minimizing) or the worst (maximizing) strategies and in either case they are essential in determining the structure of optimal controls. This typically needs to be synthesized from bang and singular controls through an analysis of the switching function. Thus singular controls generally play a major role in a synthesis of optimal controlled trajectories and this paper we analyse their existence and local for the problem in Eqs. (118)-(122).

An essential tool in this analysis is the Lie bracket of vector fields which naturally arises in the formulas for the derivatives of the switching function. Give two differentiable vector fields f dan g defined on a common open subset of $\mathbb{R}^n$, their *Lie bracket* can be defined as

$$[f,g](x) = Dg(x)f(x) - Df(x)g(x) \tag{146}$$

The Lie-bracket is anti-commutative, i.e.,$[f,g] = -[g,f]$, and for arbitrary vector fields f, g and h it satisfies the Jacobi identity [5]

$$\big[f,[g,h]\big] + \big[g,[h,f]\big] + \big[h,[f,g]\big] \equiv 0 \tag{147}$$

The following result provides an elegant and important framework for efficient computations of the derivatives of the switching functions. It is easily verified by a direct computation.

4.11 THE STRUCTURE OF SINGULAR CONTROLS OF VSEIR MODEL

We investigate the existence and local optimality of singular controls for the system in Eqs (118)-(122). By Propositions 4 the derivatives of the switching functions $\Phi_1(t) = \langle \lambda(t), g_1(x(t)) \rangle$ and $\Phi_2(t) = \langle \lambda(t), g_2(x(t)) \rangle$ are given by

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f + g_1 u + g_2 v, g_1] x(t) \rangle \tag{147}$$

$$\dot{\Phi}_2(t) = \langle \lambda(t), [f + g_1 u + g_2 v, g_2] x(t) \rangle \tag{148}$$

By anti-commutative of the Lie bracket $[g_i, g_i] \equiv 0$ and a simple computation verifies that the control vector fields g_1 and g_2 commute, i.e., $[g_1, g_2] \equiv 0$ as well. We thus have that $\dot{\Phi}_1(t) = \langle \lambda(t), [f, g_1](x, (t)) \rangle$ and $\dot{\Phi}_2(t) = \langle \lambda(t), [f, g_2](x, (t)) \rangle$.

Elementary calculations verify that

$$[f, g_1](x) = \begin{pmatrix} a_1 V \\ -\delta_1 SV - qN \\ \delta_1 SV - \alpha ES \\ \alpha ES \\ \rho IE \end{pmatrix} \quad \text{and} \quad [f, g_2](x) = \begin{pmatrix} a_3 I \\ 0 \\ 0 \\ -\rho IE \\ 0 \end{pmatrix}.$$

We first analyse the control, i.e., vaccinations schedules. Applying Propositions 2 once more to $\dot{\Phi}_1$, it follows that

$$\ddot{\Phi}_1(t) = \langle \lambda(t), [f + g_1 u + g_2 v, [f, g_1]](x(t)) \rangle \tag{149}$$

A direct calculation shows that g_2 and $[f, g_1]$ commute as well, $[g_2, [f, g_1]] \equiv \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$, and that

$$[g_1, [f, g_1]](x) = \begin{pmatrix} -a_1 V \\ \delta_1 SV - qN \\ \alpha ES - \delta_1 VS \\ -\alpha ES \\ -\rho IE \end{pmatrix}.$$

The relation

$\dot{\Phi}_1 \equiv -\lambda_1(t)(a_1 V) - \lambda_2(t)(\delta_1 SV + qN) + \lambda_3(t)(\delta_1 SV - \alpha ES) + \lambda_4(t)(\alpha ES) + \lambda_5(\rho IE) \equiv 0$

$$\lambda_4(t)(\alpha ES) + \lambda_5(\rho IE) = \lambda_1(t)(a_1 V) + \lambda_2(t)(\delta_1 SV + qN) + \lambda_3(t)(-\delta_1 SV + \alpha ES) \tag{150}$$

Implies that

$$\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle = -2\lambda_1(t)(a_1 V) - 2\lambda_2(\delta_1 SV)$$

And $\Phi_1(t) = \lambda_1(t)(a_3 + c_3) - \lambda_2(t)V - \lambda_3(t)E - \lambda_4(t)I \equiv 0$ gives that $\lambda_3(t)$ must be positive along a singular are. Hence we have that

$$\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle = -2\lambda_1(t)(a_1 V) - 2\lambda_2(\delta_1 SV) < 0$$

Singular controls of this type, i.e., for which $\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle$ does not vanish, are said to be of order 1 and it is a second-order necessary condition for minimality, the so-called *Legendre-Clebsh condition,* that this quantity be negative [9] . Thus for this model singular controls u are locally optimal. Furthermore, in this case, we taking into account that $[g_1, [f, g_1]] \equiv \begin{pmatrix} -a_1 V \\ \delta_1 SV - qN \\ \alpha ES - \delta_1 VS \\ -\alpha ES \\ -\rho IE \end{pmatrix}$, we can compute the singular control as

$$u_{sin}(t) = -\frac{\langle \lambda(t), [f, [f, g_1]](x(t)) \rangle}{\langle \lambda(t), [g_1, [f, g_1](x(t))] \rangle} \tag{151}$$

Here,

$$[f, [f, g_1]](x) = \begin{pmatrix} -a_2 \rho EI + 2a_1 qN - a_1 \mu_1 V \\ -2\delta_1 qNS + \mu_2 \delta_1 SV - \mu_1 qN \\ \alpha \rho ESI + \alpha \mu_3 SE + 2NSq\delta_1 - \mu_1 \delta_1 SV \\ \rho^2 E^2 I - \alpha \mu_2 ES \\ -\rho^2 I^2 E - \mu_3 \rho EI \end{pmatrix} \tag{152}$$

then

$$\mu_{sin}(t) = -\frac{\lambda_1[-a_2 \rho EI + 2a_1 qN - a_1 \mu_1 V] + \lambda_2[-2\delta_1 qNS + \mu_2 \delta_1 SV - \mu_1 qN]}{\lambda_1[-a_1 V] + \lambda_2[\delta_1 SV - qN] + \lambda_3[\alpha ES - \delta_1 VS] - \lambda_4[\alpha ES] - \lambda_5[\rho IE]} \tag{153}$$

$$-\frac{\lambda_3[\alpha \rho ESI + \alpha \mu_3 SE + 2NSq\delta_1 - \mu_1 \delta_1 SV] + \lambda_4[\rho^2 E^2 I - \alpha \mu_2 ES] - \lambda_5[\rho^2 I^2 E + \mu_3}{\lambda_1[-a_1 V] + \lambda_2[\delta_1 SV - qN] + \lambda_3[\alpha ES - \delta_1 VS] - \lambda_4[\alpha ES] - \lambda_5[\rho IE]}$$

Therefore, we obtain the following result

Proposition 9. *A singular control u is of order* 1 *and satisfies the Legendre-Clebsch condition for minimality. The singular control is given as a function depending both on the state and the multiplier in the form*

$$\mu_{sin}(t) = -\frac{\lambda_1[-a_2\rho EI + 2a_1qN - a_1\mu_1 V] + \lambda_2[-2\delta_1 qNS + \mu_2\delta_1 SV - \mu_1 qN]}{\lambda_1[-a_1 V] + \lambda_2[\delta_1 SV - qN] + \lambda_3[\alpha ES - \delta_1 VS] - \lambda_4[\alpha ES] - \lambda_5[\rho IE]}$$

$$-\frac{\lambda_3[\alpha\rho ESI + \alpha\mu_3 SE + 2NSq\delta_1 - \mu_1\delta_1 SV] + \lambda_4[\rho^2 E^2 I - \alpha\mu_2 ES] - \lambda_5[\rho^2 I^2 E + \mu_3\rho EI]}{\lambda_1[-a_1 V] + \lambda_2[\delta_1 SV - qN] + \lambda_3[\alpha ES - \delta_1 VS] - \lambda_4[\alpha ES] - \lambda_5[\rho IE]}$$

For treatment control, we define the switching function as

$$\Phi_2(t) = \langle \lambda(t), g_2\big(x(t)\big)\rangle = a_2 I\lambda_1 - \rho IE\lambda_4 \tag{154}$$

By using proposition 2, the first derivative of Eq. 34 we have

$$\dot{\Phi_2}(t) = (\lambda(t), [f, g_2](x)(t)) = a_2 I\lambda_1 - \rho I\lambda_4 \tag{155}$$

As we know, to check the optimally Eq 34, Eq. 35 will be zero, we have

$$(\lambda(t), [f, g_2](x)(t)) = a_2 I\lambda_1 - \rho I\lambda_4 = 0. \tag{156}$$

Hence, we have

$$\ddot{\Phi}_2 = (\lambda, g_2, [f, g_2]) = 0$$

It also shows a second-order necessary condition for minimallity, the so-called *Legendre-Clebsh condition,* that this quantity be negative [9] . Thus for this model singular controls v are not locally optimal. Therefore, we obtain the following result:

Proposition 10. *The control v is not singular.*

CHAPTER V
CONCLUSION

This research has consider VSEIR model of Tuberculosis having infectious in latent, infected, vaccination and immune period. VSEIR models have been constructed for the disease tuberculosis (TB) in northern Sumatra. The breeding rate is derived. If $\boldsymbol{R_0 \leq 1}$ the free equilibrium is stable, so that the disease is always dies out. Whereas, if $\boldsymbol{R_0 > 1}$, the disease free equilibrium become unstable in North Sumatera. Stability analysis has been performed to determine that the northern Sumatran still within safe levels. To control vaccine and treatment schedule, the singularity is analysed using the properties of the optimal singular control. The singularity properties have proven to Vaccination Susceptible Infected and Recovery (VSIR), Susceptible Exposed Infected and Recovery (SEIR) model and also to Vaccination Susceptible Exposed Infected and Recovery (VSEIR) model of Tuberculosis disease. From the result, we found that, the vaccination schedule of VSIR, SEIR and VSEIR, respectively models are controlled, whereas the only the treatment schedule of SEIR model in Northern Sumatera is controlled, otherwise. By proving the singularity of the other model, the optimal control of the models for vaccine and treatment schedule can be determined.

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Appendix

Appendix 1: Certificate

- Yulita Molliq Rangkuti[a], Marlina Setia Sinaga[a], Faridawaty Marpaung[a], and Syafruddin Side, A VSEIR model for transmission of Tuberculosis (TB) disease in North Sumatera, Indonesia (untuk pembentukan model)
- Marlina Setia Sinaga, Yulita Molliq Rangkuti[a], Faridawaty Marpaung, On Optimal Singular Controls for VSIR Model of Tuberculosis with Vaccination and Treatment (Untuk masalah optimal)
- Faridawaty Marpaung[a] Yulita Molliq Rangkuti[a], Marlina Setia Sinaga, The analysis of Optimal Singular Controls for SEIR Model of Tuberculosis with Vaccination and Treatment

Appendix 2: Articles that have been submitted to AIP Proceeding:

- Yulita Molliq Rangkuti[a], Marlina Setia Sinaga[a], Faridawaty Marpaung[a], and Syafruddin Side, A VSEIR model for transmission of Tuberculosis (TB) disease in North Sumatera, Indonesia

A VSEIR model for transmission of Tuberculosis (TB) disease in North Sumatera, Indonesia

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Abstract. *In this work, vaccination (V), Susceptible (S), Exposed (E), Infectied (I), and Recovered (R) (VSIR) model for transmission of Tuberculosis in North Sumatera is modified. An exposed class is adopted to VSIR model so called VSEIR to determine the probability of people who infectious before infected. This model is written in ordinary differential equation (ODEs) in five classes. Determinating the equilibrium point and stability analysis of modelis discussed to determine the dynamic behaviour of system. A simulation is also discussed to see the suitable model to North Sumatera data. The simulation of VSEIR model indicates Tuberculosis has not endemic in North Sumatera*

Keywords: VSEIR model; Stability analysis; equilibrium analysis.
PACS: 6460Ht;8723Cc

1. INTRODUCTION

Tuberculosis (TB) is a bacterial disease acquired through airbone infection. Mycobacterium tuberculosis (MTB) is the causative agent of tuberculosis. TB disease can affect anyone (old, young, men, women, poor, or rich) and anywhere. TB disease is usually transmitted through contaminated air with Mycobacterium tuberculosis bacteria that are released during coughing TB patients, and in children the source of infection is generally derived from adult TB patients. These bacteria often enter and when accumulated in the lungs will breed a lot (especially in people with a low immune system), and can spread through the blood vessels or lymph nodes. That is why TB infection can infect virtually all body organs such as the lungs, brain, kidneys, gastrointestinal tract, bone, lymph nodes, etc., although the organs most commonly affected are the lungs [1]. Each year, Indonesia increased by a quarter of a million new TB cases and approximately 140,000 deaths occur each year due to tuberculosis. In

fact, Indonesia is the third largest country with the problem of tuberculosis in the world [1]. According to the World Health Organization, one –third the world's population is infected, either latently or actively with tuberculosis [2].

During the year 2010, around 73.8 percent of TB patients are in North Sumatra. Based on a survey of these, Medan city is the largest number of sufferers. In general, the detection rate of TB case increased in North Sumatra. According to the North Sumatra Department of Health in 2005, we estimated that at 15,517 cases of TB sufferers and in 2010 as many as 15,614 TB-positive people in North Sumatra, while based on the estimated, it amount to 21 148 people. Based on data from the Department of Health in 2010 there are six districts/ cities in North Sumatra in 2010 with the highest number of patients based on the population in Medan around 2,397 patients, Siantar around 288 patients, Binjai around 260 patients, Tanjung Balai around 150 patients, Tebing Tinggi around 145 patients and Deli Serdang around 1,554 patients [3].

Immunization is considered important because it has some benefits for toddlers, such as preventing the spread of Tuberculosis. BCG immunization was given 1 month of age giving one the benefit prevent transmission of tuberculosis (TB) are heavy. "If the baby is not complete immunized under the age of one year as BCG has not given, it must be done if the test maontoux baby five months of age or older. This test is to determine whether the baby is negatively affected by TB. If the test result is negative, can only be given BCG immunization [1].

The mathematical model for tuberculosis found that compartmental dynamics such as Susceptible, Infected, Removed with vaccination (VSIR) [4]. Since the disease can remain latent, become active, or it can progress from latent TB to active TB either by endogenous reactivation or exogenous reinfection [5]. Based on previous statement, we modify [4] and adopt the class Exposed (E) to VSIR model. Thus, this paper will dissus about formulation of model, analysis and simulation using the fourth order Runge Kutta (KR4).

2. Model formulation

The total population size $N(t)$ is divided into four distinct epidemiological subclasses of individuals which are vaccination, susceptible, infectious, and recovered, with sizes denoted by $V(t), S(t)$, $I(t)$, and $R(t)$, respectively. Thus, $N(t)$ can be written as $N(t) = V(t) + S(t) + I(t) + R(t)$. The VSIR model [4] having vaccination, infected and recovered period is described by the following system of differential equations:

$$\frac{dV}{dt} = q - (\mu_1 + \delta_1)V, \tag{1}$$

$$\frac{dS}{dt} = \delta_1 V - (\mu_2 + \delta_2 I)S + \theta S, \tag{2}$$

$$\frac{dI}{dt} = \delta_2 IS - (\mu_4 + \mu_{TB} + \delta_4)I, \tag{3}$$

$$\frac{dR}{dt} = \delta_4 I - (\mu_5 + \theta)R, \tag{4}$$

where human birth in natural through passive vaccination ($V(t)$) at rate p, non negative parameters $\mu_1,\mu_1,\mu_3,\mu_2,,\mu_5$ denote as natural death of population of the V, the S, the I and the R, respectively. Population of infected Tuberculosis died in rate μ_{TB}. The susceptible population decreased due to coming individual from the V in rate δ_1. δ_2 denote the transfer rate from susceptible to infected population. Infected population increases due to movement of individuals from infected individuals I in rate δ_4 and decreased due to movement of individuals in to the S at rate θ. In this paper, we assume that human recovering is fully recovered. In flow of mathematical model, we assume that each compartment occurs interaction between classes. Hence, Eqs (1)-(4) can be written as

$$\frac{dV}{dt} = qN - \mu_1 V - \delta_1 VS, \tag{5}$$

$$\frac{dS}{dt} = \delta_1 VS - \mu_2 S - \delta_2 IS, \tag{6}$$

$$\frac{dI}{dt} = \delta_2 SI - (\mu_4 + \mu_m + \delta_4)I, \tag{7}$$

$$\frac{dR}{dt} = \delta_4 I - \mu_5 R. \tag{8}$$

Here, we assume that all new birth got BCG vaccination. Using a compartmental approach, one may assume that a susceptible individual first goes through a latent period (and is said to become exposed or in class $E(t)$).

The exposed individual increases from susceptible individuals in at rate α and decreases in rate ρ and μ_3 couse of death. Then, any interaction between exposed and infected in rate ρ. The exposed population The VSEIR model having infectious force, infected and recovered period is described by the following system of differential equations:

$$\frac{dV}{dt} = qN - \mu_1 V - \delta_1 VS, \tag{9}$$

$$\frac{dS}{dt} = \delta_1 VS - \mu_2 S - \alpha ES, \tag{10}$$

$$\frac{dE}{dt} = (\alpha S - \mu_3 - \rho I)E, \tag{11}$$

$$\frac{dI}{dt} = \rho EI - (\mu_4 + \mu_{TB} + \delta_4)I, \tag{12}$$

$$\frac{dR}{dt} = \delta_4 I - \mu_5 R, \tag{13}$$

with conditions

$$N = V + S + E + I + R \rightarrow R = N - V - S - I, \tag{14}$$

where the positive parameters $\mu_1, \mu_2, \mu_3, \mu_4, \mu_5$ and μ_5 are the rate of natural death of vaccination individual $(V(t))$, susceptible individual $(S(t))$, exposed individual $(E(t))$, Infected individual $(I(t))$ and recovery individual $(R(t))$, respectively. q denotes the rate of natural birth through passive vaccination. The model can be simplified by assuming the following fractions [6]

$$u = \frac{V}{N}, \ w = \frac{S}{N}, \ x = \frac{E}{N}, \ y = \frac{I}{N}, \text{ and } z = \frac{R}{N}. \tag{15}$$

Thus, the model for human populations can be simplified as follows

$$\frac{du}{dt} = q - (\mu_1 + \delta_1)u, \tag{16}$$

$$\frac{dw}{dt} = (\delta_1 u - \mu_2 - \alpha x)w, \tag{17}$$

$$\frac{dx}{dt} = (\alpha w - \mu_3 - \rho y)x, \tag{18}$$

$$\frac{dy}{dt} = \rho xy - \beta y, \tag{19}$$

$$\frac{dz}{dt} = \delta_4 y - \mu_5 z, \tag{20}$$

where $\beta = (\mu_4 + \mu_{TB} + \delta_4)$.

STABILITY ANALYSIS

Disease Free Equilibrium (DFE)

Critical point will occur while the value of

$$\frac{du}{dt} = \frac{dw}{dt} = \frac{dx}{dt} = \frac{dy}{dt} = \frac{dz}{dt} = 0. \tag{21}$$

Substitute (16)-(20) into to Eq. (21) as follows

$$q - (\mu_1 + \delta_1 w)u = 0, \tag{22}$$

$$\delta_1 uw - (\mu_2 + \alpha x)w = 0, \tag{23}$$

$$(\alpha w - \mu_3 - \rho y)x = 0, \tag{24}$$

$$\rho xy - \beta y = 0, \tag{25}$$

$$\delta_4 y - \mu_5 z = 0. \tag{26}$$

Inserting Eqs. (21)-(25) into Eq. (26) indicates the equilibrium point of the system are: $F_1 = \left(\frac{q}{\mu_1}, 0, 0, 0, 0\right)$, and $F_2 = (u_0, w_0, x_0, y_0, z_0)$ with values

$$u_0 = \frac{\mu_2}{\delta_1}, \qquad w_0 = \frac{q\delta_1 - \mu_1\mu_2}{\delta_1\mu_2}, \quad x_0 = 0, \qquad y_0 = 0, \qquad z_0 = 0. \tag{27}$$

Linearization of Eqs. (16)-(20) on the equilibrium points $\left(\frac{q}{\mu_1}, 0, 0, 0, 0\right)$, yields the following equation

$$\begin{pmatrix} \frac{d\,u}{d\,t} \\ \frac{d\,w}{d\,t} \\ \frac{d\,x}{d\,t} \\ \frac{d\,y}{d\,t} \\ \frac{d\,z}{d\,t} \end{pmatrix} = \begin{pmatrix} -\mu_1 & \frac{q\alpha}{\mu_1} & 0 & 0 & 0 \\ 0 & \frac{q\delta_1}{\mu_1} - \mu_2 & 0 & 0 & 0 \\ 0 & 0 & -\mu_3 & 0 & 0 \\ 0 & 0 & 0 & -\beta & 0 \\ 0 & 0 & 0 & \delta_4 & -\mu_5 \end{pmatrix} \begin{pmatrix} u \\ w \\ x \\ y \\ z \end{pmatrix}. \tag{28}$$

Using MAPLE, Eq (28) leads to five eigenvalue equations as follows:

$$\begin{aligned} -\lambda^5 + \left(\frac{q\delta_1}{\mu_1} - \beta - \mu_1 - \mu_2 - \mu_3 - \mu_5\right)\lambda^4 \\ + \left[\left(\frac{q\delta_1(\beta + \mu_3 + \mu_5)}{\mu_1}\right)\right. \\ \left. + (q\delta_1 - (\mu_1 + \mu_5 + \mu_2 + \mu_3)\beta - \mu_3(\mu_1 + \mu_2) - (\mu_5 + \mu_1)\mu_2)\right]\lambda^3 \\ + \left[\frac{q\delta_1(\mu_3\beta + \beta\mu_5 + \mu_5\mu_3)}{\mu_1}\right]\lambda^2 \\ + \left[\frac{q\delta_1\beta(\mu_5 - \mu_3)}{\mu_1} + q\delta_1(\mu_5 + \mu_3 + \beta) - \mu_1\mu_2(\beta + \mu_5 + \mu_3) - \mu_1\mu_5(\beta + \mu_3)\right. \\ \left. - \mu_3\mu_5(\beta + \mu_2) - \mu_2\mu_5(\beta + \mu_3) - \mu_2\mu_3(\beta + \mu_5)\right]\lambda - \mu_1\mu_2\mu_3\mu_5\beta + q\delta_1\mu_3\mu_5\beta \\ = 0, \end{aligned} \tag{29}$$

with eigenvalues

$$\lambda_1 = -\mu_1, \quad \lambda_2 = -\frac{\mu_1\mu_2 - q\delta_1}{\mu_1}, \quad \lambda_3 = -\mu_3, \quad \lambda_4 = -\beta, \quad \lambda_5 = -\mu_5. \tag{30}$$

Epidemic Equilibrium State

Linearization of Eqs (16)-(20) on the equilibrium point $(u_0, w_0, x_0, y_0, z_0)$ yields the following equation:

$$\begin{pmatrix} \frac{du}{dt} \\ \frac{dw}{dt} \\ \frac{dx}{dt} \\ \frac{dy}{dt} \\ \frac{dz}{dt} \end{pmatrix} = \begin{pmatrix} -\frac{q\delta_1 - \mu_1\mu_2}{\mu_2} - \mu_1 & -\mu_2 & 0 & 0 & 0 \\ \frac{q\delta_1 - \mu_1\mu_2}{\mu_2} & 0 & -\frac{\delta_2(q\delta_1 - \mu_1\mu_2)}{\delta_1\mu_2} & 0 & 0 \\ 0 & 0 & \frac{\alpha(q\delta_1 - \mu_1\mu_2)}{\delta_1\mu_2} - \mu_3 & 0 & 0 \\ 0 & 0 & 0 & -\beta & 0 \\ 0 & 0 & 0 & \delta_4 & -\mu_5 \end{pmatrix} \begin{pmatrix} u \\ w \\ x \\ y \\ z \end{pmatrix}. \tag{31}$$

Using MAPLE, Eq (28) leads to five eigenvalues equations as follows

$$
\begin{aligned}
-\lambda^5 + \left[-\beta - \mu_3 - \mu_5 - \frac{q(\alpha-\delta_1)}{\mu_2} - \frac{\mu_1\alpha}{\delta_1}\right]\lambda^4 \\
+ \left[-(\mu_5+\mu_3)\beta - q\delta_1 + \mu_1\mu_2 - \mu_3\mu_5 - \frac{\alpha\mu_1\beta}{\delta_1} + \frac{q\alpha\beta}{\mu_2} - \frac{q\delta_1\mu_5}{\mu_2} + \frac{\alpha q^2\delta_1}{\mu_2^2}\right. \\
\left. - \frac{q\delta_1\mu_3}{\mu_2} + \frac{q\alpha\mu_5}{\mu_2} - \frac{q\alpha\mu_1}{\mu_2}\right]\lambda^3 \\
+ \left[\frac{\delta_1 q^2\alpha}{\mu_2} + \frac{\mu_2\alpha\mu_1^2}{\delta_1} + \frac{\delta_1 q^2\alpha\beta}{\mu_2^2} + \frac{\delta_1 q^2\alpha\mu_5}{\mu_2^2} - \frac{q\delta_1\beta(\mu_3+\mu_5)}{\mu_2} - \frac{q\alpha\beta(\mu_1+\mu_5)}{\mu_2}\right. \\
- \frac{\alpha\mu_1\mu_5\beta}{\delta_1} - \delta_1 q(\mu_5-\mu_3) + \mu_2\mu_1(\mu_5+\mu_3) - \delta_1 q\beta + (\mu_2\mu_1 - \mu_3\mu_5)\beta \\
\left. - 2q\alpha\mu_1\right]\lambda^2 \\
+ \left[\frac{\delta_1\alpha q^2\beta}{\mu_2} + \frac{\delta_1\alpha q^2\mu_5}{\mu_2} + \frac{\delta_1\alpha q^2\beta\mu_5}{{\mu_2}^2} + \frac{\mu_2\alpha{\mu_1}^2\beta}{\delta_1} + \frac{\mu_2\alpha{\mu_1}^2\mu_5}{\delta_1}\right. \\
- \frac{\delta_1 q\beta\mu_5(\mu_1+\mu_3)}{\mu_2} - \delta_1 q\beta(\mu_3+\mu_5) - \delta_1 q\mu_3\mu_5 + \mu_2\mu_1\beta(\mu_3+\mu_5) \\
\left. + \mu_2\mu_1\mu_3\mu_5 - 2q\alpha\mu_1(\beta-\mu_5)\right]\lambda \\
+ \left[\frac{\delta_1 q^2\alpha\mu_5\beta}{\mu_2} + \frac{\mu_2\alpha\mu_1^2\beta\mu_5}{\delta_1} - \delta_1 q\beta\mu_3\mu_5 + \beta\mu_1\mu_2\mu_3\mu_5 - 2q\alpha\beta\mu_1\mu_5\right] = 0
\end{aligned} \tag{32}
$$

with eigenvalues

$$
\lambda_1 = -\frac{q\delta_1 - \sqrt{q^2\delta_1^2 - 4q\delta_1\mu_2^2 + 4\mu_1\mu_2^3}}{2\mu_2}, \quad \lambda_2 = -\frac{q\delta_1 + \sqrt{q^2\delta_1^2 - 4q\delta_1\mu_2^2 + 4\mu_1\mu_2^3}}{2\mu_2},
$$

$$
\lambda_3 = -\frac{\delta_1\mu_2\mu_3 - q\delta_1\alpha + \alpha\mu_1\mu_2}{\mu_2\delta_1}, \quad \lambda_4 = -\beta, \quad \lambda_5 = -\mu_5. \tag{33}
$$

Since $R_e(\lambda_1) < 0$, $R_e(\lambda_2) < 0, R_e(\lambda_3) < 0, R_e(\lambda_4) < 0$, $R_e(\lambda_5) < 0$, then it is asymptomatically stable.

Equilibrium point of VSEIR model for North Sumatera Indonesia

Parameters of this model are variously determined. Some parameters are took from annualy Health fact [1] and supplement data from previous study by Momoh et al. [4]. The parameter is known as $q = 0.11, \mu_1 = 0.1, \mu_2 = 0.133, \mu_3 = 0.14, \mu_5 = 0.133, \delta_1 = 0.675, \delta_2 = 0.544, \delta_3 = 0.644, \delta_4 = 0.7$ and $\mu_{TB} = 0.05$. The equilibrium points were determined using VSEIR model with set parameters for the state of north Sumatera.

$$
\frac{du}{dt} = 0.15 - 0.1u - 0.675uw, \tag{34}
$$

$$
\frac{dw}{dt} = 0.675\,uw - 0.03w - 0.544wx, \tag{35}
$$

$$
\frac{dx}{dt} = 0.544wx - 0.04x - 0.644xy \tag{36}
$$

$$
\frac{dy}{dt} = 0.644xy - 0.904y, \tag{37}
$$

$$
\frac{dz}{dt} = 0.7y - 0.133z. \tag{38}
$$

Then to obtain the critical point of Eqs. (34) to (38) are equal to zero, as below

$$
0.15 - 0.1u - 0.675uw = 0, \tag{39}
$$

$$
0.675\,uw - 0.03w - 0.544wx = 0, \tag{40}
$$

$$
0.544wx - 0.04x - 0.644xy = 0, \tag{41}
$$

$$
0.644xy - 0.904y = 0. \tag{42}
$$

$$
0.7y - 0.133z = 0. \tag{43}
$$

The equilibrium point of VSEIR model are

$$
(u, w, x, y, z) = (V, S, E, I, R) = (1.11,0,0,0,0) \tag{44}
$$

and

$$(u, w, x, y, z) = (0.197037037, 0.686438318, 0, 0\ ,0). \quad (45$$

The second equilibrium points is $(0.197037037, 0.686438318, 0, 0\ ,0)$,whereas, other points are not logic for equilibrium points because any negative point indeed. By using MAPLE, the eigen value (λ) are investigated; as follow: at equilibrium point $(1.11,0,0,0,0)$, eigen values $\lambda_1 = 0.61625, \lambda_2 = -0.904, \lambda_3 = -0.1, \lambda_4 = -0.14$ and $\lambda_5 = -0.133$. At equilibrium point $(0.197037037, 0.686438318, 0, 0\ ,0)$ has eigen value, such as $\lambda_1 = 0.233422445, \lambda_2 = -0.1329999996, \lambda_3 = -0.1485765736, \lambda_4 = -0.4147692913$ and $\lambda_5 = -0.9040000006$.

VSEIR model for stability analysis in North Sumatera Indonesia

Result of VSEIR model in searching the equilibrium point and eigenvalues are discussed in Table 1. Based on the table, The equilibrium points of VSEIR model in North Sumatera is saddle points. It indicates that no occurrence of infected Tuberculosis since there are no infected human when 1.11 human are suspected of TB. Every human in the population are health and there aren't human that infected by virus.

Table (1). Equilibrium points and Stability Analysis

Equilibrium points (V, S, E, I, R)	Eigen values	Stability analysis
$(1.11,0,0,0,0)$	Real and opposite sign	Saddle point
$(0.197037037, 0.686438318, 0, 0\ ,0)$	Real and opposite sign	Saddle point

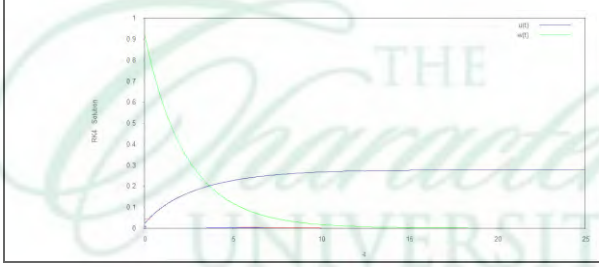
RESULT AND DISCUSSION

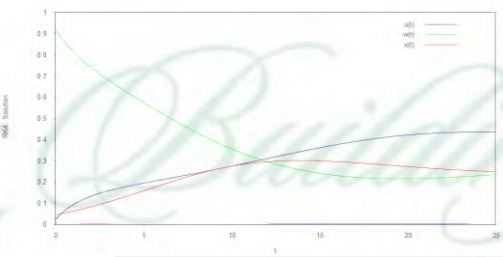
VSEIR Model of tuberculosis in North Sumatera

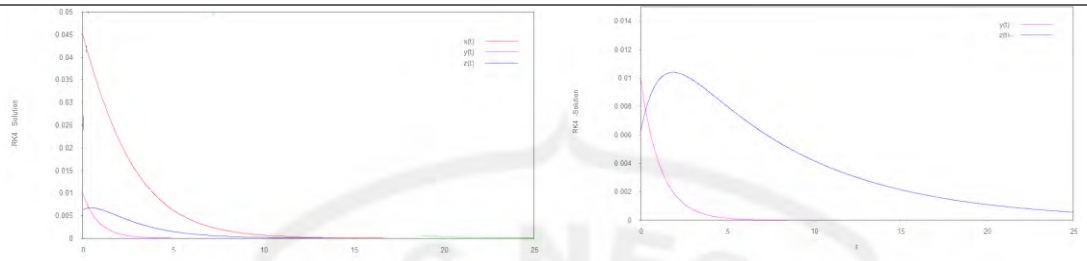
Several investigation have done for VSEIR model of Tuberculosis in this paper. This model is suitable for the state of North Sumatera. Some parameters are took from annually Health fact [1] and supplement data from previous study by Momoh et al. [4]. The parameter is known as $q = 0.11, \mu_1 = 0.1, \mu_2 = 0.133, \mu_3 = 0.14, \mu_5 = 0.133, \delta_1 = 0.675, \alpha = 0.544, \rho = 0.644, \delta_4 = 0.7$ and $\mu_{TB} = 0.05$. The initial polulation is reported by health department of North Sumatera[3]. Table 1 show the stability analysis looking from equilibrium and eigen valus. From table, all equilibrium points were saddle point. Determining a breeding rate on VSEIR is important in Epidemiology problem since this rate shows the infected population will occur in main state. The determination of R_0 was proposed by [7]. $R_0 > 1$ implies that endemic steady state is stable and the infection for a population. $R_0 \leq 1$ implies that the uninfected steady state is stable. The other hand, the tuberculosis infects an individual, if $R_0 > 1$, otherwise.

$$R_0 = \frac{q\delta_1\beta - \mu_1\mu_2\mu_4}{\mu_1\mu_2(\delta_4 + \mu_{TB})} \quad (46)$$

A simulation carried out using MAPLE. Stability analysis tended to asymptotically stable. Illustration of the dynamics of each epidemic giving in Figure 1(a) and 1(b). Figure 1a shows the probability of vaccination, susceptible, exposed, infected and recovery individuals that have $R_0 \leq 1$. It shows that North Sumatra is free disease area of TB. Otherwise, in Figure 1(b), $R_0 > 1$, it indicates North Sumatera is epidemic area of TB.







(a) dynamic system for $R_0 \leq 1$ (b) dynamic system for $R_0 > 1$

Figure 1. Transmission of Tuberculosis with initial condition

CONCLUSIONS

3. This paper has consider VSEIR model of Tuberculosis having infectious in latent, infected, vaccination and immune period. The breeding rate is derived. If $\boldsymbol{R_0 \leq 1}$ the free equilibrium is stable. So that the disease always dies out. Whereas, if $\boldsymbol{R_0 > 1}$, the disease free equilibrium become unstable in North Sumatera.

4. Acknowledgments

We gratefully acknowledge, the financial support received from Direktorat Jenderal Pendidikan Tinggi (DIKTI) dan universitas Negeri Medan (UNIMED) Indonesia for hibah bersaing 2014.

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Appendix 3: Yulita's Certificate

THE 3rd INTERNATIONAL CONFERENCE ON QUANTITATIVE SCIENCES AND ITS APPLICATIONS (ICOQSIA 2014)

CERTIFICATE OF PRESENTATION

This is to certify that

YULITA MOLLIQ RANGKUTI

has presented in

The 3rd International Conference on Quantitative Sciences and Its Applications (ICOQSIA 2014)

held on August 12 - 14, 2014 in Langkawi, Kedah, MALAYSIA

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Appendix 4: The Outcomes of articles that have been submitted to AIP Proceeding: Faridawaty Marpaung[a] Yulita Molliq Rangkuti[a], Marlina Setia Sinaga, The analysis of Optimal Singular Controls for SEIR Model of Tuberculosis with Vaccination and Treatment

The analysis of Optimal Singular Controls for SEIR Model of Tuberculosis with Vaccination and Treatment

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The optimally of singular control for SEIR model of Tuberculosis is analyzed. There are controls that correspond to time of the vaccination and treatment schedule. The optimally of singular control is obtained by differentiate a switching function of the model. The result shows that vaccination and treatment control are singular.

Keywords: SEIR model, Optimal singular control, Switching function, Tuberculosis.
PACS: Xx; 02.30.Yy

6. 1. INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by bacteria Mycobacterium tuberculosis. TB is usually transmitted through contaminated air with Mycobacterium tuberculosis bacteria that are released during coughing TB patients, and in children the source of infection is generally derived from adult TB patients. These bacteria often enter and when accumulated in the lungs will breed a lot (especially in people with a low immune system), and can spread through the blood vessels or lymph nodes. That is why TB infection can infect virtually all body organs such as the lungs, brain, kidneys, gastrointestinal tract, bone, lymph nodes, etc., although the organs most commonly affected are lungs.[1].

Mathematical models have been widely used in different form for studying the transmission dynamics of TB epidemics [2]. Mathematical models have become an important tool in describing the dynamics of the spread of an infectious disease and the effects that vaccination and treatment have on its dynamics. We assume that a susceptible individual goes through a latent period before coming to infectious. The models are conducted as Susceptible Exposed Infected (SEI), Susceptible Exposed Infected Recovery (SEIR) [3] or Susceptible Exposed Infected Susceptible (SEIRS) or so on.

Despite some successes associated with the use of BCG vaccine and some TB treatment therapies, this pandemic has continued to increase and has led to a growing consensus that new control strategies will be needed for disease eradication. The optimal control has a long history of being analyzed to problems in epidemiology problems. Bowong [4] control a tuberculosis model indicating how a control term on the chemoprophylaxis should be introduced in the population to reduce the number of individuals with active TB. Yang et al. [5] focus primarily on controlling the disease using an objective function based on a combination of minimizing the number of TB infections and minimizing the cost of control strategies. In this work, main emphasis is on a complete analysis of the optimally properties corresponding to trajectories. There controls are natural candidates for optimally and are widely used in medical treatment were a maximum dose of treatment is given repeatedly with breaks in between. We develop simple and easily verifiable conditions which allow us to determine the locally of bang-bang control. In this paper, we investigate the optimality singular controls of SEIR models of tuberculosis with vaccination and treatment theoretically. These are controls correspond to time-vary the vaccination and treatment schedules.

7. 2. EPIDEMIOLOGIC MODELS

The epidemiology model is of type SEIR [4] which has four classes. The class, *S* represents the susceptible who

do not have the disease, E represents the exposed who are infected but are yet to show any sign of symptoms, I represents the infective who have the disease and can transmit it to others, R, denotes the recovered class of those who went through infection and emerge with permanent or temporary infection-acquired immunity. In this paper, we only consider an SIER model [1]. We assume that the treatment in rate s, the recruitment due to immigration in rate γ, the slow and fast progression in rate ϑ, ρ , respectively was omitted. The immunity in the class R may not be permanent and the class R should be followed by the class S of individuals who regain their susceptibility when temporary immunity ends.

Let $S(t)$ represent the number of susceptible individuals, $E(t)$ represent exposed individuals, $I(t)$ the number of infective ones and $R(t)$ the number of recovered ones, all at time. We also denote the total number of individuals by $N, N = S + E + I + R$, and in [4] assume that all new births enter the susceptible class S. Therefore we consider the following dynamics:

$$\dot{S} = \pi - \beta IS - \mu S \tag{1}$$

$$\dot{E} = \beta IS - \mu E, \tag{2}$$

$$\dot{I} = DIS + DE - (\mu + \mu_T)I, \tag{3}$$

$$\dot{R} = \varepsilon I - sI - \beta IR - \mu R, \tag{4}$$

Thus, the controlled mathematical model is written as follow

$$\dot{S} = \pi - \beta IS - \mu S - Su, \tag{5}$$

$$\dot{E} = \beta IS - \mu E - Eu, \tag{6}$$

$$\dot{I} = DIS + DE - (\mu + \mu_T)I - Iv, \tag{7}$$

where π, represents the rate of recruitment of susceptible individuals, βIS, represents the loss of the number of susceptible individuals that are being infected by individuals from class I with the parameter β standing for the average number of adequate contacts (i.e., contacts sufficient for transmission) of a person per unit of time.

The last term of equation (5), Su represents the effect of vaccination, and it is assumed that vaccination removes the fraction Su of individuals from the class S and makes them resistent. In equation (2), the E decreased by natural death of the Eu, and individual class E to class is infectious (I) and increased as a result of disease transmission βIS, the last term Eu, represents the effect of vaccination of E. The variabel u is a control that represents the rate at which susceptible individuals are vaccinated. It takes values in a compact interval, $0 \leq u \leq u_{max}$. In the I, Eq.3, D, represents detection rate of TB . The additional outflow Iv is related to the cure of infected individuals due to treatment and v represents the rate at which infectious individuals are treated at each time period, the second control in the model with values in the interval $0 \leq v \leq\leq v_{max}$.

Thus there are two possible mechanisms as controls: immunization of the susceptible and exposed individuals and treatment of the infected ones. These actions are modeled by the two controls u dan v that for mathematical reasons are taken as Lebesque-measurable functions. The action of both controls enriches the class R of the recovered individuals by removing them from the class of susceptible and infected ones, respectively. The class R is defined as $R = N - I - S - E$. For the model to be realistic, we need to make sure that all the variables including R remain positive. The initial numbers of individuals in each of the populations are positive numbers denoted by

$$N(0) = N_0, S(0) = S_0 \text{ , } E(0) = E_0 \text{ and } I(0) = I_0. \tag{8}$$

Note that if there are no infected individuals initially,$I_0 = 0$, I remains identically zero. The model, thus don't represent the on the set of infection, but only its course. From biological considerations, a closed set

$$Q = \{(S, E, I, R): 0 < S, 0 < E, 0 < I, S + E + I + R < N\},$$

where $\mathbb{R}^4$*, denote the non-negative cone and its lower dimensional faces. It can be verified that* Q *is posively invariant with respect to (1-4).* We denote by ∂Q and $\dot{Q}$ the boundary and the interior of Q.

3. FORMULATION AS AN OPTIMAL CONTROL PROBLEM

Let the population sizes of all there classes, S_0, E_0, I_0 and $R_0$are given, find the best strategy in terms of combined efforts of vaccination and treatment that would minimize the number of people who die from the

infection while at the same time also minimizing the cost vaccination and treatment of the population.

In this paper, we consider the following objective for a fixed terminal time T:

$$J(u,v) = \int_0^T aE(t) + bI(t) + cu(t) + dv(t)dt \tag{9}$$

The first term in the objective, $aE(t)$ represents the number of exposed who are infected but are yet to show any sign of symptoms at time t, $bI(t)$, represents the number of people who are exposed and infected at time t and are taken as b measure for the deaths associated with the outbreak. The terms, $cu(t)$ and $dv(t)$ represent the cost of vaccination and treatment, respectively, and are assumed to be proportional to the vaccination and treatment rates.

We shall apply methods of geometric optimal control theory to analyze the relations between optimal vaccination and treatment schedules. These techniques become more transparent if the problem is formulated as a Mayer –type optimal control problem : that is , one where we only minimize a penalty term at the terminal point. Such a structure can easily be achieved at the cost of one more dimension if the objective is adjoined as an extra variable. Defining

$$\dot{Z} = aE + bI + cu + dv, \qquad Z(0) = 0. \tag{10}$$

We therefore consider the following optimal control problem. For a fixed terminal time , minimize the value $Z(T)$ subject to the dynamics

$$\dot{Z} = aE + bI + cu + dv, \qquad Z(0) = 0, \tag{11}$$
$$\dot{S} = \pi - \beta IS - \mu S - Su \qquad S(0) = 0, \tag{12}$$
$$\dot{E} = \beta IS - \mu E - Eu, \qquad E(0) = 0, \tag{13}$$
$$\dot{I} = DIS + DE - (\mu + \mu_T)I - Iv, \qquad I(0) = 0, \tag{14}$$

Over all Lebesque measurable function

$$u: [O,T] \to [0, u_{max}] \quad \text{and} \quad v: [0,T] \to [0, v_{max}]$$

Introducing the state $\dot{x} = (Z,S,E,I)^T$, the dynamics of the system is a multiinput control-affine system of the form

$$\dot{x} = f(x) + g_1(x)u + g_2(x)v, \tag{15}$$

with drift vector field f given by

$$f(x) = \begin{pmatrix} aE + bI \\ \pi - \beta IS - \mu S \\ \beta IS - \mu E \\ DIS + DE - (\mu + \mu_T)I \end{pmatrix}, \tag{16}$$

and control vector fields g_1 and g_2 given by

$$g_1 = \begin{pmatrix} c \\ -S \\ -E \\ 0 \end{pmatrix} \quad \text{and} \quad g_2(x) = \begin{pmatrix} d \\ 0 \\ 0 \\ -I \end{pmatrix}. \tag{17}$$

We call an admissible control pair (u,v) with corresponding solution x a controlled trajectory of the system.

4. NECESSARY CONDITIONS FOR OPTIMALITY

First-order necessary conditions for optimality of a controlled trajectory by the *Pontryagin maximum principle* [4,15] : For a row-vector $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4) \in (\mathbb{R}^4)$, we define the Hamiltonian $H = H(\lambda, x, u, v)$ as the dot product, $\langle ., . \rangle$ of the row vector λ with the column vector that defines the dynamics, that is

$$\begin{aligned} H &= \langle \lambda, f(x) + g_1(x)u + g_2(x)v \rangle \\ &= \lambda_1(aE + bI + cu + dv) + \lambda_2(\pi - \beta IS - \mu S - Su) + \lambda_3(\beta IS - \mu E - Eu) \\ &\quad + \lambda_4(DIS + DE - (\mu + \mu_t)I - Iv). \end{aligned} \tag{18}$$

Then, if (u_*, v_*) is an optimal control defined over the interval $[0,T]$ with corresponding trajectory $x_* = (Z_*, S_*, E_*, I_*)^T$, there exists an absolutely continuous co-vector, $\lambda: [0,T] \to (\mathbb{R}^4)^*$, such that following conditions hold [6]

(a) λ satisfies the adjoin equation (written as row vector and with D_f and D_{gi} denoting the Jacobian matrices

of the partial derivatives)

$$\dot{\lambda} = -\lambda(Df(x_*) + Dg_1(x_*)u_* + Dg_2(x_*)v_*), \tag{19}$$

with terminal condition

$$\lambda(T) = \left(\frac{\pi}{\mu}, \quad 0, \quad 0, \quad 0\right) \tag{20}$$

(b) for almost every time $t\epsilon[0,T]$ the optimal controls $\big(u_*(t), v_*(t)\big)$ minimize the Hamiltonian along $\big(\lambda(t), x_*(t)\big)$ over the control set $[0, u_{max}] \times [0, v_{max}]$ and,
(c) the Hamiltonian is constant along the optimal solution.

We call a pair $\big(x,(u,v)\big)$ consisting of admissible controls (u,v) with corresponding trajectory x for wich there exist multipliers λ such that the conditions of the Maximum Principle are satisfied an *external* (pair) and the triple $(x,(u,v),\lambda)$ is an external lift. Note that the dynamics does not depend on the auxiliary variable Z and thus by the adjoint equation (6) the multiplier λ_1 is constant; by the terminal condition (20) , it is thus given by $\lambda_1(t) \equiv \frac{\pi}{\mu}$. In particular, the overall multiplier $\lambda(t)$ is never zero. For almost any time t, the optimal controls $\big(u_*(t), v_*(t)\big)$ minimize the Hamiltonian $H(\lambda(t), x_*(t), u, v)$ over the compact interval $[0, u_{max}] \times [0, v_{max}]$. Since H is linear in the controls, this minimization problem s plits into separate one-dimensional problems that can easily be solved. Defining the so-called *switching functions* Φ_1 and Φ_2 as

$$\Phi_1(t) = \langle\lambda(t).\, g_1\big(x_*(t)\big)\rangle = c - \lambda_3(t)S_*(t) \tag{21}$$

and

$$\Phi_2(t) = \langle\lambda(t).\, g_2\big(x_*(t)\big)\rangle = d - \lambda_4(t)I_*(t) \tag{22}$$

It follows that the optimal controls satisfy

$$u_*(t) = \begin{cases} 0 & if \quad \Phi_1(t) > 0 \\ u_{max} & if \quad \Phi_1 < 0 \end{cases} \qquad \text{and} \qquad v_*(t) = \begin{cases} 0 & if \quad \Phi_2(t) > 0 \\ v_{max} & if \quad \Phi_2(t) < 0 \end{cases}$$

The minimum condition alone does determine the controls at times when $\Phi_1(t) = 0$. if $\Phi_1(\tau) = 0$, but $\Phi_1(\tau) \neq 0$, then the control switches between the value 0 and its maximum value depending on the sign of $\dot{\Phi}\imath(\tau)$. Controls with this property are called bang-bang controls and we refer to the constant controls with values in the endpoints of the control intervals as *bang* controls. The other extreme occurs when a switching function vanishes over an open interval. In this case also derivatives of $\Phi_1(t)$ must vanish and this typically allows to compute such a control. Controls of this kind are called *singular* [6]. While the name might give impression that these controls are less important, quite the contrary is true. Singular controls (if they exist) tend to be either that best (minimizing) or the worst (maximizing) strategies and in either case they are essential in determining the structure of optimal controls. This typically needs to be synthesized from bang and singular controls through an analysis of the switching function. Thus singular controls generally play a major role in a synthesis of optimal controlled trajectories and this paper we analyse their existence and local for the problem in Eqs. (11)-(14).

An essential tool in this analysis is the Lie bracket of vector fields which naturally arises in the formulas for the derivatives of the switching function. Give two differentiable vector fields f dan g defined on a common open subset of $\mathbb{R}^n$, their *Lie bracket* can be defined as

$$[f,g](x) = Dg(x)f(x) - Df(x)g(x) \tag{23}$$

The Lie-bracket is anti-commutative, i.e.,$[f,g] = -[g,f]$, and for arbitrary vector fields f, g and h it satisfies the Jacobi identity [5]

$$\big[f,[g,h]\big] + \big[g,[h,f]\big] + \big[h,[f,g]\big] \equiv 0 \tag{24}$$

The following result provides an elegant and important framework for efficient computations of the derivatives of the switching functions. It is easily verified by a direct computation.

Proposition 1. *Let $\big(x,(u,v)\big)$be a controlled trajectory of the system and let λ be a solution to the corresponding adjoint equations. Given a continuously differentiable vector field h , define*

$$\psi(t) = \langle\lambda(t), h\big(x(t)\big)\rangle \tag{25}$$

Then the derivative of ψ is given by

$$\psi(t) = \langle\lambda(t), [f + \dot{g}_1 u + g_2 v, h]\big(x(t)\big)\rangle \tag{26}$$

5. THE STRUCTURE OF SINGULAR CONTROLS

We investigate the existence and local optimality of singular controls for the system in Eqs (11)-(14). By

Propositions 1 the derivatives of the switching functions $\Phi_1(t) = \langle \lambda(t), g_1(x(t)) \rangle$ and $\Phi_2(t) = \langle \lambda(t), g_2(x(t)) \rangle$ are given by

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f + \dot{g}_1 u + g_2 v, g_1] x(t) \rangle \quad (27)$$

$$\dot{\Phi}_2(t) = \langle \lambda(t), [f + \dot{g}_1 u + g_2 v, g_2] x(t) \rangle \quad (28)$$

By anti-commutative of the Lie bracket $[g_i, g_i] \equiv 0$ and a simple computation verifies that the control vector fields g_1 and g_2 commute, i.e., $[g_1, g_2] \equiv 0$ as well. We thus have that

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f, g_1](x, (t)) \rangle \quad \text{and} \quad \dot{\Phi}_2(t) = \langle \lambda(t), [f, g_2](x, (t)) \rangle.$$

Elementary calculations verify that

$$[f, g_1](x) = \begin{pmatrix} aE \\ -\pi \\ 0 \\ DIS + DE \end{pmatrix} \quad \text{and} \quad [f, g_2](x) = \begin{pmatrix} bI \\ -\beta IS \\ \beta IS \\ -DE \end{pmatrix}.$$

We first analyse the control, i.e., vaccinations schedules. Applying Propositions 2 once more to $\dot{\Phi}_1$, it follows that

$$\ddot{\Phi}_1(t) = \langle \lambda(t), [f + g_1 u + g_2 v, [f, g_1]](x(t)) \rangle \quad (29)$$

A direct calculation shows that g_2 and $[f, g_1]$ commute as well, $[g_2, [f, g_1]] \equiv \begin{pmatrix} 0 \\ 0 \\ 0 \\ ED \end{pmatrix}$, and that

$$[g_1, [f, g_1]](x) = \begin{pmatrix} -aE \\ -\pi \\ 0 \\ -DSI - DE \end{pmatrix}.$$

The relation

$$\ddot{\Phi}_1 \equiv -\lambda_1(t) aE(t) - \lambda_2(t)\pi(t) + \lambda_4(t)(DSI + DE)(t) \equiv 0 \quad (30)$$

Implies that

$$\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle = -2\lambda_4(t)(DSI + DE)(t)$$

And $\Phi_1(t) = c - \lambda_3(t) S(t) \equiv 0$ gives that $\lambda_3(t)$ must be positive along a singular are. Hence we have that

$$\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle = -2\lambda_4(t)(DSI + DE)(t) < 0$$

Singular controls of this type, i.e., for which $\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle$ does not vanish, are said to be of order 1 and it is a second-order necessary condition for minimallity, the so-called *Legendre-Clebsh condition*, that this quantity be negative [9] . Thus for this model singular controls u are locally optimal. Furthermore, in this case, we taking into account that $[g_2, [f, g_1]] \equiv \begin{pmatrix} 0 \\ 0 \\ 0 \\ DE \end{pmatrix}$, we can compute the singular control as

$$u_{sin}(t) = -\frac{\langle \lambda(t), [f, [f, g_1]](x(t)) \rangle}{\langle \lambda(t), [g_1, [f, g_1](x(t))] \rangle} \quad (31)$$

Here,

$$[f, [f, g_1]](x) = \begin{pmatrix} a\beta IS - a\mu E - bDIS - bDE \\ -\pi\beta I - \pi\mu + \pi\beta S^2 DI + \pi\beta SDE \\ \pi\beta I - \beta S^2 DI - \beta SDE \\ 2DI\pi - DI^2\beta S - DI\mu S + D\beta IS + \mu_T \end{pmatrix} \quad (32)$$

Since $\langle \lambda(t), [f, g_1](x(t)) \rangle \equiv 0$, it follows from (31) that

$$\mu_{sin}(t) = -\frac{1}{2\lambda_2 \pi}\left[-\lambda_2(a\beta IS + bDIS + bDE) + \psi(t)(\lambda_2 - \lambda_3) - \mu - \frac{\lambda_4}{2\lambda_2}\left(\frac{\mu + \mu_T}{\pi}\right) DE\right], \quad (33)$$

where, $\psi(t) = \beta I\pi - \pi\beta S^2 DI - \pi\beta SDE$. Therefore, we obtain the following result

Proposition 2. *A singular control u is of order* 1 *and satisfies the Legendre-Clebsch condition for minimality. The singular control is given as a function depending both on the state and the multiplier in the form*

$$\mu_{sin}(t) = -\frac{1}{2\lambda_2\pi}\left[-\lambda_2(a\beta IS + bDIS + bDE) + \psi(t)(\lambda_2 - \lambda_3) - \mu - \frac{\lambda_4}{2\lambda_2}\left(\frac{\mu + \mu_T}{\pi}\right)DE\right]$$

where $\psi(t) = \beta I\pi - \pi\beta S^2 DI - \pi\beta SDE$.

For treatment control, we define the switching function as

$$\Phi_2(t) = \langle\lambda(t), g_2(x(t))\rangle \tag{34}$$

By using proposition 2, the first derivative of Eq. 34 we have

$$\dot{\Phi_2}(t) = (\lambda(t), [f, g_2](x)(t)) = \lambda_1 bI - \lambda_2\beta IS + \lambda_3\beta IS - \lambda_4 DE \tag{35}$$

As we know, to check the optimally Eq 34, Eq. 35 will be zero, we habe

$$(\lambda(t), [f, g_2](x)(t)) = \lambda_1 bI - \lambda_2\beta IS + \lambda_3\beta IS - \lambda_4 DE = 0. \tag{36}$$

Hence, we have

$$\begin{aligned}\ddot{\Phi}_2 = (\lambda, f, [f, g_2]) &= -\lambda_1(bI\mu - bDIS - 2bDE + a\beta IS) - \lambda_2(\beta S^2 DI + \beta SDE + \beta^2 I^2 S - \pi\beta SDE)\\ &+ \lambda_3(\pi\beta I - \mu\beta IS + \beta S^2 DI + 2\beta SDE) - \lambda_4(2D\beta IS - DI^2\beta S - D^2 ES + 2DE\mu_T) < 0\end{aligned}$$

It also shows a second-order necessary condition for minimallity, the so-called *Legendre-Clebsh condition*, that this quantity be negative [9] . Thus for this model singular controls u are locally optimal. Furthermore, in this case,and taking

$$v_{sin}(t) = -\frac{\langle\lambda(t), [f, [f, g_2]](x(t))\rangle}{\langle\lambda(t), [g_2, [f, g_2]](x(t))\rangle}. \tag{37}$$

Here, we have

$(\lambda, f, [f, g_2]) = -\lambda_1(bI\mu - bI\mu_T - bDIS - 2bDE + a\beta IS) - \lambda_2(\beta S^2 DI + \mu_T\beta IS + \beta SDE + \beta^2 I^2 S - \pi\beta SDE) + \lambda_3(\pi\beta I - \mu\beta IS + \beta S^2 DI - \mu_T\beta IS + 2\beta SDE) - \lambda_4(2D\beta IS - DI^2\beta S - D^2 ES - DE\mu_T)$ and $\left(\lambda(g_2(f, g_2))\right) = -\lambda_1 bI - \lambda_4 DE$

we can compute the singular control as

$$\begin{aligned}v_{sin}(t) = \frac{1}{-(\lambda_1 bI + \lambda_4 DE)}&(\lambda_1 bDIS + 2\lambda_1 bDE - \lambda_1 bI\mu - \lambda_1 bI\mu_T - \lambda_1 a\beta IS - \lambda_2\beta S^2 DI\\ &- \lambda_2\beta SDE + \lambda_2\beta SI\mu_T - \lambda_2\beta^2 I^2 S + \lambda_2\pi\beta SDE + \lambda_3\pi\beta I - \lambda_3\mu\beta IS + \lambda_3\beta S^2 DI\\ &+ 2\lambda_3\beta SDE + \lambda_3\beta SI\mu_T - 2\lambda_4 D\beta IS + \lambda_4 DI^2\beta S + \lambda_4 D^2 ES - \lambda_4 DE\mu_T)\end{aligned} \tag{38}$$

Therefore, we obtain the following result:

Proposition 3. *The control v can be singular.*

CONCLUSION

The optimal singular control problem for an SEIR-model of Tuberculosis was discussed. The structure singular controls was analized to determine singularity properties of the model. We apply Lie bracket of vector field to check whether the second order of switching function was vanish or not. For the calculation we used Maple. Based on our computation, we found that the vaccination and treatment schedules are singulars. The optimality of vaccination and treatment for other epidemology problem can be analized in future.

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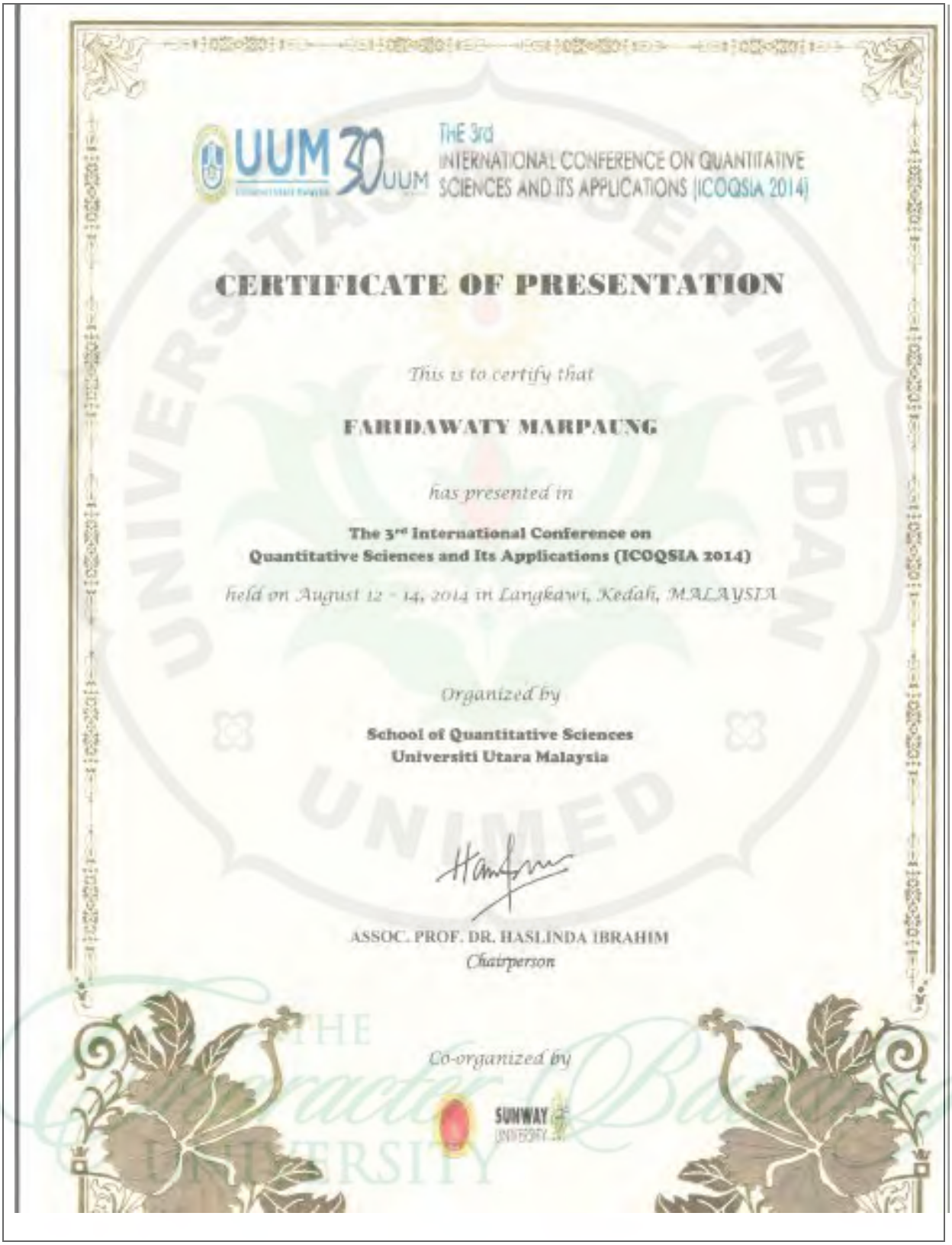

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On Optimal Singular Controls for VSIR Model of

Tuberculosis with Vaccination and Treatment

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A VSIR model of Tuberculosis is considered to obtain the optimally singular control. Existence and local optimality of singular controls is analized by showing the second derivative of switching function. To find the derivative, we uses a Lie bracket. From the result, it is shows that the optimal vaccination schedule can be singular, but treatment schedules is not singular.

Keywords: VSIR model, Optimal control, Singular controls, Epidemiology
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5 INTRODUCTION

Tuberculosis (TB) is an infectious bacterial disease caused by Mycobacterium Tuberculosis, which most commonly affects the lungs. It is transmitted from person to person via contaminated air with Mycobacterium tuberculosis bacteria that are released during coughing TB patients, and in children the source of infection is generally derived from adult TB patients [1]. Immunization is considered important because it has some benefits for toddlers, such as preventing the spread of TB. BCG immunization was given1 month of age giving one the benefit prevent transmission of TB are heavy. "If the baby is not complete immunized under the age of one year as BCG has not given, it must be done if the test maontoux baby five months of age or older. This test is to determine whether the baby is negatively affected by TB. If the test result is negative, so it can only be given BCG immunization [2].

The standard models in epidemiology include three compartments typically denoted by S, I and R. In this work, we present the model VSIR [3] which V denotes passively immune infant, normally it gives for new birth, S means susceptible, I denotes infected class, and R is Recovery class. Momoh et al. [3] stated that progression to active TB among the population epidemiology significant and interventions should focus on vaccinations and treatment of infected. Since the latent infections can eventually become active, even people without symptoms should receive medical treatment. Medication can help get rid of the inactive bacteria before they become active. It was virtually wiped out with the help of antibiotics, but the disease has resurfaced in potent new forms –multidrug-resistant TB and extensively drug-resistant TB. So if you have TB –its active or latent state—you must seek medical treatment. TB is treatable with a six-month course of antibiotics [4].

To date, an analysis approach to problems of optimal control for Tuberculosis was restricted to apply Potryagin maximal principle [5]. This analysis focused on optimally of singular controls. Using the Legendre-Clebsch condition (a high-order necessary condition for optimally of singular arc), we should that these arcs are indeed locally minimizing rather than locally minimizing, and thus eliminated the singular controls for candidate optimally [6]. Ledzewicz and Schattler [8] analysis the optimal singular controls of general SIR model with vaccination and treatment and it showed that control for vaccination was singular but treatment control was not singular. Based on [8], we will show the optimal singular control of Vaccination Susceptible Infected Recovery (VSIR) Model in [3] of Tuberculosis. In next section, this paper will discuss about epidemiologic models, formulation as an optimal control problem, necessary conditions for optimality, the structure of singular controls, and the end, we will get the conclusion.

6 epidemiologic models

The models in tuberculosis we consider for four class denoted by V, S, I, R The class V represent infants with passive immunity, S stands for the class susceptible individuals, I represent the class of infected ones and R denotes the recovered class of those who went through infection and emerge with permanent or temporary infection-acquired immunity. In this paper, for tuberculosis case the infant with vaccination immunete can not

enter to class S. Furthermore, for tuberculosis the immunity in the class R may not be permanent and the class R should be followed by the class S of individuals who regain their susceptibility when temporary immunity ends. Since the immunity is waning so the immunity is not permanent. The model can be splited become c_1 and c_2, where c_1 and c_2 denote as cost for child vaccinate and adult vaccinate, respectively.

Individuals are recruited into V class via natural birth at the rate Q through passive vaccination, the population of the V decreases due to natural death at rate μ and movement of the individuals into S as a result of warning out of vaccines used in passive vaccination at the rate δ. The population of the S increases due to coming of individuals from the V and R classes at the rates δ and θ. The population of the S class decreases due to the movement of individuals into the infected class at the rate β and natural death at a rate μ. The population of the I decreases due to treatment againts TB at the rate ψ and natural death at the rate μ and death as result of TB infention at the rate μ_m. The model above is thus described by the following set of ordinary differential equations similar to [3]

$$\dot{V} = Q - (\mu + \delta)V - V_u \quad (1)$$
$$\dot{S} = \delta V - (\mu + \beta I)S + \theta S - S_u \quad (2)$$
$$\dot{I} = \beta SI - (\mu + \mu_m + \psi)I - I_v \quad (3)$$

where Q is natural birth rate, V is passively immune infant, S is susceptible class, I is infected class, μ is natural death rate, δ is rate of the duration of vaccine efficacy, β is TB contact rate, μ_m is death as result of TB infection, ψ is rate of recovery from TB infection, θ is rate at which individuals become susceptible.

We consider that all new births getting vaccination and thus the natural birth Q enters to equation (1), and V_u represent the effect control vaccination for child. Susceptible dynamic in equation (2), βIS, represents the loss of the number of susceptible individuals can being infected to class I in rate β per unit time. The last term, Su, represents the effect of vaccination. The variable u is a control that represents the rate at which susceptible individuals are vaccinated. It takes values in a compact interval, $0 \leq u \leq v_{max}$.

In the I-dynamics, equation (3), βIS thus represents the newly infected individuals from class S. The term ψI outflow of infected individuals that recovery, $(\mu + \mu_m)I$ represent deaths from the infection. Iv is related to the cure of infected individuals due to treatment and represents the rate at which infectious individuals are treated at each time period, the second control in the model with values in the interval $0 \leq v \leq v_{max}$.

Thus the are two possible mechanisms available as controls: immunization of the susceptible individuals and treatment of the infected individuals. These actions are modeled by the two controls u and v that are taken as Lebesgue-measurable functions. The action of both controls enriches the class R of the recovered individuals by removing them from the class of passively immune infant, susceptible and infected individuals, respectively. The class R is defined as $R = N - V - I - S$ like in [6]. For the model to be realistic, we need to make sure that all the variables including R remain positive. The initial numbers of individuals in each of the populations are positive numbers denoted by

$$N(0) = N_0, V(0) = V_0, S(0) = S_0, and\ I(0) = I_0.$$

From biological considerations, we study (1-3) in the closed set

$$\mathcal{M} = \{(N, V, S, I): 0 < N, 0 < V, 0 < S, 0 < I, V + S + I < N\},$$

where $\mathbb{R}^4_+$ denotes the non-negative cone and its lower dimensional faces. It can be verified that $\mathcal{M}$ is posively *invariant* with respect to (1-3) [7].

7 FORMULATION AS AN OPTIMAL CONTROL PROBLEM

Our aim is to solve the following problem: firstly, we define the given initial population sizes of all four classes, V, S, I, and R. Find the best strategy in terms of combined efforts of vaccination and treatment that would minimize the number of people who die from the infection while at the same time, also minimizing the cost of vaccination and treatment of the population. For tuberculosis since the immunity is waning so the immunity is not permanent, and in this paper we splited the model of vaccinated control becomes c_1 and c_2, where c_1 and c_2 denote as cost for vaccinated child and adult ones, respectively for a fixed terminal time T, we consider the following objective:

$$J(u, v) = \int_0^T aV(t) + bI(t) + (c_1 + c_2)u(t) + dv(t)dt \quad (4)$$

The first term in the objective, $aV(t)$, represent infants individual with passive immunity at time t, $aI(t)$,

represents the number of people who are infected at time t and is taken as a measure for the deaths associated with the outbreak. The terms, $(c_1 + c_2)u(t)$ and $dv(t)$ represent the cost of vaccination and treatment, respectively.

For a fixed terminal time T, minimize the value $Z(T)$subject to the dynamics, similar to [3].

$$\dot{Z} = aV + bI + (c_1 + c_2)u + dv \qquad Z(0) = 0 \qquad (5)$$
$$\dot{V} = Q - (\mu + \delta)V - Vu \qquad V(0) = 0 \qquad (6)$$
$$\dot{S} = \delta V - (\mu + \beta I)S + \theta S - Su \qquad S(0) = 0 \qquad (7)$$
$$\dot{I} = \beta SI - (\mu + \mu_m + \psi)I - Iv \qquad I(0) = 0 \qquad (8)$$

Over all Lebesgue measurable functions

$$u: [0,T] \to [0, u_{max}] \text{ and } v: [0,T] \to [0, v_{max}]$$

Introducing the state $x = (Z, V, S, I)^T$, the dynamics of the system is a multi input control-affine system of the form

$$\dot{x} = f(x) + g_1(x)u + g_2(x)v$$

With drift vector field f given by

$$f(x) = \begin{pmatrix} aV + bI \\ Q - (\mu + \delta)V \\ \delta V - (\mu + \beta I)S + \theta S \\ \beta IS - (\mu + \mu_m + \psi)I \end{pmatrix}$$

and control vector fields g_1 and g_2 given by

$$g_1(x) = \begin{pmatrix} c_1 + c_2 \\ -V \\ -S \\ 0 \end{pmatrix} \text{ and } g_2(x) = \begin{pmatrix} d \\ 0 \\ 0 \\ -I \end{pmatrix}.$$

We call an admisisible control pair (u, v) with corresponding solution x a *controlled trajectory* of the system.

8 NECESSARY CONDITIONS FOR OPTIMALITY

Let a first order necessary conditions for optimality of a controlled trajectory are given by *Pontryagin maximum* principle and let a row vector $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4) \epsilon (\mathbb{R}^4)^*$, we defined the Hamiltonian $H = H(\lambda, x, u, v)$ as the dot product, $\langle ,.,. \rangle$, of the row vector λ with the column vector that defines the dynamics, as necesssary conditions for optimality given by the *Pontryagin maximum principle* [2,6], that is

$$H = \langle \lambda, f(x) + g_1(x)u + g_2(x)v \rangle$$
$$= \lambda_1(aV + bI + (c_1 + c_2)u + dv) + \lambda_2(Q - (\mu + \delta)V - V_u) + \lambda_3(\delta V + \theta S - (\mu + \beta I)S - S_u) +$$
$$\lambda_4(\beta IS) - (\mu + \mu_m + \psi)I - Iv)$$

Then, if (u_*, v_*) is an optimal control defined over the interval $[0, T]$ with corresponding trajectory $x_* = (Z_*, V_*, S_*, I_*)^T$, there exists an absolutely continuous co-vector, $\lambda: [0,T] \to (\mathbb{R}^4)^*$ such that the following conditions hold:

(d) λ satisfies the adjoint equations (written as a row vector and Df and Dg_i denoting the Jacobian matrices of the partial derivatives)

$$\dot{\lambda} = -\lambda\,(Df(x_*) + Dg_1(x_*)u_* + Dg_2(x_*)v_*) \qquad (9)$$

With terminal condition

$$\lambda(T) = \left(\frac{Q}{\mu + \delta}, \frac{\delta Q}{(\mu + \delta)(\mu - \theta)}, 0, 0\right) \qquad (10)$$

(e) for almost every time $t \epsilon [0,T]$ the optimal controls $(u_*(t), v_*(t))$ minimize the hamiltonian along

$(\lambda(t), x_*, (t))$ over the control set $[0, u_{max}]x[0, v_{max}]$ and

(f) the Hamiltonian is constant along the optimal solution.

We call a pair $\big(x, (u, v)\big)$ consisting of admissible controls (u, v) with corresponding trajectory x for which there exist multipliers λ such that the conditions of the maximum Principle are satisfied an *extremal* (pair) and the triple $(x, (u, v), \lambda)$ is an extremal lift (to the cotangent bundle).

Note that the dynamics does not depend on the auxiliary variable Z and thus by the adjoint equation (9) the multiplier λ_1 is constant; by the terminal condition (10) it is thus given by $\lambda_1(t) \equiv \frac{Q}{\mu+\delta}$. In particular, the overall multiplier $\lambda(t)$ is never zero. For almost any time t, the optimal controls $(u_*(t), v_*(t))$ minimize the Hamiltonian $H(\lambda(t), x_*(t), u, v)$ over the compact interval $[0, u_{max}]x[0, v_{max}]$. Since H is linear in the controls, this minimization problem splits into two separate one-dimensional problems that can easily be solved. Defining the so-called *switching functions* Φ_1 and Φ_2 like in [7] as

$$\Phi_1(\mathrm{t}) = \langle \lambda(\mathrm{t}), \mathrm{g}_1(\mathrm{x}_*(\mathrm{t})) \rangle = (c_1 + c_2) - \lambda_2(t)V_*(t) - \lambda_3(\mathrm{t})\mathrm{S}_*(\mathrm{t})$$

and

$$\Phi_2(\mathrm{t}) = \langle \lambda(\mathrm{t}), \mathrm{g}_2(\mathrm{x}_*(\mathrm{t})) \rangle = d - \lambda_4(\mathrm{t})\mathrm{I}_*(\mathrm{t})$$

it follows that the optimal controls satisfy

$$u_*(t) = \begin{cases} 0 & if\ \Phi_1(t) > 0 \\ u_{max} & if\ \Phi_1(t) < 0 \end{cases} \text{ and } v_*(t) = \begin{cases} 0 & if\ \Phi_1(t) > 0 \\ v_{max} & if\ \Phi_1(t) < 0 \end{cases}.$$

The minimum condition alone does not determine the control at times when $\Phi_{\mathrm{i}}(\mathrm{t}) = 0$. If $\Phi_{\mathrm{i}}(\tau) \neq 0$, then the control switches between the value 0 and its maximum value depending on the sign of $\dot{\Phi}_i(\tau)$. Controls with this property are called bang-bang controls and we refer to the constant controls with values in the andpoints of the control intervals as *bang* controls. The other extreme occurs when a switching function vanishes over an open interval. In this case all derivatives of $\dot{\Phi}_i(t)$ must vanish and this typically allows to compute such a control. Controls of this kind are called *singular* [9]. While the name (which has historical reasons) might give the impression that these controls are less important, quite the contrary is true. According Singular controls (if they exist) tend to be either the best (minimizing) or the worst (maximizing) strategies and in either case they are essential in determining the structure of optimal controls. These typically then need to be synthesized from bang and singular controls through an analysis of the switching function. Thus singular controls generally play a major role in a synthesis of optimal controlled trajectories and in this paper we analyze their existence and loocal optimality for the problem in (5) - (8).

An essential tool in this analysis is the Lie bracket of vector fields which naturally arises in the formulas for the derivatives of the switching function. Given two differentiable vector fields f and g defined on a common open subset of $\mathbb{R}^n$, their *Lie bracket* can be defined as

$$[f, g](x) = Dg(x)f(x) - Df(x)g(x)$$

The Lie-bracket is anti-commutative, i.e., $[f, g] = -[g, f]$, and for arbitary vector fields f, g and h it satisfies the Jacobi identity[8]

$$\big[f, [g, h]\big] + \big[g, [h, f]\big] + [h, [f, g]] \equiv 0 \qquad 11$$

The following result provides an important framework for efficient computations of the derivatives of the switching functions. It is easily verified by a direct *computation*.

Proposition 1. *Let (x,(u,v)) be a controlled trajectory of the system and let λ be a solution to the corresponding adjoint equations. Given a continuously differentiable vector field h, define*

$$\Psi(t) = \langle \lambda(t), h(x(t)) \rangle$$

Then the derivative of Ψ *is given by*

$$\dot{\Psi}(t) = \langle \lambda(t), [f + g_1 + g_2 v, h](x(t)) \rangle.$$

9 THE STRUCTURE OF SINGULAR CONTROLS

Now, we start by investigating the existence and local optimality of singular controls for the system in (5) - (8). By proposition 1 the derivatives of the switching functions $\Phi_1(t) = \langle \lambda(t), g_1(x(t)) \rangle$ and $\Phi_2(t) = \langle \lambda(t), g_2(x(t)) \rangle$ are given by

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f + g_1 u + g_2 v, g_1](x(t)) \rangle$$
$$\dot{\Phi}_2(t) = \langle \lambda(t), [f + g_1 u + g_2 v, g_2](x(t)) \rangle$$

By anti-commutativity of the Lie bracket $[g_i, g_i] \equiv 0$ and a simple computation verifies that the control vector fields g_1 and g_2 commute, i.e., $[g_1, g_2] \equiv 0$ as well. We thus have that

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f, g_1](x(t)) \rangle \text{ and } \dot{\Phi}_2(t) = \langle \lambda(t), [f, g_2](x(t)) \rangle$$

Elementary calculations verify that

$$[f, g_1](x) = \begin{pmatrix} aV \\ -Q \\ 0 \\ \beta SI \end{pmatrix}$$

and

$$[f, g_2](x) = \begin{pmatrix} bI \\ 0 \\ -\beta SI \\ 0 \end{pmatrix}$$

We first analyze the control u, i.e., vaccination schedules. Applying Proposition 2 once more to $\ddot{\Phi}_1$, it follows that

$$\ddot{\Phi}_1(t) = \langle \lambda(t), [f + g_1 u + g_2 v, [f, g_1]](x(t)) \rangle \quad (12)$$

and

$$[g_1, [f, g_1]](x) = \begin{pmatrix} -aV \\ -Q \\ 0 \\ -\beta SI \end{pmatrix} \quad (1$$

The switching function of (13) is

$$\dot{\Phi}_1(t) \equiv \lambda_1(t) aV(t) - \lambda_2(t) Q + \lambda_4(t) \beta S(t) I(t). \quad (14)$$

Implies that

$$\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle = -(2\lambda_1(t) aV(t) + 2\lambda_4(t) \beta S(t) I(t)) \quad (15)$$

and $\Phi_1(\mathrm{t}) = (c_1 + c_2) - \lambda_2(t) V_*(t) - \lambda_3(\mathrm{t}) \mathrm{S}_*(\mathrm{t}) \equiv 0$ gives that $\lambda_2(t)$ and $\lambda_3(t)$ must be positive along a singular arc. Hence we have that

$$\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle = -(2\lambda_1(t) aV(t) + 2\lambda_4(t) \beta S(t) I(t)) < 0.$$

Singular controls of this type , i.e., for which $\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle$ does not vanish, are said to be of order 1 and it is a second-order necessary condition for minimality, the are so called *legendre-Clebsch condition*, that this quantity be negative [9]. Thus for this model singular controls u are locally optimal. Furthermore, we can compute the singular control as

$$u_{sin}(t) = -\frac{\langle \lambda(t), [f, [f, g_1]](x(t)) \rangle}{\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle} \quad (16)$$

To evaluate the vector fields, this equation can be simplified. A direct, but some what lengthy computation

shows

$$[f,[f,g_1]](x) = \begin{pmatrix} 2aQ - aV\mu - a\delta V - b\beta SI \\ -(\mu+\delta)Q \\ \delta Q + \beta^2 S^2 I \\ \beta I\delta V - \mu\beta IS + \theta\beta IS + \beta^2 I^2 S \end{pmatrix}$$

and

$$\begin{aligned} &\langle \lambda(t), [f,[f,g_1]](x(t))\rangle \\ &= \lambda_1(t)\Big((a\big(2Q - \mu V(t) - \delta V(t)\big) - b\beta S(t)I(t)\Big) - \lambda_2(t)(\mu+\delta)Q \\ &+ \lambda_3(t)(\delta Q + \beta^2 S^2(t)I(t)) + \lambda_4(\beta I(t)S(t)(\theta + \beta I(t)S(t) - \mu) + \beta\delta I(t)V(t)) \end{aligned} \tag{17}$$

we can write

$$[f,[f,g_1]](x) = \mu[f,g_1](x) + \frac{\delta}{2}[g_1,[f,g_1]] + \omega(x),$$

where

$$\omega(x) = \lambda_1(2aQ - a\delta V - b\beta IS) + \lambda_3(\delta Q + \beta^2 S^2 I) + \lambda_4(\delta\beta IV - \beta^2 I^2 S + \beta IS\theta).$$

Since $\langle \lambda(t), [f,g_1](x(t))\rangle \equiv 0$, it follows from (16) that

$$u_{sin}(t) = -\frac{1}{2}\delta + \frac{1}{2}\frac{\omega(x)}{\lambda_1 aV + \lambda_4\beta IS}$$

Once more using (14), we simplified the second term to $\frac{\omega(x)}{2\lambda_2 Q}$ and we obtain the following result:

Proposition 2. *A singular control u is of order 1 and satisfied the Legendre-Clebsch condition for minimality. The singular control is given as a function depending both on the state and the multiplier in the form*

$$u_{sin}(t) = \frac{1}{2}\Big(\frac{\omega(x)}{\lambda_2 Q} - \delta\Big).$$

Based on the structure of singular control we apply the same way to analysis treatment control (v). Let switching function Φ_2 give

$$\Phi_2(t) = \langle \lambda(t), g_2(x(t))\rangle$$

The first derivative of Φ_2 is

$$\dot{\Phi}_2(t) = \langle \lambda(t), [f + g_1 u + g_2 v, g_2](x(t))\rangle$$

and the second derivative is given by

$$\ddot{\Phi}_2(t) = \langle \lambda(t), [f, +g_1 u + g_2 v, [f,g_2]](x(t))\rangle.$$

Furthermore, a direct calculation verifies that

$$[g_2,[f,g_2]] = \begin{pmatrix} -bI \\ 0 \\ \beta IS \\ 0 \end{pmatrix} = -[f,g_2](x)$$

Since $g_2$and $[f,g_1\cdot]$ commute, it follows from the Jacobi identity that $[g_1,[f,g_2]] = [g_2,[f,g_1]] \equiv 0$. we found $\langle \lambda(t), [f,g_2](x(t))\rangle \equiv 0$ and thus also

$$\langle \lambda(t), [g_2,[f,g_2]](x(t))\rangle \equiv 0$$

and $[f,f,g_2]$ and $[g_2,[f,g_2]] \equiv 0$. Thus there is no singular on V, we obtain the following result

Proposition 3. *The control v cannot be singular.*

CONCLUSION

The optimal singular control problem for an VSIR-model with vaccination and treatment were discussed. The structure singular controls was analized to determine singularity properties of the model. We apply Lie bracket of vector field to check whether the second order of switching function was vanish or not. For the calculation we used Maple. Based on our computation, we found that the vaccination schedule is singular but the treatment cannot be singular. The optimality of vaccination and treatment for other epidemology problem can be analized in future.

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10.

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Appendix 5: ACTIVITY'S PHOTO

Photo 1. The activity to prepare some papers for conference

Photo 2. Presentation of first result in Langkawi

Photo 2. Presentation for the second paper

Photo 4. The submission report for the fourth paper to journal of Applied Mathematics

FOTOCOPY OF RESEARCH APPOITMENT LETTER

DEPARTEMEN PENDIDIKAN DAN KEBUDAYAAN
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SURAT PERJANJIAN PENELITIAN
No.:062/UN33.8/LL/2014
Tanggal: 1 April 2014

Pada hari ini Selasa tanggal satu bulan April tahun dua ribu empat belas, kami yang bertanda tangan di bawah ini:

1. Prof. Drs. Manihar Situmorang, M.Sc., Ph.D : Ketua Lembaga Penelitian Universitas Negeri Medan, dan atas nama Rektor UNIMED, dan dalam perjanjian ini disebut **PIHAK PERTAMA**.
2. Martina Setia Sinaga, S.Si.M.Si : Dosen FMIPA bertindak sebagai Peneliti/ Ketua pelaksana Penelitian, selanjutnya disebut **PIHAK KEDUA**.

Kedua belah pihak secara bersama-sama telah sepakat mengadakan Surat Perjanjian Pelaksanaan Pengadaan Penelitian untuk meiaksanakan Penelitian Desentralisasi BOPTN Tahun 2014 yang dibiayai dari Anggaran DIPA Universitas Negeri Medan Tahun 2014 untuk dengan ketentuan sebagai berikut:

Pasal 1

PIHAK PERTAMA memberi tugas kepada PIHAK KEDUA, dan PIHAK KEDUA menerima tugas tersebut untuk melaksanakan penelitian dengan judul: "**Pengembangan Model Vaksin dengan Pengaruh Vaksinasi untuk Mengurangi Penyebaran Penyakit TB Di Sumatera Utara.**" yang menjadi Penelitian Desentralisasi BOPTN Tahun 2014 tanggung jawab PIHAK KEDUA dengan masa kerja 8 (delapan) bulan terhitung mulai bulan April s/d November 2014.

Pasal 2

Pekerjaan dilaksanakan oleh PIHAK KEDUA atas dasar ketentuan yang merupakan bagian yang tidak terpisahkan dari DP2M dan Universitas Negeri Medan.

Pasal 3

Untuk pelaksanaan pengawasan dan pengendalian pekerjaan adalah Lembaga Penelitian Unimed dan sistem pengendalian internal (SPI) Unimed.

Pasal 4

1. PIHAK PERTAMA memberikan dana penelitian tersebut pada pasal 1 sebesar Rp.38.000.000,- (Tiga puluh delapan juta rupiah) secara bertahap, berdasarkan Surat Keputusan Rektor Universitas Negeri Medan Nomor: 0240/A/UN33/KEP/2014, Tanggal 25 Maret 2014 tentang Penetapan Hibah Penelitian Desentralisasi BOPTN Tahun 2014, Skim Penelitian Hibah Bersaing.
2. Tahap pertama sebesar 70%, yaitu Rp. 26.600.000,- (Dua puluh enam juta enam ratus ribu rupiah), dibayarkan setelah Surat Perjanjian Penggunaan dana (SPPD) ini ditandatangani oleh kedua belah pihak.
3. Tahap kedua sebesar 30%, yaitu Rp. 11.400.000,- (Sebelas juta empat ratus ribu rupiah) dibayarkan setelah menyerahkan Laporan Akhir Penelitian.
4. Jangka waktu pelaksanaan pekerjaan sampai 100% yang disebut pada pasal 1 perjanjian ini ditetapkan selama 8 (Delapan) bulan terhitung sejak tanggal 01 April 2014 s/d 29 November 2014. Waktu penyelesaian tersebut tidak bisa dirubah oleh PIHAK KEDUA.
5. PIHAK KEDUA membayar pajak (PPh) sesuai dengan peraturan yang berlaku dan fotocopy bukti pembayaran diserahkan ke Lembaga Penelitian Universitas Negeri Medan.

Pasal 5

1. PIHAK KEDUA menyelesaikan dan menyerahkan Laporan Hasil penelitian sebagaimana dimaksud dalam pasal 1 selambat-lambatnya tanggal 29 November 2014.
2. PIHAK KEDUA menyerahkan Laporan Kemajuan Pelaksanaan Penelitian paling lambat bulan Juli 2014 dan memasukkan Laporan Kemajuan Penelitian secara *online* di aplikasi SIMLITABMAS Dikti Kemendiktisd.
3. PIHAK KEDUA harus melakukan Monitoring dan Evaluasi yang dilakukan secara Internal untuk penelitian lapangan oleh Lembaga Penelitian Unimed pada bulan Juli 2014, dan secara Eksternal oleh DITLITABMAS DIKTI DEPDIKBUD pada bulan Agustus 2014, dan hasil penilaian diunggah secara online di simlitabmas.dikti.go.id.
4. PIHAK KEDUA harus memasukkan Draft Hasil Penelitian secara *online* di aplikasi SIMLITABMAS Dikti Kemendiktisd dengan menguggah ke simlitabmas.dikti.go.id, dan menyerahkan hard copy paling lambat pada Minggu ke 4 bulan Oktober 2014, dibuat rangkap 2.
5. Sebelum Laporan Akhir Penelitian, PIHAK KEDUA harus melakukan DESIMINASI Hasil Penelitian melalui forum resmi yang Dikoordinasi oleh Lemlit Unimed pada Minggu ke 1-2 bulan November 2014.
6. PIHAK KEDUA harus menyampaikan naskah artikel ilmiah hasil Penelitian dalam bentukcompacktc disk (CD) untuk diterbitkan pada Jurnal Nasional, Nasional terakreditasi atau Jurnal Internasional, dan bukti pengiriman dilampirkan di dalam Laporan penelitian.
7. PIHAK KEDUA harus menyelesaikan Laporan Hasil Pelaksanaan Penelitian sesuai Panduan Pelaksanaan Penelitian DP2M Edisi IX tahun 2013 secara *online* di aplikasi SIMLITABMAS Dikti Kemendiktisd dan menyerahkan hard copy Laporan Hasil Pelaksanaan Penelitian kepada PIHAK PERTAMA sebanyak 8 (delapan) exemplar dan 3 soft copy bersama-sama Draft Publikasi Ilmiah paling lambat tanggal 14 November 2014 dalam bentuk pdf. Laporan Akhir Penelitian ini dibuat rangkap 8 (delapan) diperuntukkan sebagai berikut: 1 (satu) pada Perpustakaan Nasional, 1 (satu) pada PDII-LIPI, 1 (satu) pada BAPENAS, 1 (satu) perpustakaan Unimedi, 1 (satu) pada Lembaga Penelitian Unimed, 1 (satu) untuk fakultas ybs, dan 1 (satu) untuk jurusan/prodi ybs.
8. Sistematika laporan akhir penelitian harus memenuhi ketentuan sesuai ketentuan yang ditetapkan di dalam Panduan Pelaksanaan Penelitian DP2M Edisi IX tahun 2013, paling sedikit sebagai berikut:
   a. Bentuk ukuran kertas kwarto
   b. Warna cover disesuaikan dengan ketentuan yang ditetapkan oleh sesuai Panduan Pelaksanaan Penelitian DP2M Edisi IX Tahun 2013
   c. Dibawah bagian kulit cover depan ditulis: dibiayai berdasarkan Surat Perjanjian Penelitian, Nomor 062/UN33.8/LL/2014 , Tanggal 01 April 2014.
   d. Melampirkan Surat Perjanjian Penelitian pada lampiran Laporan Hasil Penelitian tahun 2014.
   e. PIHAK KEDUA wajib menyerahkan artikel dan ringkasan eksekutif kepada PIHAK PERTAMA sebanyak dua rangkap dan soft copy saat menyerahkan Laporan Hasil Penelitian sesuai dengan format dan ketentuan yang telah ditentukan pada templet SIMLITABMAS Dikti Kemendiktisd (dalam format Microsoft word).
9. PIHAK KEDUA wajib menyampaikan laporan realisasi dana pelaksanaan pekerjaan penelitian kepada PIHAK PERTAMA sebanyak (2) rangkap dan menunggah secara *online* di aplikasi SIMLITABMAS Dikti Kemendiktisd penelitian paling lambat tanggal 14 November 2014 yang pembiayannya dibebankan pada PIHAK KEDUA. Bukti pengeluaran keuangan (kwitansi) dan RAB menjadi arsip pada PIHAK KEDUA.
10. PIHAK KEDUA harus menyimpan segala dokumen yang berhubungan dengan penelitian dan dapat diberikan bila diperlukan.
11. Apabila Ketua pelaksana sebagaimana dimaksud pada Pasal 1 tidak dapat menyelesaikan pelaksanaan penelitian ini, maka PIHAK KEDUA dapat menunjuk pengganti Ketua Pelaksana yang merupakan salah satu anggota tim setelah mendapat persetujuan tertulis dari Rektor Universitas Negeri Medan.
12. Apabila PIHAK KEDUA tidak melaksanakan tugas sebagaimana dimaksud dalam pasal 1 maka harus mengembalikan dana yang telah diterimanya ke Kas Negara serta menyerahkan fotocopy bukti pengembalian ke Kas Negara yang akan divalidasi oleh KPPN.
13. Apabila dikemudian hari terbukti bahwa judul penelitian sebagaimana dimaksud dalam Pasal 1 dijumpai adanya indikasi duplikasi dengan penelitian lain/atau diperoleh indikasi ketidak jujuran/tikat tidak baik yang tidak sesuai dengan kaidah ilmiah, maka kegiatan penelitian tersebut dinyatakan batal dan PIHAK KEDUA wajib mengembalikan dana yang telah diterimanya ke Kas Negara dan divalidasi oleh KPPN.

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Pasal 6

1. Apabila PIHAK KEDUA tidak dapat menyelesaikan penelitiann sebagaimana tersebut dalam Pasal 5 maka PIHAK KEDUA dikenakan sanksi harus mengembalikan dana yang telah diterimanya ke Kas Negara.
2. Apabila batas waktu pelaksanaan penelitian ini PIHAK KEDUA belum menyerahkan hasil pekerjaan seluruhnya kepada PIHAK PERTAMA, maka PIHAK KEDUA dikenakan denda sebesar 1(satu) permil setiap hari keterlambatan sampai dengan setinggi-tingginya 5% (lima persen) dari nilai Surat Perjanjian ini, terhitung dari tanggal jatuh tempo yang telah ditetapkan sampai dengan batas akhir pembayaran dana penugasan penelitian oleh Universitas Negeri Medan.

Pasal 7

1. Hak kekayaan intelektual yang dihasilkan dari hasil penelitian tersebut diatur dan dikelola sesuai dengan peraturan dan perundang-undangan yang berlaku.
2. Hasil penelitian berupa peralatan dan/atau alat yang dibeli dari kegiatan ini adalah milik negara yang dapat dihibahkan kepada lembaga/institusi/masyarakat melalui Surat Keterangan Hibah.

Pasal 8

1. Apabila terjadi perselisihan antara PIHAK PERTAMA dan PIHAK KEDUA dalam pelaksanaan perjanjian ini maka akan dilakukan penyelesaian secara musyawarah dan mufakat, dan apabila tidak tercapai penyelesaian secara musyawarah dan mufakat maka penyelesaian dilakukan melalui proses hukum yang berlaku.
2. Hal-hal yang belum diatur dalam perjanjian ini akan diatur kemudian oleh kedua belah pihak. Demikian surat Perjanjian Penelitian ini diperbuat untuk dikerahui dan dilaksanakan sebagaimana mestinya.

PIHAK PERTAMA,	PIHAK KEDUA,
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