OPTIMAL CONTROL OF INFECTIOUS DISEASES VIA VACCINATION, QUARANTINE AND TREATMENT: A THEORETICAL APPROACH

BOLARIN, G.[1], BAMIGBOLA, O. M.[2], & COLE, A. T.[1]
[1]Mathematics Department, FUT, Minna, Niger State, Nigeria
[2]Mathematics Department, Unilorin, Ilorin, Kwara State, Nigeria
E-mail: g.bolarin@futminna.edu.ng **Phone No:** +234-818-714-1978

Abstract
The focus of this paper is to examine the problem of controlling spread of infectious diseases through the use of Vaccines, quarantine and Treatment. Through the use of Pontryagin's maximum principle, we were able to ascertain the existence of the control systems. We also apply optimal control theory to minimizing the spread of infection in a population; the optimality was measured by the minimization of the probability of infectious individuals and maximization of the recovered individuals.

Keyword: *Optimal Control Theory, Pontryagin's maximum principle, Hamiltonian, Langragian, Infectious Diseases, Vaccination*

Introduction
Epidemiologist and Health workers all over the world are always seeking a way to eradicate infectious diseases in a given population. It has been noted that if proper and timely steps are taken in the course of an outbreak of a disease, eradication is possible. Notable ways of preventing or eradicating an infection include but not limited to (i) vaccination (ii) enlightenment campaign (iii) treatment etc.

Optimal control theory and its applications to models were first proposed by Pontryagin in the 1950s and improved on by Pontryagin et al (1986). Recently his work has been extended and used to make decisions in epidemiological models.

Optimal control theory is a useful tool that can be used to control the spread of a disease for which vaccine and /or treatment are available; see Yusuf and Benyah (2012), Zaman et al (2007), Zaman et al (2008) and Zaman et al (2009) for examples. The authors of aforementioned articles concentrated on the use of SIR models and they either applied optimal vaccination alone or with treatment, but in this study we applied the theory to a MSEIR model with standard incidence and we included quarantine as a control variable. The derivation and analysis of the MSEIR model used in this work can be found in Bolarin (2014).

Optimal Control
Optimal Vaccination
We consider the control variable $u(t) \in U_{\max}$ to be the percentage of susceptible individuals being vaccinated per unit time. Here,
$U_{\max} = \{u \mid u(t) \text{ is lebesque measurable, } 0 \le u(t) \le 0.87,\ t \in [0,T]\}$.

Now we consider an optimal control problem to minimize the objective functional

$$J(u) = \int_0^T \left[A_1 M(t) + A_2 S(t) + A_3 E(t) + A_4 I(t) + \frac{1}{2}\kappa u^2(t) \right] dt \qquad (1.1)$$

Subject to

$$
\left.
\begin{aligned}
&\frac{dM}{dt} = K - (\delta + \alpha)M - \mu S \\
&\frac{dS}{dt} = -\frac{\beta SI}{N} + \delta M + (\mu - \alpha - u(t))S + \rho R \\
&\frac{dE}{dt} = \frac{\beta SI}{N} - (\varepsilon + \alpha)E \\
&\frac{dI}{dt} = \varepsilon E - (\gamma + \alpha + \varphi)I \\
&\frac{dR}{dt} = \gamma I - (\rho + \alpha)R + u(t)S(t) \\
&with \\
&M(0) = M_0 \geq 0 \\
&S(0) = S_0 \geq 0 \\
&E(0) = E_0 \geq 0 \\
&I(0) = I_0 \geq 0 \\
&R(0) = R_0 \geq 0
\end{aligned}
\right\} \qquad (1.2)
$$

$A_i (i = 1,2,3,4)$ are small positive constants to keep a balance in the size of $M(t), S(t), E(t)$ and $I(t)$ respectively. κ is a positive weight parameter such that $0 < \kappa < N$ which is associated with the control $u(t)$. In this work, what we intend to do is to minimize the $M(t), S(t), E(t)$ and $I(t)$ classes and to maximize the total number of recovered class $R(t)$ using possible minimal control variable $u(t)$.

First, we show the existence for the control system (1.2). Let $M(t), S(t), E(t)$ and $I(t)$ be state variables with control variable $u(t)$. For existence, we consider a control system (1.2) with initial conditions. We rewrite (1.2) in the following form:

$$\phi_t = A\phi + F(\phi) \qquad (1.3)$$

where $\phi = \begin{bmatrix} M(t) \\ S(t) \\ E(t) \\ I(t) \\ R(t) \end{bmatrix}$; $A = \begin{bmatrix} -(\delta+\alpha) & -\mu & 0 & 0 & 0 \\ \delta & (\mu-\alpha-u(t)) & 0 & 0 & \rho \\ 0 & 0 & -(\varepsilon+\alpha) & 0 & 0 \\ 0 & 0 & \varepsilon & -(\gamma+\alpha+\varphi) & 0 \\ 0 & u(t) & 0 & \gamma & -(\rho+\alpha) \end{bmatrix}$

and $F(\phi) = \begin{bmatrix} K \\ \frac{-\beta SI}{N} \\ \frac{\beta SI}{N} \\ 0 \\ 0 \end{bmatrix}$

and ϕ_t denotes the derivates of ϕ with respect to time t. (1.3) is a non-linear system with a bounded coefficient. We set

$$G(\phi) = A\phi + F(\phi) \tag{1.4}$$

The second term on the right hand side of (1.4) satisfies;
$|F(\phi_1) - F(\phi_2)| \leq D(|M_1(t) - M_2(t)| + |S_1(t) - S_2(t)| + |E_1(t) - E_2(t)| + |I_1(t) - I_2(t)|)$ where the positive constant D is independent of the state variables $M(t), S(t), E(t) \text{ and } I(t) \leq N(t)$. Moreso,
$|G(\phi_1) - G(\phi_2)| \leq L|\phi_1 - \phi_2|$ where $L = \max\{D, \|A\|\} < \infty$. So it follows that G is uniformly Lipschitz continuous.

Following the argument to Birkhoff and Rota (1986), from definition of the control $u(t)$ and the restriction on $M(t), S(t), E(t), I(t) \text{ and } R(t) \geq 0$, we see that the solution of the system (1.3) exists.

In order to find the optimal solution of our control problems (1.1) and (1.2) we first find the lagrangian and Hamiltonian for the optimal control problem.
The lagrangian is given by;

$$L(M, S, E, I, u) = A_1 M(t) + A_2 S(t) + A_3 E(t) + A_4 I(t) + \frac{1}{2}\kappa u^2(t) \tag{1.5}$$

What we seek is the minimal value of (1.5). So we define the following Hamiltonian H for the control problem in order to achieve this.

$$\left.\begin{aligned} \mathrm{H}(M, S, E, I, R, u, \lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, t) = L(M, S, E, I, u) + \lambda_1(t)\frac{dM(t)}{dt} + \lambda_2(t)\frac{dS(t)}{dt} + \lambda_3(t)\frac{dE(t)}{dt} \\ \lambda_4(t)\frac{dI(t)}{dt} + \lambda_5(t)\frac{dR(t)}{dt} \end{aligned}\right\} \tag{1.6}$$

Theorem 1
There exists an optimal control $u^*(t)$ such that $J(u^*(t)) = \min J(u(t))$ subject to the control (1.2) with initial conditions.

Proof:
We will use the result in Lukes (1982) to prove the existence of an optimal control. The control and the state variables are positive. In this minimizing problem, the necessary convexity of the objective functional in $u(t)$ is satisfied. The control space $U_{\max} = \{u \mid u(t) \text{ is lebesque measurable and } 0 \leq u(t) \leq 0.87,\ t \in [0, T]\}$ is also convex and closed by definition. The optimal system is bounded which is the condition for compactness needed for the existence of the optimal control.

More so, the integral in the functional $A_1M(t)+A_2S(t)+A_3E(t)+A_4I(t)+\frac{1}{2}\kappa u^2(t)$ is convex on the control $u(t)$. Lastly there exist a constant $v>1$, positive numbers ω_1 and ω_2 such that

$J(u(t)) \geq \omega_2 + \omega_1(|u(t)|^2)^{v/2}$ which completes the existence of an optimal control.

Now to find the optimal solution, we apply the Pontryagin's maximum principle as applied in Lenhart and John (2007) and Morton and Nancy (2000) to the Hamiltonian.

$$H(t,x(t),u(t),\lambda(t)) = f(t,x(t),u(t)) + \lambda(t)g(t,x(t),u(t)) \qquad (1.7)$$

Lemma 1 (Zaman et al, 2008**)**

If $(x^*(t),u^*(t))$ is an optimal solution of an optimal control problem, then there exists a non-trivial vector function $\lambda(t)=(\lambda_1(t),\lambda_2(2),\ldots\lambda_n(t))$ satisfying the following inequalities:

$$\left.\begin{aligned} \frac{dx}{dt} &= \frac{\partial H(t,x^*(t),u^*(t),\lambda(t))}{\partial \lambda}, \\ 0 &= \frac{\partial H(t,x^*(t),u^*(t),\lambda(t))}{\partial u}, \\ \lambda^{'}(t) &= \frac{\partial H(t,x^*(t),u^*(t),\lambda(t))}{\partial x} \end{aligned}\right\} \qquad (1.8)$$

It follows from the derivation above that,

$$\left.\begin{aligned} &u^* = 0 \quad if\ \frac{\partial H}{\partial u} < 0 \\ &0 \leq u^* \leq 0.87 \quad if\ \frac{\partial H}{\partial u} = 0 \\ &u^* = 0.87 \quad if\ \frac{\partial H}{\partial u} > 0 \end{aligned}\right\} \qquad (1.9)$$

Now we apply the necessary conditions to the Hamiltonian (1.7).

Theorem 2

Let $M^*(t), S^*(t), E^*(t), I^*(t)$ and $R^*(t)$ be the optimal state solutions with associated optimal control variable $u^*(t)$ for the optimal control (1.1) and (1.2). Then there exist adjoint variables $\lambda_1,\lambda_2,\lambda_3,\lambda_4$ and λ_5 satisfying

$$\left.\begin{aligned} \lambda_1^{'}(t) &= (\lambda_1(t)-\lambda_2(t))\delta + \alpha\lambda_1(t) - A_1 \\ \lambda_2^{'}(t) &= \mu\lambda_1(t) + (\lambda_2(t)-\lambda_5(t))\frac{\beta I^*(t)}{N(t)} + (\alpha-\mu)\lambda_2(t) + (\lambda_2(t)-\lambda_5(t))u^*(t) - A_2 \\ \lambda_3^{'}(t) &= \varepsilon(\lambda_3(t)-\lambda_4(t)) + \alpha\lambda_3(t) - A_3 \\ \lambda_4^{'}(t) &= (\lambda_2(t)-\lambda_3(t))\frac{\beta S^*(t)}{N(t)} + (\gamma+\alpha+\varphi)\lambda_4(t) - \gamma\lambda_5(t) - A_4 \\ \lambda_5^{'}(t) &= (\lambda_5(t)-\lambda_2(t))\rho + \alpha\lambda_5(t) \end{aligned}\right\} \qquad (1.10)$$

with transversality conditions,

$$\lambda_i(T) = 0 \qquad i = 1,2,3,4,5 \qquad (1.11)$$

Furthermore, the optimal control $u^*(t)$ is given as

$$u^*(t) = \max\left\{\min\left\{\frac{S^*(t)(\lambda_2(t) - \lambda_5(t))}{\kappa}, 0.87\right\}, 0\right\} \tag{1.12}$$

Proof:

To determine the adjoint equations and the transversality conditions we use the Hamiltonian (1.6). By setting $M(t) = M^*(t), S(t) = S^*(t), E(t) = E^*(t), I(t) = I^*(t)$ and $R(t) = R^*(t)$ and differentiating the Hamiltonian (1.7) with respect to $M(t), S(t), E(t), I(t)$ and $R(t)$ we obtain,

$$\lambda_1^{'}(t) = \frac{-\partial H}{\partial M} = \left(\lambda_1(t) - \lambda_2(t)\right)\delta + \alpha\lambda_1(t) - A_1$$

$$\lambda_2^{'}(t) = \frac{-\partial H}{\partial S} = \mu\lambda_1(t) + \left(\lambda_2(t) - \lambda_5(t)\right)\frac{\beta I^*(t)}{N(t)} + (\alpha - \mu)\lambda_2(t) + (\lambda_2(t) - \lambda_5(t))u^*(t) - A_2$$

$$\lambda_3^{'}(t) = \frac{-\partial H}{\partial E} = \varepsilon\left(\lambda_3(t) - \lambda_4(t)\right) + \alpha\lambda_3(t) - A_3$$

$$\lambda_4^{'}(t) = \frac{-\partial H}{\partial I} = \left(\lambda_2(t) - \lambda_3(t)\right)\frac{\beta S^*(t)}{N(t)} + \left(\gamma + \alpha + \varphi\right)\lambda_4(t) - \gamma\lambda_5(t) - A_4$$

$$\lambda_5^{'}(t) = \frac{-\partial H}{\partial R} = \left(\lambda_5(t) - \lambda_2(t)\right)\rho + \alpha\lambda_5(t)$$

Using the optimality conditions, we have

$$\frac{\partial H}{\partial u} = \kappa u^* - S^*(t)\lambda_2(t) + S^*(t)\lambda_5(t) = 0$$

$$\Rightarrow \kappa u^*(t) = S^*(t)(\lambda_2(t) - \lambda_5(t))$$

which gives

$$u^*(t) = \frac{S^*(t)(\lambda_2(t) - \lambda_5(t))}{\kappa} \tag{1.13}$$

from (1.9) and (1.13) we have

$$u^*(t) = \begin{cases} 0 & \text{if } \dfrac{S^*(t)(\lambda_2(t) - \lambda_5(t))}{\kappa} \le 0 \\ \dfrac{S^*(t)(\lambda_2(t) - \lambda_5(t))}{\kappa}, & \text{if } 0 < \dfrac{S^*(t)(\lambda_2(t) - \lambda_5(t))}{\kappa} < 0.87 \\ 0.87 & \text{if } \dfrac{S^*(t)(\lambda_2(t) - \lambda_5(t))}{\kappa} \ge 0.87 \end{cases}$$

It can be rewritten in the following form $u^*(t) = \max\left\{\min\left\{\frac{S^*(t)(\lambda_2(t) - \lambda_5(t))}{\kappa}, 0.87\right\}, 0\right\}$

The characterization of the optimal control is given by (1.12).

To obtain the optimal control and state we solve the optimality system consisting of the state system (1.2) with boundary conditions, the adjoint systems (1.10) and (1.11) and the characterization of the optimal control (1.12).

By substituting the values of $u^*(t)$ in the control system we get the following system

$$\left.\begin{aligned}
\frac{dM^*(t)}{dt} &= K-(\delta+\alpha)M^*(t)-\mu S^*(t)\\
\frac{dS^*(t)}{dt} &= -\frac{\beta S^*(t)I^*(t)}{N}+\delta M^*(t)+(\mu-\alpha)S^*(t)-S^*(t)\left(\max\left\{\min\left\{\frac{S^*(t)(\lambda_2(t)-\lambda_5(t))}{\kappa},0.87\right\},0\right\}\right)+\rho R\\
\frac{dE^*(t)}{dt} &= \frac{\beta S^*(t)I^*(t)}{N}-(\varepsilon+\alpha)E^*(t)\\
\frac{dI^*(t)}{dt} &= \varepsilon E^*(t)-(\gamma+\alpha+\varphi)I^*(t)\\
\frac{dR^*(t)}{dt} &= \gamma I^*(t)-(\rho+\alpha)R^*(t)+S^*(t)\left(\max\left\{\min\left\{\frac{S^*(t)(\lambda_2(t)-\lambda_5(t))}{\kappa},0.87\right\},0\right\}\right)
\end{aligned}\right\} \quad (1.14)$$

with the Hamiltonian H^* at $(t, M^*, S^*, E^*, I^*, R^*, u^*, \lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5)$

$$\left.\begin{aligned}
H^* = {} & M^*(t)+S^*(t)+E^*(t)+I^*(t)+\frac{1}{2}\left[\kappa\left(\max\left\{\min\left\{\frac{S^*(t)(\lambda_2(t)-\lambda_5(t))}{\kappa},0.87\right\},0\right\}\right)^2\right]\\
& +\lambda_1(t)\left[K-(\delta+\alpha)M^*(t)-\mu S^*(t)\right]+\lambda_2(t)\left[\begin{aligned}&-\frac{\beta S^*(t)I^*(t)}{N}+\delta M^*(t)+(\mu-\alpha)S^*(t)\\ &-S^*(t)\left(\max\left\{\min\left\{\frac{S^*(t)(\lambda_2(t)-\lambda_5(t))}{\kappa},0.87\right\},0\right\}\right)\\ &+\rho R\end{aligned}\right]\\
& +\lambda_3(t)\left[\frac{\beta S^*(t)I^*(t)}{N}-(\varepsilon+\alpha)E^*(t)\right]+\lambda_4(t)\left[\varepsilon E^*(t)-(\gamma+\alpha+\varphi)I^*(t)\right]\\
& +\lambda_5(t)\left[\gamma I^*(t)-(\rho+\alpha)R^*(t)+S^*(t)\left(\max\left\{\min\left\{\frac{S^*(t)(\lambda_2(t)-\lambda_5(t))}{\kappa},0.87\right\},0\right\}\right)\right]
\end{aligned}\right\} \quad (1.15)$$

Optimal Vaccination and Treatment

We define our objective functional as;

$$J(u)=\int_0^T [A_1M(t)+A_2S(t)+A_3E(t)+A_4I(t)]dt+\frac{1}{2}\int_0^T (C_1u_1^2+C_2u_2^2)dt$$

subject to

$$\frac{dM(t)}{dt}=K-(\delta+\alpha)M(t)-\mu S(t)$$

$$\frac{dS(t)}{dt}=-\frac{\beta S(t)I(t)}{N(t)}+\delta M(t)+(\mu-\alpha-u_1(t))S(t)+\rho R(t) \quad (1.16)$$

$$\frac{dE(t)}{dt}=\frac{\beta S(t)I(t)}{N(t)}-(\varepsilon+\alpha)E(t)$$

$$\frac{dI(t)}{dt}=\varepsilon E(t)-(\gamma+\alpha+\varphi+u_2(t))I(t)$$

$$\frac{dR(t)}{dt}=\gamma I(t)-(\rho+\alpha)+u_1(t)S(t)+u_2(t)I(t)$$

where

$$U=\left\{(u_1(t),u_2(t))\,|\,0\le u_1\le u_{1\max}\le 1, 0\le u_2\le u_{2\max}\le 1, t\in[0,T]\right\} \quad (1.17)$$

and it is measurable in lebesque sense.

A_i *for* $i=1,2,3,4$ are small positive constant to keep a balance in the size of our compartments.

C_1 and C_2 are the relative weights attached to the cost of the interventions. u_1 and u_2 are proportions of vaccinated susceptible and treated infected respectively.

Following the approach above we have;

For existence:

Let $M(t), S(t), E(t)$ and $I(t)$ be the state variables with a control variable u (as given in 1.17). For existence we consider a control system (1.16) with initial conditions. We can rewrite (1.16) in the following form

$$\phi_t=A\phi+F(\phi) \quad (1.18)$$

Where

$$\phi=\begin{bmatrix} M(t)\\ S(t)\\ E(t)\\ I(t)\\ R(t)\end{bmatrix};$$

$$A=\begin{bmatrix} -(\delta+\alpha) & -\mu & 0 & 0 & 0 \\ \delta & (\mu-\alpha-u(t)) & 0 & 0 & \rho \\ 0 & 0 & -(\varepsilon+\alpha) & 0 & 0 \\ 0 & 0 & \varepsilon & -(\gamma+\alpha+\varphi+u_2) & 0 \\ 0 & u(t) & 0 & (\gamma+u_2) & -(\rho+\alpha) \end{bmatrix}$$

$$F(\phi)=\begin{bmatrix} K \\ \frac{-\beta SI}{N} \\ \frac{\beta SI}{N} \\ 0 \\ 0 \\ \end{bmatrix}$$

and ϕ_t denote the derivative of ϕ with respect to time *t.* As we know (1.18) is a non-linear system with a bounded coefficient. Now we have

$$G(\phi)=A\phi+F(\phi) \tag{1.19}$$

The second term on the RHS of (1.19) satisfies
$\left|F(\phi_1)-F(\phi_2)\right| \le L\left(\left|M_1(t)-M_2(t)\right|+\left|S_1(t)-S_2(t)\right|+\left|E_1(t)-E_2(t)\right|+\left|I_1(t)-I_2(t)\right|\right)$ where L (positive constant) is independent of the state variable $M(t), S(t), E(t)$ and $I(t) \le N(t)$.

More so,
$\left|G(\phi_1)-G(\phi_2)\right| \le H\left|\phi_1-\phi_2\right|$ where $\mathrm{H}=\max\{L, \|K\|\}$ with restriction on

$M(t), S(t), E(t), I(t)$ and $R(t) \ge 0$ and the definition of u , we can see that the solution of the system (1.16) exists and G is uniformly Lipschitz continuous.

To find the optimal solution of (1.16) and (1.17) we find the Lagrangian and Hamiltonian for the optimal control problem.

The Lagrangian is given by,

$$L(M,S,E,I,U)=A_1M(t)+A_2S(t)+A_3E(t)+A_4I(t)+\frac{1}{2}C_1u_1^2+C_2u_2^2 \tag{1.20}$$

We seek the minimal value of (1.20). So we define the following Hamiltonian H for the control problem.

$$\left.\begin{aligned} \mathrm{H}(M,S,E,I,R,u,\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5,t) &= L(M,S,E,I,u)+\lambda_1(t)\frac{dM(t)}{dt}+\lambda_2(t)\frac{dS(t)}{dt}+\lambda_3(t)\frac{dE(t)}{dt} \\ &\lambda_4(t)\frac{dI(t)}{dt}+\lambda_5(t)\frac{dR(t)}{dt} \end{aligned}\right\} \tag{1.21}$$

Theorem 3

Let $M^*(t), S^*(t), E^*(t), I^*(t)$ and $R^*(t)$ be optimal state solutions with associated optimal control pair $u_1^*(t)$ and $u_2^*(t)$ for the optimal control problem (16) and (17) then there exists an adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4$ and λ_5 which satisfy:

$$\left.\begin{aligned}
\lambda_1^{'}(t) &= \frac{-\partial H}{\partial M} = \left(\lambda_1(t)-\lambda_2(t)\right)\delta + \alpha\lambda_1(t) - A_1 \\
\lambda_2^{'}(t) &= \frac{-\partial H}{\partial S} = \mu\lambda_1(t) + \left(\lambda_2(t)-\lambda_5(t)\right)\frac{\beta I^*(t)}{N(t)} + (\alpha-\mu)\lambda_2(t) + (\lambda_2(t)-\lambda_5(t))u_1^*(t) - A_2 \\
\lambda_3^{'}(t) &= \frac{-\partial H}{\partial E} = \varepsilon\left(\lambda_3(t)-\lambda_4(t)\right) + \alpha\lambda_3(t) - A_3 \\
\lambda_4^{'}(t) &= \frac{-\partial H}{\partial I} = \left(\lambda_2(t)-\lambda_3(t)\right)\frac{\beta S^*(t)}{N(t)} + (\lambda_4-\lambda_5)\gamma + \left(\alpha+\varphi\right)\lambda_4(t) + (\lambda_4-\lambda_5)u_2^* - A_4 \\
\lambda_5^{'}(t) &= \frac{-\partial H}{\partial R} = \left(\lambda_5(t)-\lambda_2(t)\right)\rho + \alpha\lambda_5(t)
\end{aligned}\right\} \quad (1.22)$$

with transversality conditions $\lambda_i(T) = 0 \quad i = 1,2,3,4,5$ (1.23)

Further more, the optimal control $u = (u_1^*, u_2^*)$ is given as

$$\left.\begin{aligned}
u_1^*(t) &= \max\left\{\min\left\{0, \frac{S^*(t)(\lambda_2(t)-\lambda_5(t))}{C_1}, u_{1\max}\right\}, 0\right\} \\
u_2^*(t) &= \max\left\{\min\left\{0, \frac{I^*(t)(\lambda_4(t)-\lambda_5(t))}{C_5}, u_{2\max}\right\}, 0\right\}
\end{aligned}\right\} \quad (1.24)$$

Proof:

From (21) our Hamiltonian is given as

$$\frac{1}{2}\left(C_1u_1 + C_2u_2\right) + A_1M(t) + A_2S(t) + A_3E(t) + A_4I(t) + \lambda_1(A-(\delta+\alpha)M(t)-\mu S(t))$$
$$+\lambda_2\left(\frac{-\beta S(t)I(t)}{N} + \delta M + (\mu-\alpha-u_1)S(t) + \rho R(t)\right) + \lambda_3\left(\frac{\beta S(t)I(t)}{N} - (\varepsilon+\alpha)E(t)\right)$$
$$+\lambda_4\left(\varepsilon E(t) - (\gamma+\alpha+\varphi+u_2)I(t)\right) + \lambda_5\left(\gamma I(t) - (\rho+\alpha)R(t) + u_1S(t) + u_2I(t)\right)$$

So from the third equation of system (8) and by setting $M(t) = M^*(t), S(t) = S^*(t)$, $E(t) = E^*(t), I(t) = I^*(t) \text{ and } R(t) = R^*(t)$ we have

$$\left.\begin{aligned}
\lambda_1^{'}(t) &= \frac{-\partial H}{\partial M} = \left(\lambda_1(t)-\lambda_2(t)\right)\delta + \alpha\lambda_1(t) - A_1 \\
\lambda_2^{'}(t) &= \frac{-\partial H}{\partial S} = \mu\lambda_1(t) + \left(\lambda_2(t)-\lambda_5(t)\right)\frac{\beta I^*(t)}{N(t)} + (\alpha-\mu)\lambda_2(t) + (\lambda_2(t)-\lambda_5(t))u_1^*(t) - A_2 \\
\lambda_3^{'}(t) &= \frac{-\partial H}{\partial E} = \varepsilon\left(\lambda_3(t)-\lambda_4(t)\right) + \alpha\lambda_3(t) - A_3 \\
\lambda_4^{'}(t) &= \frac{-\partial H}{\partial I} = \left(\lambda_2(t)-\lambda_3(t)\right)\frac{\beta S^*(t)}{N(t)} + (\lambda_4-\lambda_5)\gamma + \left(\alpha+\varphi\right)\lambda_4(t) + (\lambda_4-\lambda_5)u_2^* - A_4 \\
\lambda_5^{'}(t) &= \frac{-\partial H}{\partial R} = \left(\lambda_5(t)-\lambda_2(t)\right)\rho + \alpha\lambda_5(t)
\end{aligned}\right\}$$

Now the Hamiltonian is maximized with respect to controls at the optimal control pair. So by optimality conditions, we have

$$\frac{\delta H}{u_1} = 0 \text{ and } \frac{\delta H}{u_2} = 0$$

$$\Rightarrow \left.\begin{array}{l} C_1u_1 - \lambda_2 S(t) + \lambda_5 S(t) = 0 \\ C_2u_2 - \lambda_4 I(t) + \lambda_5 I(t) = 0 \end{array}\right\} \quad (1.25)$$

which gives

$$\left.\begin{array}{l} u_1 = \dfrac{(\lambda_2 - \lambda_5)S(t)}{C_1} \\ u_2 = \dfrac{(\lambda_4 - \lambda_5)I(t)}{C_2} \end{array}\right\} \quad (1.26)$$

by setting $u_1(t) = u_1^*(t), u_2(t) = u_2^*(t), S(t) = S^*(t)$ and $I(t) = I^*(t)$, from (25) we have

$$\left.\begin{array}{l} u_1^* = \dfrac{(\lambda_2 - \lambda_5)S^*(t)}{C_1} \\ u_2^* = \dfrac{(\lambda_4 - \lambda_5)I^*(t)}{C_2} \end{array}\right\}$$

So if we impose the bounds $0 \le u_1 \le u_{1\max}$ and $0 \le u_2 \le u_{2\max}$, in compact form we have

$$\left.\begin{array}{l} u_1^*(t) = \max\left\{\min\left\{0, \dfrac{S^*(t)(\lambda_2(t) - \lambda_5(t))}{C_1}, u_{1\max}\right\}, 0\right\} \\ u_2^*(t) = \max\left\{\min\left\{0, \dfrac{I^*(t)(\lambda_4(t) - \lambda_5(t))}{C_5}, u_{2\max}\right\}, 0\right\} \end{array}\right\}.$$

So we have (16) and (22) as our resulting optimality system.

Quarantine, Vaccination and Treatment

We now consider an additional optimality parameter, quarantine.

Define the objective function as:

$$J(u) = \int_0^T [A_1M(t) + A_2S(t) + A_3E(t) + A_4I(t)]dt + \frac{1}{2}\int_0^T (C_1u_1^2 + C_2u_2^2 + C_2u_2^2)dt$$

subject to

$$\left.\begin{array}{l} \dfrac{dM(t)}{dt} = K - (\delta + \alpha)M(t) - \mu S(t) \\ \dfrac{dS(t)}{dt} = -\dfrac{\beta S(t)I(t)}{N(t)} + \delta M(t) + (\mu - \alpha - u_1(t))S(t) + \rho R(t) \\ \dfrac{dE(t)}{dt} = \dfrac{\beta S(t)I(t)}{N(t)} - (\varepsilon + \alpha)E(t) \\ \dfrac{dI(t)}{dt} = \varepsilon E(t) - (\gamma + \alpha + \varphi + u_2(t))I(t) \\ \dfrac{dR(t)}{dt} = \gamma I(t) - (\rho + \alpha) + u_1(t)S(t) + u_2(t)I(t) + u_3R(t) \end{array}\right. \quad (1.27)$$

where

$$U = \{(u_1(t), u_2(t)), u_3(t) \mid 0 \le u_1 \le u_{1\max} \le 1, 0 \le u_2 \le u_{2\max} \le 1, 0 \le u_2 \le u_{2\max} \le 1, t \in [0, T]\} \quad (1.28)$$

A_i *for* $i = 1, 2, 3, 4$ are small positive constant to keep a balance in the size of our compartments.

C_1, C_2 and C_3 are the relative weights attached to the cost of the interventions. u_1, u_2 and u_3 are proportions of vaccinated susceptible, quarantine exposed and treated infected respectively.

Similarly, we can show the existence for the optimality system by following the reasoning above.

To find the optimal solution of (1.27) and (1.28) we find the Lagrangian and Hamiltonian for the optimal control problem.

The Lagrange is given by

$$L(M,S,E,I,U) = A_1M(t) + A_2S(t) + A_3E(t) + A_4I(t) + \frac{1}{2}C_1u_1^2 + C_2u_2^2 + C_3u_3^2 \quad (1.29)$$

We seek the minimal value of (1.29), so we define the following Hamiltonian H for the control problem.

$$\left.\begin{aligned} \mathrm{H}(M,S,E,I,R,u,\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5,t) = L(M,S,E,I,u) + \lambda_1(t)\frac{dM(t)}{dt} + \lambda_2(t)\frac{dS(t)}{dt} + \lambda_3(t)\frac{dE(t)}{dt} \\ \lambda_4(t)\frac{dI(t)}{dt} + \lambda_5(t)\frac{dR(t)}{dt} \end{aligned}\right\} \quad (1.30)$$

Theorem 4

Let $M^*(t), S^*(t), E^*(t), I^*(t)$ and $R^*(t)$ be optimal state solutions with associated optimal control pair $u_1^*(t)$ and $u_2^*(t)$ for the optimal control problem (1.16) and (1.17) then there exists an adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4$ and λ_5 which satisfy:

$$\left.\begin{aligned}
\lambda_1'(t) &= \frac{-\partial H}{\partial M} = \left(\lambda_1(t) - \lambda_2(t)\right)\delta + \alpha\lambda_1(t) - A_1 \\
\lambda_2'(t) &= \frac{-\partial H}{\partial S} = \mu\lambda_1(t) + \left(\lambda_2(t) - \lambda_5(t)\right)\frac{\beta I^*(t)}{N(t)} + (\alpha - \mu)\lambda_2(t) + (\lambda_2(t) - \lambda_5(t))u_1^*(t) - A_2 \\
\lambda_3'(t) &= \frac{-\partial H}{\partial E} = \varepsilon\left(\lambda_3(t) - \lambda_4(t)\right) + \alpha\lambda_3(t) + (\lambda_3(t) - \lambda_5(t))u_2^*(t) - A_3 \\
\lambda_4'(t) &= \frac{-\partial H}{\partial I} = \left(\lambda_2(t) - \lambda_3(t)\right)\frac{\beta S^*(t)}{N(t)} + (\lambda_4 - \lambda_5)\gamma + \left(\alpha + \varphi\right)\lambda_4(t) + (\lambda_4 - \lambda_5)u_3^* - A_4 \\
\lambda_5'(t) &= \frac{-\partial H}{\partial R} = \left(\lambda_5(t) - \lambda_2(t)\right)\rho + \alpha\lambda_5(t)
\end{aligned}\right\} \quad (1.31)$$

with transversality conditions $\lambda_i(T) = 0 \quad i = 1,2,3,4,5$ (1.32)

Proof:

The proof follows from Theorem 3

Conclusion

In this work a MSEIR model was used to study application of optimal control technique to epidemiology. Pontryagin's Maximum Principle was used in this work. We have shown the existence of the control systems, where we focused on the application of optimal control theory to minimizing the spread of measles in a population, the optimality was measured by the minimality of the probability of infectious individuals and maximization of the recovered individuals. We derived the necessary conditions for the control problems by studying three scenarios namely; (i) Vaccination alone (ii) Vaccination and Treatment (iii) Vaccination, Quarantine and Treatment.

References

Birkhoff, G., & Rota, G. C. (1989). Ordinary differential equations, fourth ed. *John Wiley and Sons*, New York.

Gbolahan, B. (2014). On the dynamical analysis of a new model for measles infection. *International Journal of Mathematical Trends and Technology (IJMTT),* 7, 144 - 155.

Lenhart, S. & John, T. W. (2007). *Optimal control applied to biological models*. Chapman and Hall/CRC. *London*, UK: Mathematical and computational biology series.

Lukes, D. L. (1982). *Differential equations: Classical to Controlled. Mathematics in Science and Engineering*, New York: *Academic Press*, 162, 182.

Morton, I. K., & Nancy, L. S. (2000). Dynamics optimization: The calculus of variations and optimal control in economics and management. *Elsevier Science*, The Netherlands, 218 – 234.

Pontryagin, L. S., Boltyanskii, V. G., Gamkrelidze, R. V., & Mishchenko, E. F. (1986). The mathematical theory of optimal processes. *Gordon and Breach Science Publishers*.

Yusuf, T. T., & Benyah, F. (2012). Optimal control of vaccination and treatment for SIR epidemiological model. *World Journal of Modelling and Simulation*, 8, 3,194-204.

Zaman, G., Kang, Y. H. & Jung, I. H. (2009). Optimal treatment of an SIR epidemic model with time delay. *BioSystems*, 98, 43 - 50.

Zaman, G., Kang, Y. H. & Jung, I. H. (2008). Stability analysis and optimal vaccination of an SIR epidemic model. *Biosytems*, 93, 240 – 249.

Zaman, G., Kang, Y. H., & Jung, I. H. (2007). Optimal vaccination and treatment in the *SIR* epidemic model. *Proc. KSIAM,* 3, 31 – 33.