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Optimal Control and Cost Effectiveness Analysis for the Transmission Dynamics of Yaws Infection

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ABSTRACT

This work considered a neglected bacterial disease for which non-linear model of yaws infection with time dependent control measures was developed to study the effect of the control measures in tackling the disease transmission in the population. Optimal control strategy was developed in order to investigate and analyze the optimal cost for controlling the transmission of the diseases in the population. Pontryagin's Maximum Principles (PMP) was applied to carry out economic evaluations in order to optimize the cost of the intervention in the models and also to optimize the objective functional so as to establish the most optimal control strategy in tackling the spread of the infections. Numerical simulations had been carried-out for the model using forward-backward Runge-Kutta of order four to study the effect of the control strategies and also to calculate the incremental cost effectiveness ratios (ICERs) for the implementation of various combinations of the control parameters for the yaws infection in order to determine the most cost effective strategy that could check the spread of the disease. The findings showed that the most cost-effective strategy to check the spread of yaws infection is the combination of personal hygiene and treatment for infection as a single control strategy.

1. Introduction

Yaws belongs to a class of long-term bacterial illnesses called endemic treponematoses. Treponema spiral bacteria, which also cause endemic syphilis (bejel) and pinta, are the cause of these disorders. Out of these three infections, yaws is the most prevalent. Treponema pallidum subspecies pertenue, the pathogenic organism, shares genetic similarities with T. pallidum subspecies pallidum, the causative agent of syphilis, bejel, and pinta. Poor populations in warm, humid, tropical forest regions of Africa, Asia, Latin America, and the Pacific are the main locations for the disease's prevalence. The majority of those impacted reside at the "end of the road," far from medical facilities. Yaws can spread more easily in situations of poverty, low socioeconomic status, and inadequate personal cleanliness. Children make up about 75–80% of those impacted by yaws. Males and females are equally affected, with the peak incidence occurring in youngsters between the ages of 6 and 10. Minor injuries are spread by direct contact between people. Yaws's original lesion is teeming with microorganisms. The limbs are where most lesions arise. Ninety to ninety-nine days, on average, are spent in incubation. Chronic deformity and incapacity can result from infection if left untreated. The World Health Organization (WHO) divides nations into three epidemiological groups: Group A consists of nations whose endemic status is currently known; Group B consists of nations whose status was previously known to be endemic but is uncertain at this time; and Group C consists of nations without a history of yellow fever (Yaws) (WHO, 2022). Thirteen nations were identified as endemic for yellow fever in 2013. Since then, two other nations Liberia and the Philippines have reported verified instances, while three more Colombia, Ecuador, and Haiti have reported suspected cases of yaws as a result of intensive surveillance efforts. A 5-year-old Malaysian child was the only known incidence of yaws in 2021. The WHO lists Malaysia as one of the countries where the disease was formerly prevalent but not has been confirmed as so at this time. Additional research is necessary (WHO, 2021). One spirochaete that cannot be grown in vitro is

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Treponema pallidum. It is convenient to categorize the clinical characteristics of yaws into primary, secondary, and tertiary illness. While patients may come with a combination of clinical indications, it is important to keep in mind that this classification is clinically beneficial (Marks, *et al.* 2015). At least 76 of the nations and territories that were recognized as endemic in the 1950s are included in group B and require evaluation to see if the disease is currently prevalent there. This can be accomplished by integrated surveillance with other illnesses, particularly neglected tropical diseases connected to the skin. Only 346 of the 87,877 suspected cases of yaws that were reported to the WHO in 2020 from 11 countries were confirmed; the bulk of cases were from Papua New Guinea, the Solomon Islands, and Vanuatu in the Western Pacific Region (WHO, 2021). Treponemal infections (such syphilis and yaws) are typically diagnosed with laboratory-based serological tests like Treponema Pallidum Particle Agglutination (TPPA) and rapid plasma reagin (RPR). However, because these tests are unable to differentiate between yaws and syphilis, careful clinical assessment is necessary when interpreting test findings in people residing in yaws endemic areas. The unrelated H. ducreyi bacteria is responsible for about 40% of ulcers that are clinically misdiagnosed as yaws. Treponemal quick tests are inexpensive and generally accessible, but they are not able to differentiate between an infection and one that is present now, thus their utility in tracking transmission interruption is restricted. Chembio Diagnostics, USA's Dual Path Platform Syphilis Screen and Confirm assay is capable of identifying both active and latent infections. The DPP test is quite expensive, hence treponemal testing can be used to screen suspected instances of YAWS before the DPP confirms positive results. However, if expense is not an issue, nations may decide to utilize solely DPP. By finding the DNA in the skin lesions, polymerase chain reaction (PCR) technology is used to conclusively diagnose yaws. It can also be used to track resistance to azithromycin. Following widespread treatment and post-elimination observation, this will be helpful (WHO, 2022). Either of the two antibiotics—benzathine penicillin or azithromycin—can be used to treat yaws. Patients who cannot be treated with azithromycin or who have suspected clinical treatment failure after azithromycin should use benzathine penicillin, which can be administered intramuscularly at a dose of 1.2 million units for adults over the age of 10 or 30 mg/kg for children. Four weeks after starting antibiotic therapy, patients should be reexamined. More than 95% of cases will show complete clinical recovery. According to WHO (2022), any patient whose therapy is thought to have failed must undergo testing for macrolide resistance and be treated with benzathine penicillin. As of right now, yaws has no known vaccine. Reducing transmission requires both better personal hygiene and health education. Empirical care should be given to contacts of yaws patients. The eradication strategy involves mass therapy, also known as total community treatment, or TCT, in which all residents in areas known to harbor yaws get oral azithromycin (30 mg/kg, maximum 2g) at a minimum coverage rate of 90%. The absence of new serologically confirmed indigenous cases for three years in a row, the absence of any case confirmed by PCR, and the lack of evidence of transmission for three years in a row as determined by sero-surveys conducted on children aged one to five years are the three requirements for the elimination of yaws (WHO, 2022). In order to examine the effectiveness and economics of two disease prevention strategies—community mobility restriction to stop disease transmission and vaccine intervention—Adi, Irsalinda, and Ndii (2022) introduce an optimal control problem in a two-strain SIR epidemic model with viral mutation and vaccine administration. We take into account the time-dependent control scenario and construct the essential criteria for the best possible control of the disease using Pontryagin's Maximum Principle. In order to assess the cost-effectiveness of any potential strategy for the control measures, we additionally compute the Average Cost-Effectiveness Ratio (ACER) and the Incremental Cost-Effectiveness Ratio (ICER). The study's findings suggest that immunization plus mobility restriction is the most economical way to reduce disease. Marks, Mitjà, Fitzpatrick, Asiedu, Solomon, Mabey and Funk (2020) created a model of the spread of yaws by altering the treatment's coverage and number of rounds. Between 1.08 and 3.32 were the expected number of cases that resulted from an index case basic reproduction number. Eight rounds of treatment with 80% coverage were needed at low estimations of the basic reproduction number (1.45) in order to achieve an 80% chance of eradication. At high estimates of fundamental reproduction number (2.47), this requirement rose to 95%. At all estimations of the fundamental reproduction number, increasing the treatment interval to 12 months resulted in higher requirements. Seidu, Makinde, and Daabo (2016) investigate the dynamics of HIV/AIDS in a population of varying sizes, comprising an infecting AIDS group and two groups of infectious individuals with distinct behavioral characteristics. The fundamental model was transformed into an optimal control issue. To find the most economical approach that reduced the spread, they looked at implementing several combinations of the control settings. The most cost-effective technique was the one that included all of the control parameters, as demonstrated by the incremental cost-effective ratio analysis performed on the different control

schemes. An extended SIR-type model for anthroponotic visceral leishmaniasis transmission was created by Biswas, Subramanian, ELMojtaba, Chattopadhyay, and Sarkar (2017). Seasonal changes were represented as a periodic sandfly biting rate. We estimate the model parameters and compare the model predictions with known instances of visceral leishmaniasis, fitting the model for actual data reported from South Sudan. They investigate the effects of common control methods, such as spraying insecticides, treating infected patients with drugs, and treating symptomatic individuals with bednets, on the dynamics of infected human and vector populations, using the idea of optimum control. Rather of using the best possible combinations of the aforementioned measures, they suggested that the tactics continue to be ineffectual in controlling the disease on their own. They discovered that, after testing the model for several ideal combinations and taking into account sporadic seasonal swings, the best combination of individual treatment and pesticide sprays controls the disease effectively for the duration of the intervention. They discovered that the same method also works well and is economical after conducting a cost-effective analysis. Lastly, they proposed that our model could help policy makers anticipate which intervention measures work best for particular time periods and how to deploy them appropriately to eradicate visceral leishmaniasis. Darmawati, *et al*. (2022) examined the cost-effectiveness, optimal control, and sensitivity of several filariasis intervention techniques. They looked at bed net use, insecticide use, and the use of both bed nets and pesticide in combination as intervention options. They described the ideal controls using Pontryagin's maximal concept. The most economical course of action is determined using the Infection Averted Ratio (IAR) and Average Cost-Effectiveness Ratio (ACER). In addition, we calculate the basic reproduction number and examine its sensitivity to various parameters pertaining to the usage of insecticides and bed nets. Insecticide intervention is the most economical method of controlling filariasis, according to the ACER values. However, the IAR values show that the most economical course of action is the bed-net use intervention. Moreover, it is the most successful method of curing filariasis. The results of the sensitivity analysis demonstrate that lowering the basic reproduction number and the spread of filariasis is mostly dependent on the control parameter linked to bed net use and treatment. Comparing various solutions based on their prices and outcomes has been defined as economic appraisal. Because of this, every economic evaluation technique compares one alternative intervention, therapy, or program against another. As a result, we can evaluate two or more options along two dimensions—costs and consequences—and with each other (Drummond et al. 2005). An approach known as the Morges strategy was put forth by Holmes, Tildesley, Solomon, Mabey, et al. (2020). It entails cycles of total community therapy, which treats the entire population, and total targeted treatment, or TTT, which treats clinical cases and contacts. The usefulness of household-based contact tracing for a TTT strategy is diminished, nevertheless, by modeling and empirical research suggesting that asymptomatic infections frequently are not detected in the same households as clinical cases. They predicted the possibility of eliminating transmission under various intervention plans and the degree of systematic non-treatment resulting from the intervention using a model fitted to data from the Solomon Islands. According to their findings, treating at-risk individuals with TTT is not as beneficial as introducing additional treatment rounds through whole community treatment. In order to determine the best malaria reduction strategies, Keno, Dano, and Ganati (2022) applied the maximum principle of Pontryagin to a deterministic mathematical model of malaria transmission with a climate variation factor. These strategies are described with three control measures: treated bed nets, infected human treatment, and indoor residual spraying. They came to the conclusion that the most effective and affordable method of eliminating malaria is to combine treatment with indoor spraying after analyzing the optimality system. As a result, a yaws infection model with control parameters was developed to address the dynamics of yaws infection transmission.

2. Material and Methods

2.1 Description of the Model

A time dependent controls model was developed and partitioned into nine (9) sub-populations; susceptible populations $S(t)$, exposed populations $E(t)$, primary yaws populations $M_Y(t)$, secondary yaws populations $D_Y(t)$, tertiary yaws populations $T_Y(t)$, individuals with reversible disfigurement $D_S(t)$, irreversible disfigurement $I_S(t)$, recovered individuals with disfigurement $R_S(t)$, and individuals recovered without disfigurement $R_Y(t)$. Susceptible population $S(t)$ increases by recruitment rate Λ and individuals who recovered from yaws after losing their temporary immunity at a rate h. However, the susceptible population decreases by those who acquired the

yaws inactions at a rate $(1-u_1)\phi\left(\frac{M_Y + x_1 D_Y + x_2 D_S}{N}\right)$ where x_1 and x_2 are alteration parameters which signify fewer disease transmission. ϕ is the contact rate between the susceptible and the infectious individuals and is reduced by natural rate μ.

The exposed population $E(t)$ increase by the individuals who got infected after getting in touch with the contagious individuals at the rate, $(1-u_1)\phi\left(\frac{M_Y + x_1 D_Y + x_2 D_S}{N}\right)$ and it lessen by individuals who move to primary phase of yaws illness at the rate β_1 and the secondary phase of illness at the rate β_2, it is also lessen due to natural mortality rate μ.

While, the primary yaws infected population $M_Y(t)$ increases by those who move from exposed stage at the rate β_1, but lessen by the individuals who develop temporary disfigure at a rate κ_1, those who advance to secondary stage of yaws illness and tertiary stage of the illness at the rates κ_2 and κ_3. It is also reduces by those that got healed due to treatment and recovered from primary yaws at the rate z_1 and by the natural death rate μ.

The secondary yaws $D_Y(t)$, increase by those that move out from exposed population and primary yaws at the rates β_2 and κ_3 respectively. But it trim down by those that progress to tertiary yaws at the rate b_3 and those that develops reversible disfigurements at the rate ζ. It is also lessened by the proportion ς that recovered from the infection due to treatment at the rate z_3 and by those that dies naturally at the rate μ.

The population of tertiary yaws T_Y increases by the progression rate κ_2 from primary yaws and by the progression rate b_3 from secondary yaws. The population decreases by those that develop reversible disfigurement at the rate b_1 and by those that recovered from the infection b_2 as a results of treatment at the rate z_2. It also reduces due to natural death rate, μ.

The reversible disfigurements population $D_S(t)$ increases by those that develop reversible scars from primary, secondary and tertiary yaws at the rates κ_1, b_1 and ζ, respectively. However, it also decreases by the individual that develop irreversible scars at the rate φ_2 and those that recovered at the rate φ_1 after being treated from the infection at the rate z_4. It also decreases by natural mortality rate, μ.

The irreversible disfigurements $I_S(t)$, compartment increases by the individuals who moves from reversible disfigurements at the rate φ_2, but it reduces by those that recovered from the infection only but remains with disfigurements at the rate n after the infection is successfully treated at the rate z_5 and by the natural death rate μ.

The population of individuals who recovered only from the infection but remain with disfigurements $R_S(t)$, increases by those that are treated from the infection only at the rate n and by those that dies naturally at the rate μ.

Lastly, the recovered compartment increases by those that were treated from primary yaws at the rate m, secondary yaws at a rate ς, tertiary yaws at the rate b_2 and the reversible disfigurements at a rate φ_1, respectively. But it decreases by those that lost their temporary immunity at the rate η and by the natural death rate μ.

Therefore, based on the description above, we come out with the model equations below;

2.1.1 Yaws model equations with controls

$$\frac{dS}{dt} = \Lambda + \eta R_Y - (1-u_1)\phi\left(\frac{M_Y + x_1 D_Y + x_2 D_S}{N}\right)S - \mu S \tag{1.1}$$

$$\frac{dE}{dt} = (1-u_1)\phi\left(\frac{M_Y + x_1 D_Y + x_2 D_S}{N}\right)S - (\beta_1 + \beta_2 + \mu)E \tag{1.2}$$

$$\frac{dM_Y}{dt} = \beta_1 L - (u_2 z_1 m + k_1 + k_2 + k_3 + \mu)M_Y \tag{1.3}$$

$$\frac{dD_Y}{dt} = \beta_2 L + k_3 M_Y - (b_3 + \zeta + u_2 z_3 \varsigma + \mu)D_Y \tag{1.4}$$

$$\frac{dT_Y}{dt} = k_2 M_Y + b_3 D_Y - (b_1 + u_2 z_2 b_2 + \mu)T_Y \tag{1.5}$$

$$\frac{dD_S}{dt} = k_1 M_Y + b_1 T_Y + \zeta D_Y - (u_3 z_4 \varphi_1 + \varphi_2 + \mu)D_S \tag{1.6}$$

$$\frac{dI_S}{dt} = \varphi_2 D_S - (u_2 z_5 n + \mu)I_S \tag{1.7}$$

$$\frac{dR_Y}{dt} = u_2 z_1 m M_Y + u_2 z_2 b_2 T_Y + u_2 z_3 \varsigma D_Y + u_3 z_4 \varphi_1 D_S - (\eta + \mu)R_Y \tag{1.8}$$

$$\frac{dR_S}{dt} = u_2 z_5 n I_S - \mu R_S \tag{1.9}$$

3. Analysis

3.1 Economic Evaluation for Yaws Model

The foundation of economic evaluation is the understanding that while information about an intervention's efficacy is important, it is not sufficient for making decisions. Explicit consideration of the costs, particularly the opportunity costs or benefits lost, of various options must also be made, (Weinstein and Manning, 1997). Comparing competing solutions based on their prices and outcomes is known as economic appraisal. Because of this, every economic evaluation technique compares one alternative intervention, therapy, or program against another. As a result, we have two (or more) options to compare as well as two metrics (costs and consequences) to do so, (Drummond *et al*. 2005).

Thus, we determine the most cost effective strategy needed to control the transmission dynamics of yaws infection, which is done by minimizing the cost objective functional which is formulated by adopting the derivation approach of Lenhart and Workman (2007).

$$J(u_1, u_2, u_3) = \int_0^{t_f} \left(\left\{ C_{hy} u_1(t) S(t) + C_{tt} u_2(t)\left(z_1 m M_Y(t) + z_2 b_2 T_Y(t) + z_3 \varsigma D_Y(t) + z_5 n I_S(t)\right) + C_{st} u_3(t) z_4 \varphi \right\} e^{-\varphi_Y t} \right) dt \tag{2.1}$$

Utilizing the cost objective functional provided in (2.1) for economic evaluation subject to (1.1) – (1.9). As a result, the matching Hamiltonian is provided by

$$
\begin{aligned}
H_C \quad = \quad & C_{hy}u_1(t)S(t)e^{-\varphi_Y t} + C_{tt}u_2(t)z_1 mM_Y(t)e^{-\varphi_Y t} + C_{tt}u_2(t)z_3\varsigma D_Y(t)e^{-\varphi_Y t} \\
+ \quad & C_{tt}u_2(t)z_2 b_2 T_Y(t)e^{-\varphi_Y t} + C_{st}u_3(t)z_4\varphi_1 D_S(t)e^{-\varphi_Y t} + C_{tt}u_2(t)z_5\, nI_S(t)e^{-\varphi_Y t} \\
+ \quad & \lambda_{S_Y}\left[\Lambda + \eta R_Y - (1-u_1)\phi\left(\frac{M_Y + x_1 D_Y + x_2 D_S}{N}\right)S - \mu S\right] \\
+ \quad & \lambda_E\left[(1-u_1)\phi\left(\frac{M_Y + x_1 D_Y + x_2 D_S}{N}\right)S - (\beta_1 + \beta_2 + \mu)E\right] \\
+ \quad & \lambda_{M_Y}\left[\beta_1 E - (u_2 z_1 m + k_1 + k_2 + k_3 + \mu)M_Y\right] \\
+ \quad & \lambda_{D_Y}\left[\beta_2 E + k_3 M_Y - (b_3 + \zeta + u_2 z_3\varsigma + \mu)D_Y\right] \\
+ \quad & \lambda_{T_Y}\left[k_2 M_Y + b_3 D_Y - (b_1 + u_2 z_2 b_2 + \mu)T_Y\right] \\
+ \quad & \lambda_{D_S}\left[k_1 D_Y + b_1 T_Y + \zeta A_Y - (u_3 z_4\varphi_1 + \varphi_2 + \mu)D_S\right] \\
+ \quad & \lambda_{I_S}\left[\varphi_2 D_S - (u_2 z_5 n + \mu)I_S\right] \\
+ \quad & \lambda_{R_Y}\left[u_2 z_1 mM_Y + u_2 z_2 b_2 T_Y + u_2 z_3\varsigma D_Y + u_3 z_4\varphi_1 D_S - (\eta + \mu)R_Y\right] \\
+ \quad & \lambda_{R_S}\left[u_2 z_5 nI_S - \mu R_S\right]
\end{aligned}
\qquad (2.2)
$$

3.1.1 Economic evaluation of personal hygiene

When we differentiate (2.2) based on u_1 (personal hygiene) as the control parameter, we obtain

$$
\begin{aligned}
\frac{\partial H_C}{\partial u_1} &= C_{hy}S\lambda_{C_Y}e^{-\varphi_Y t} + \frac{\eta(M_Y + x_1 D_Y + x_2 D_S)S}{N}\lambda_S - \frac{\eta(M_Y + x_1 D_Y + x_2 D_S)S}{N}\lambda_E \\
\frac{\partial H_C}{\partial u_1} &= C_{hy}S\lambda_{C_Y}e^{-\varphi_Y t} + \frac{\eta(M_Y + x_1 D_Y + x_2 D_S)S}{N}(\lambda_S - \lambda_E)
\end{aligned}
\qquad (2.3)
$$

The expression $\frac{\phi(M_Y + x_1 D_Y + x_2 D_S)S}{N}(\lambda_S - \lambda_E)$ in (2.3) is the total marginal benefit for the use of personal hygiene and the $C_{hy}S\lambda_{C_Y}e^{-\varphi_Y t}$ is the marginal cost. The ideal policy is implemented if the marginal cost of personal cleanliness equals the marginal benefit..

$$
\left.
\begin{aligned}
u_1(t) = 0 \quad & if \quad C_{hy}S\lambda_{C_Y}e^{-\varphi_Y t} > \frac{\phi(M_Y + x_1 D_Y + x_2 D_S)S}{N}(\lambda_S - \lambda_E) \\
u_1(t) \in (0,1) \quad & if \quad C_{hy}S\lambda_{C_Y}e^{-\varphi_Y t} = \frac{\phi(M_Y + x_1 D_Y + x_2 D_S)S}{N}(\lambda_{S_Y} - \lambda_E) \\
u_1(t) = 1 \quad & if \quad C_{hy}S\lambda_{C_Y}e^{-\varphi_Y t} < \frac{\phi(M_Y + x_1 D_Y + x_2 D_S)S}{N}(\lambda_S - \lambda_E)
\end{aligned}
\right\}
\qquad (2.4)
$$

Accordingly, personal cleanliness will only be most effective in avoiding yaws if the predicted marginal benefit outweighs the marginal cost.

3.1.2 Economic evaluation for treatment of yaws infections

Differentiating (2.2) with respect u_2 (treatments of yaws infection) as control parameter, we get

$$
\frac{\partial H_C}{\partial u_2} = \begin{cases} C_{tt}mz_1 M_Y^* e^{-\varphi_Y t} + C_{tt}z_2 b_2 T_Y^* e^{-\varphi_Y t} + C_{tt}z_3 f_2 D_Y^* e^{-\varphi_Y t} + C_{tt}z_5 nI_S e^{-\varphi_Y t} + mz_1 M_Y^*\lambda_{M_Y} \\ +mz_1 M_Y^*\lambda_{R_Y} - b_2 z_2 T_Y^*\lambda_{T_Y} + b_2 z_2 T_Y^*\lambda_{R_Y} - \varsigma z_3 D_Y\lambda_{A_Y} + \varsigma z_3 D_Y\lambda_{R_Y} - z_5 nI_S\lambda_{I_S} + z_5 nI_S\lambda_{R_S} \end{cases}
$$

$$\frac{\partial H_C}{\partial u_2} = \begin{cases} C_{tt}\left(mz_1M_Y^* + z_2b_2T_Y^* + z_3f_2D_Y^* + z_5nI_S\right)e^{-\varphi_Y t} + mz_1M_Y^*\left(\lambda_{R_Y} - \lambda_{M_Y}\right) \\ +b_2z_2T_Y^*\left(\lambda_{R_Y} - \lambda_{T_Y}\right) + \varsigma z_3D_Y^*\left(\lambda_{R_Y} - \lambda_{D_Y}\right) + z_5nI_S^*\left(\lambda_{R_S} - \lambda_{I_S}\right) \end{cases} \quad (2.5)$$

The marginal cost for treatments of primary yaws M_Y infection is given by $C_{tt}\left(mz_1M_Y^* + z_2b_2T_Y^* + z_3f_2D_Y^* + z_5nI_S\right)e^{-\varphi_Y t}$ while $mz_1M_Y^*\left(\lambda_{R_Y} - \lambda_{M_Y}\right) + b_2z_2T_Y^*\left(\lambda_{R_Y} - \lambda_{T_Y}\right) + \varsigma z_3D_Y^*\left(\lambda_{R_Y} - \lambda_{D_Y}\right) + z_5nI_S^*\left(\lambda_{R_S} - \lambda_{I_S}\right)$ given the little advantage obtained from treating basic yaws infection. Then the optimal policy will be achieved if

$$\begin{aligned} u_2(t) = 0 \quad & if \quad C_{tt}\left(mz_1M_Y^* + z_2b_2T_Y^* + z_3f_2D_Y^* + z_5nI_S\right)e^{-\varphi_Y t} > \begin{cases} mz_1M_Y^*\left(\lambda_{R_Y} - \lambda_{M_Y}\right) + b_2z_2T_Y^*\left(\lambda_{R_Y} - \lambda_{T_Y}\right) \\ +\varsigma z_3M_Y^*\left(\lambda_{R_Y} - \lambda_{M_Y}\right) + z_5nI_S^*\left(\lambda_{R_S} - \lambda_{I_S}\right) \end{cases} \\ u_2(t) \in (0,1) \quad & if \quad C_{tt}\left(mz_1M_Y^* + z_2b_2T_Y^* + z_3f_2D_Y^* + z_5nI_S\right)e^{-\varphi_Y t} = \begin{cases} mz_1M_Y^*\left(\lambda_{R_Y} - \lambda_{M_Y}\right) + b_2z_2T_Y^*\left(\lambda_{R_Y} - \lambda_{T_Y}\right) \\ +\varsigma z_3D_Y^*\left(\lambda_{R_Y} - \lambda_{D_Y}\right) + z_5nI_S^*\left(\lambda_{R_S} - \lambda_{I_S}\right) \end{cases} \\ u_2(t) = 1 \quad & if \quad C_{tt}\left(mz_1M_Y^* + z_2b_2T_Y^* + z_3f_2D_Y^* + z_5nI_S\right)e^{-\varphi_Y t} < \begin{cases} mz_1M_Y^*\left(\lambda_{R_Y} - \lambda_{M_Y}\right) + b_2z_2T_Y^*\left(\lambda_{R_Y} - \lambda_{T_Y}\right) \\ +\varsigma z_3D_Y^*\left(\lambda_{R_Y} - \lambda_{D_Y}\right) + z_5nI_S^*\left(\lambda_{R_S} - \lambda_{I_S}\right) \end{cases} \end{aligned} \quad (2.6)$$

Yaws infection therapies are optimal if the marginal benefit of using them outweighs the marginal cost of doing so.

3.1.3 Economic evaluation of surgery for reversible disfigurement

Differentiating (2.2) with respect u_3 (surgery for reversible disfigurement) as control parameter, we get

$$\frac{\partial H_C}{\partial u_3} = C_{st}z_4\varphi_1D_S^*e^{-\varphi_Y t} + z_4\varphi_1D_S^*\lambda_{D_S} + z_4\varphi_1D_S^*\lambda_{R_Y}$$

$$\frac{\partial H_C}{\partial u_3} = C_{st}z_4\varphi_1D_S^*e^{-\varphi_Y t} + z_4\varphi_1D_S^*\left(\lambda_{R_Y} + \lambda_{D_S}\right) \quad (2.7)$$

The expression $z_4\varphi_1D_S^*\left(\lambda_{R_Y} + \lambda_{D_S}\right)$ in (2.7) is the total marginal benefit for the use of surgery for reversible disfigurements and the $C_{st}z_4\varphi_1D_S^*e^{-\varphi_Y t}$ is the marginal cost. The surgery for reversible disfigurements optimal policy is reached if the marginal cost of the procedure is less than the marginal benefit.

$$\left.\begin{aligned} u_3(t) = 0 \quad & if \quad C_{st}z_4\varphi_1D_S^*e^{-\varphi_Y t} > z_4\varphi_1D_S^*\left(\lambda_{R_Y} + \lambda_{D_S}\right) \\ u_3(t) \in (0,1) \quad & if \quad C_{st}z_4\varphi_1D_S^*e^{-\varphi_Y t} = z_4\varphi_1D_S^*\left(\lambda_{R_Y} + \lambda_{D_S}\right) \\ u_3(t) = 1 \quad & if \quad C_{st}z_4\varphi_1D_S^*e^{-\varphi_Y t} < z_4\varphi_1T_S^*\left(\lambda_{R_Y} + \lambda_{T_S}\right) \end{aligned}\right\} \quad (2.8)$$

This indicates that only when the predicted marginal benefit outweighs the marginal cost will surgery for reversible disfigurements be used optimally.

3.2 Optimal Control

The optimal control problem is formulated for model (1.1) – (1.9) to introduce time-dependent control variables $u_1(t)$, $u_2(t)$ and $u_3(t)$ in order to identify the best preventive measures (hygiene, treating primary yaws infections in individuals, treating secondary and tertiary yaws infections, treating infections causing irreversible disfigurements in individuals, and treating and operating on reversible disfigurements) with the least amount of implementation implications. We consider the control variables $u(t) = \left[u_1(t), u_2(t), u_3(t)\right] \in U$ in respect to the state variables $S(t), E(t), M_Y(t), D_Y(t), T_Y(t), D_S(t), I_S(t), R_Y(t), R_S(t)$ for the optimal control system problem, where

control variables are bounded and measured with $\{U = (u_1, u_2, u_3)\}$ is a Lebesgue measurable on [0, 1], $0 \le u_i(t) \le 1,\ t \in [0,\ tf\ ],\ i = 1, 2, 3.$

The objective functional is given as

$$J(u_1, u_2, u_3) = \int_0^{t_f} \left(A_1 \left(M_Y(t) + D_Y(t) + I_S(t) \right) + A_2 D_S(t) + \left(\frac{C_1}{2} u_1^2(t) + \frac{C_2}{2} u_2^2(t) + \frac{C_3}{2} u_3^2(t) \right) e^{-\varphi_Y t} \right) dt \qquad (2.9)$$

where t_f is the final time and the coefficients A_1, A_2, C_1, C_2, C_3 are positive weights for stability of the factors. The terms $A_1\left(M_Y(t), D_Y(t), I_S(t)\right), A_2 D_S(t)$ are the cost of infection while $C_1 u_1^2, C_2 u_2^2, C_3 u_3^2$ are the costs related with $u_1(t)$ (personal hygiene), $u_2(t)$ (treatment for yaws primary infected individual's, secondary infections, tertiary yaws infections and infection for irreversible disfigurements individual's) and $u_3(t)$ (treatment and surgery for reversible disfigurements).

We seek optimal control u_1, u_2 and u_3 such that

$$J\left(u_1^*, u_2^*, u_3^*\right) = \min\left\{ J\left(u_1, u_2, u_3\right), \left(u_1, u_2, u_3 \in U\right) \right\} \qquad (2.10)$$

The requirements that an ideal control must meet in order to fulfill Pontryagin's Maximum Principle (PMP), which transforms (1.1) – (1.9) into a pointwise Hamiltonian minimization problem with respect to u_1, u_2, u_3.

Theorem 1

Lenhart and Workman (2007) states that if $u_i^*(t)$ and $x^*(t)$ are optimal for problem (1.1) – (1.9), then there exists a piecewise differentiable adjoint variable $\lambda(t)$ such that

$H(t, x^*(t), u(t), \lambda(t)) \le H(t, x^*(t), u^*(t), \lambda(t))$ For all controls u at each time t, where the Hamiltonian H is

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

and

$$\lambda'(t) = -\frac{\partial H_Y(t, x^*(t), u^*(t), \lambda(t))}{\partial x},$$

$\lambda(t) = 0.$

Thus, our Hamiltonian is

$$
\begin{aligned}
H = \quad & A_1\left(M_Y(t)+D_Y(t)+I_S(t)\right)+A_2D_S(t)+\frac{C_1}{2}u_1^2(t)e^{-\varphi_Y t}+\frac{C_2}{2}u_2^2(t)e^{-\varphi_Y t}+\frac{C_3}{2}u_3^2(t)e^{-\varphi_Y t} \\
& + \lambda_S\left[\Lambda+\eta R_Y-(1-u_1)\phi\left(\frac{M_Y+x_1D_Y+x_2D_S}{N}\right)S-\mu S\right] \\
& + \lambda_E\left[(1-u_1)\phi\left(\frac{M_Y+x_1D_Y+x_2D_S}{N}\right)S-(\beta_1+\beta_2+\mu)E\right] \\
& + \lambda_{M_Y}\left[\beta_1E-(u_2z_1m+k_1+k_2+k_3+\mu)M_Y\right] \\
& + \lambda_{D_Y}\left[\beta_2E+k_3M_Y-(b_3+\zeta+u_2z_3\varsigma+\mu)D_Y\right] \\
& + \lambda_{T_Y}\left[k_2M_Y+b_3D_Y-(b_1+u_2z_2b_2+\mu)T_Y\right] \\
& + \lambda_{D_S}\left[k_1M_Y+b_1T_Y+\zeta D_Y-(u_3z_4\varphi_1+\varphi_2+\mu)D_S\right] \\
& + \lambda_{I_S}\left[\varphi_2D_S-(u_2z_5n+\mu)I_S\right] \\
& + \lambda_{R_Y}\left[u_2z_1mM_Y+u_2z_2b_2T_Y+u_2z_3\varsigma D_Y+u_3z_4\varphi_1D_S-(\eta+\mu)R_Y\right] \\
& + \lambda_{R_S}\left[u_2z_5nI_S-\mu R_S\right] \\
& + \lambda_{C_Y}\left[C_{hy}u_1(t)S(t)+C_{tt}u_2\left((t)z_1mM_Y(t)+z_3\varsigma D_Y(t)+z_2b_2T_Y(t)+z_5nI_S(t)\right)+C_{st}u_3(t)z_4\varphi_1D_S(t)\right]
\end{aligned}
\tag{2.11}
$$

where λ_S, λ_E, λ_{M_Y}, λ_{D_Y}, λ_{T_Y}, λ_{D_S}, λ_{I_S}, λ_{R_Y}, λ_{R_S}, λ_{C_Y} are the adjoint variables or co-state variables.

We utilize Lenhart and Workman's (2007) optimal control existence result and Pontryagin's Maximum Principle to determine the required conditions for this optimal control.

Theorem 2

The optimal controls u_1^*, u_2^*, u_3^* and solutions S, E, M_Y, D_Y, T_Y, D_S, I_S, R_Y, R_S of the corresponding state system that minimizes $J(u_1, u_2, u_3)$ over $\prod$. Then there exists adjoint variables λ_S, λ_E, λ_{M_Y}, λ_{D_Y}, λ_{T_Y}, λ_{D_S}, λ_{I_S}, λ_{R_Y}, λ_{R_S}, λ_{C_Y} satisfying

$$\left.\begin{aligned}
\frac{\partial H}{\partial S} &= \left[-(1-u_1)\frac{\phi(M_Y + x_1 D_Y + x_2 D_S)}{N}\lambda_S - \mu\lambda_S + (1-u_1)\frac{\phi(M_Y + x_1 D_Y + x_2 D_S)}{N}\lambda_S + C_{hy}u_1\lambda_{C_Y} \right] \\
\frac{\partial H}{\partial E} &= \left[-(\beta_1 + \beta_2 + \mu)\lambda_E + \beta_1\lambda_{M_Y} + \beta_2\lambda_{D_Y} \right] \\
\frac{\partial H}{\partial M_Y} &= \left[A_1 - (1-u_1)\frac{\phi S}{N}\lambda_S + (1-u_1)\frac{\phi S}{N}\lambda_E - (u_2 z_1 m + k_1 + k_2 + k_3 + \mu)\lambda_{M_Y} + k_3\lambda_{A_Y} + k_2\lambda_{T_Y} + k_1\lambda_{D_S} + u_2 z_1 m\lambda_{R_Y} + C_{tt}u_2 z_1 m\lambda_{C_Y} \right] \\
\frac{\partial H}{\partial D_Y} &= \left[A_1 - (1-u_1)\frac{\phi x_1 S}{N}\lambda_S + (1-u_1)\frac{\phi x_1 S}{N}\lambda_E - (b_3 + \zeta + u_2 z_3\varsigma + \mu)\lambda_{D_Y} + b_3\lambda_{T_Y} + \zeta\lambda_{D_S} + u_2 z_3\varsigma\lambda_{R_Y} + C_{tt}u_2 z_3\varsigma\lambda_{C_Y} \right] \\
\frac{\partial H}{\partial T_Y} &= \left[-(b_1 - u_2 z_2 b_2 + \mu)\lambda_{T_Y} + b_1\lambda_{D_S} + u_2 z_2 b_2\lambda_{R_Y} + C_{tt}u_2 z_2 b_2\lambda_{C_Y} \right] \\
\frac{\partial H}{\partial D_S} &= \left[A_2 - (1-u_1)\frac{\phi x_2 S}{N}\lambda_S + (1-u_1)\frac{\phi x_2 S}{N}\lambda_E - (u_3 z_4\varphi_1 + \varphi_2 + \mu)\lambda_{D_S} + \varphi_2\lambda_{I_S} + u_3 z_4\varphi_1\lambda_{R_Y} + C_{st}u_3 z_4\varphi_1\lambda_{C_Y} \right] \\
\frac{\partial H}{\partial I_S} &= \left[A_1 - (u_2 z_5 n + \mu)\lambda_{I_S} + u_2 z_5 n\lambda_{R_S} + C_{tt}u_2 z_5 n\lambda_{C_Y} \right] \\
\frac{\partial H}{\partial R_Y} &= \left[\eta\lambda_S - (\eta + \mu)\lambda_{R_Y} \right] \\
\frac{\partial H}{\partial R_S} &= \left[-\mu\lambda_{R_S} \right] \\
\frac{\partial H}{\partial C_Y} &= 0
\end{aligned}\right\} \quad (2.12)$$

with transversality conditions:

$$\lambda_S(t_f) = \lambda_E(t_f) = \lambda_{M_Y}(t_f) = \lambda_{D_Y}(t_f) = \lambda_{T_Y}(t_f) = \lambda_{D_S}(t_f) = \lambda_{I_S}(t_f) = \lambda_{R_Y}(t_f) = \lambda_{R_S}(t_f) = 0 \quad (2.13)$$

And the controls u_1^*, u_2^*, u_3^* satisfy the optimality conditions:

$$\left.\begin{aligned}
u_1^* &= \max\left\{0,\ \min\left(1,\ \frac{\partial H_Y}{\partial u_1}\right)\right\} \\
u_2^* &= \max\left\{0,\ \min\left(1,\ \frac{\partial H_Y}{\partial u_2}\right)\right\} \\
u_3^* &= \max\left\{0,\ \min\left(1,\ \frac{\partial H_Y}{\partial u_3}\right)\right\}
\end{aligned}\right\} \quad (2.14)$$

Proof

By differentiating the Hamiltonian function, which is evaluated at the optimal control, the differentiable equations controlling the adjoint variables can be found. The adjoint system can therefore be expressed as

$$\frac{\partial H}{\partial S(t)} = -\frac{d\lambda_S}{dt},\ \frac{\partial H}{\partial E(t)} = -\frac{d\lambda_E}{dt},\ \frac{\partial H}{\partial M_Y(t)} = -\frac{d\lambda_{M_Y}}{dt},\ \frac{\partial H}{\partial D_Y(t)} = -\frac{d\lambda_{D_Y}}{dt},\ \frac{\partial H}{\partial T_Y(t)} = -\frac{d\lambda_{T_Y}}{dt},$$

$$\frac{\partial H}{\partial D_S(t)} = -\frac{d\lambda_{D_S}}{dt},\ \frac{\partial H}{\partial I_S(t)} = -\frac{d\lambda_{I_S}}{dt},\ \frac{\partial H}{\partial R_Y(t)} = -\frac{d\lambda_{R_Y}}{dt} \text{ and } \frac{\partial H}{\partial R_S(t)} = -\frac{d\lambda_{R_S}}{dt} \quad (2.15)$$

then,

$$\left.\begin{aligned}
\frac{d\lambda_S}{dt} &= \left[(1-u_1)\frac{\phi\left(M_Y + x_1D_Y + x_2D_S\right)}{N}\left(\lambda_S - \lambda_E\right) + \mu\lambda_S - C_{hy}u_1\lambda_{C_{f2}}\right]\\
\frac{d\lambda_E}{dt} &= \left[\beta_1\left(\lambda_E - \lambda_{M_Y}\right) + \beta_2\left(\lambda_E - \lambda_{D_Y}\right) + \mu\lambda_E\right]\\
\frac{d\lambda_{M_Y}}{dt} &= \left[(1-u_1)\frac{\phi S}{N}\left(\lambda_S - \lambda_E\right) + u_2z_1m\left(\lambda_{M_Y} - \lambda_{R_Y} - C_{tp}\lambda_{C_{f2}}\right) + k_1\left(\lambda_{M_Y} - \lambda_{D_S}\right) + k_2\left(\lambda_{M_Y} - \lambda_{T_Y}\right) + k_3\left(\lambda_{M_Y} - \lambda_{D_Y}\right) + \mu\lambda_{M_Y} - A_1\right]\\
\frac{d\lambda_{D_Y}}{dt} &= \left[(1-u_1)\frac{\phi x_1S}{N}\left(\lambda_S - \lambda_E\right) + b_3\left(\lambda_{D_Y} - \lambda_{T_Y}\right) + \zeta\left(\lambda_{D_Y} - \lambda_{D_S}\right) + u_3z_3\varsigma\left(\lambda_{D_Y} - \lambda_{R_Y} - C_{tt}\lambda_{C_{f2}}\right) + \mu\lambda_{D_Y} - A_1\right]\\
\frac{d\lambda_{T_Y}}{dt} &= \left[b_1\left(\lambda_{T_Y} - \lambda_{D_S}\right) + u_3z_2b_2\left(\lambda_{T_Y} - \lambda_{R_Y} - C_{tt}\lambda_{C_{f2}}\right) + \mu\lambda_{T_Y}\right]\\
\frac{d\lambda_{D_S}}{dt} &= \left[(1-u_1)\frac{\phi x_2S}{N}\left(\lambda_S - \lambda_E\right) + u_4z_4\varphi_1\left(\lambda_{T_Y} - \lambda_{R_Y} - C_{st}\lambda_{C_{f2}}\right) + \varphi_2\left(\lambda_{D_S} - \lambda_{I_S}\right) + \mu\lambda_{D_S} - A_2\right]\\
\frac{d\lambda_{I_S}}{dt} &= \left[u_5z_5n\left(\lambda_{I_S} - \lambda_{R_S} - C_{tr}\lambda_{C_{f2}}\right) + \mu\lambda_{I_S} - A_1\right]\\
\frac{d\lambda_{R_Y}}{dt} &= \left[\phi\left(\lambda_{R_Y} - \lambda_S\right) + \mu\lambda_{R_Y}\right]\\
\frac{d\lambda_{R_S}}{dt} &= \left[\mu\lambda_{R_S}\right]
\end{aligned}\right\}$$

with transversality conditions:

$$\lambda_S(t_f) = \lambda_E(t_f) = \lambda_{M_Y}(t_f) = \lambda_{D_Y}(t_f) = \lambda_{T_Y}(t_f) = \lambda_{D_S}(t_f) = \lambda_{I_S}(t_f) = \lambda_{R_Y}(t_f) = \lambda_{R_S}(t_f) = 0$$

Hence, solving $\frac{\partial H}{\partial u_1} = 0,\ \frac{\partial H}{\partial u_2} = 0,\ \frac{\partial H}{\partial u_3} = 0$ gives the characterization of controls.

$$\frac{\partial H}{\partial u_1} = C_1u_1^*(t)e^{-\varphi_Y t} + \frac{\phi\left(M_Y + x_1D_Y + x_2D_S\right)S^*}{N}\lambda_S - \frac{\phi\left(M_Y + x_1D_Y + x_2D_S\right)S^*}{N}\lambda_E + C_{hy}S^*\lambda_{C_{f2}}$$

$$u_1^*(t) = \frac{\phi\left(M_Y + x_1D_Y + x_2D_S\right)S^*}{C_1Ne^{-\varphi_Y t}}\left(\lambda_S - \lambda_E\right) - \frac{C_{hy}S^*\lambda_{C_Y}}{C_1e^{-\varphi_Y t}}$$

$$\frac{\partial H_Y}{\partial u_2} = \begin{cases} C_2u_2^*(t)e^{-\varphi_Y t} - mz_1M_Y^*\lambda_{M_Y} + mz_1M_Y^*\lambda_{R_Y} + C_{tp}mz_1M_Y^*\lambda_{C_Y} - b_2z_2T_Y^*\lambda_{T_Y} + b_2z_2T_Y^*\lambda_{R_Y} + C_{tt}z_2b_2T_Y^*\lambda_{C_Y} \\ -\varsigma z_3D_Y\lambda_{D_Y} + \varsigma z_3D_Y\lambda_{R_Y} + C_{tt}z_3f_2D_Y^*\lambda_{C_Y} - z_5nI_S\lambda_{I_S} + z_5nI_S\lambda_{R_S} + C_{tt}z_5nI_S\lambda_{C_Y} \end{cases}$$

$$u_2^*(t) = \frac{mz_1M_Y^*\left(\lambda_{M_Y} - \lambda_{R_Y} - C_{tp}\lambda_{C_Y}\right) + b_2z_2T_Y^*\left(\lambda_{T_Y} - \lambda_{R_Y} - C_{tt}\lambda_{C_Y}\right) - \varsigma z_3D_Y^*\left(\lambda_{D_Y} + \lambda_{R_Y} + C_{tt}\lambda_{C_Y}\right) + z_5nI_S^*\left(\lambda_{I_S} - \lambda_{R_S} - C_{tt}\lambda_{C_Y}\right)}{C_2e^{-\varphi_Y t}}$$

$$\frac{\partial H_Y}{\partial u_3} = C_3u_3^*(t)e^{-\varphi_Y t} - z_4\varphi_1D_S^*\lambda_{D_S} + z_4\varphi_1D_S^*\lambda_{R_Y} + C_{st}z_4\varphi_1D_S^*\lambda_{C_Y} = 0$$

$$u_3^*(t) = \frac{z_4\varphi_1D_S^*\left(\lambda_{D_S} - \lambda_{R_Y} - C_{st}\lambda_{C_L}\right)}{C_3e^{-\varphi_Y t}}$$

Using the usual controls argument from Kirschner, Lenhart, and Serbin (1997) and Joshi (2002), we argue that the bound on the controls are;

$$u_1^* \begin{cases} 0 & if \quad u_1^c \le 0 \\ u_1^c & if \quad 0 < u_1^c < 1 \\ 1 & if \quad u_1^c \ge 1 \end{cases} \qquad u_2^* \begin{cases} 0 & if \quad u_2^c \le 0 \\ u_2^c & if \quad 0 < u_2^c < 1 \\ 1 & if \quad u_2^c \ge 1 \end{cases} \qquad u_3^* \begin{cases} 0 & if \quad u_3^c \le 0 \\ u_3^c & if \quad 0 < u_3^c < 1 \\ 1 & if \quad u_3^c \ge 1 \end{cases}$$

The uniqueness of the optimality system (2.12) – (2.14) is attained because the solutions to the state and adjoint equations are apriori bounded. The uniqueness of the optimality system (2.12) – (2.14) is attained because the solutions to the state and adjoint equations are apriori bounded to [0, t_f].

4. Numerical Simulation

The optimality systems were solved numerically by the use of the forward-backward iterative approach. The state system and the adjoint system make up the optimality system, which must be solved in order to find the optimal control solution. We employ the fourth-order Runge–Kutta approach to solve the state equations with an assumption for the controls over the simulated time due to the transversality conditions. The study examined the impact of optimal control measures on the spread of yaws infection within a population, utilizing the parameters and variables listed in tables 1 for comparison.

Table 1: Parameter Values for the Yaws Model

Parameters	Descriptions	Values	Sources
Λ	Recruitment rate	1000	Assumed
μ	Natural Mortality rate	0.02	Mushabaya, *et, al.*, (2011)
ϕ	Contact rate between the susceptible with infectious individuals	0.0175	Assumed
x_1	Modification parameter for secondary infectious individuals	1.30	Mushabaya, *et, al.*, (2011)
x_2	Modification parameter for temporary scarred and infectious individuals	0.77	Mushabaya, *et, al.*, (2011)
β_1	Progression rate from exposed individuals to primary infectious individuals	0.0033	Assumed
β_2	Progression rate from exposed individuals to secondary infectious individuals	0.0502	Assumed
η	Rate at which individuals who recovered without deformity become susceptible	0.575	Assumed
k_1	Rate at which primary infected individuals develops temporary scars	0.25	Assumed
k_2	Rate at which primary infected individual progresses to tertiary yaws infection	0.5	Assumed
k_3	Rate at which primary infected individual progresses to secondary yaws infection	0.0278	Marks, *et, al.*, (2020)
z_1	Rate of treatment for primary yaws infection	0.95	Marks, *et, al.*, (2020)
z_2	Rate of treatment for tertiary yaws infection	0.042	Kimball, *et, al.*, (2022)
z_3	Rate of treatment for secondary yaws infection	0.65	Marks, *et, al.*, (2020)
z_4	Rate of treatment of infection for temporary scarred	0.125	Kimball, *et, al.*, (2022)
z_5	Rate of treatment of infection only for permanent scarred	0.042	Kimball, *et, al.*, (2022)
m	Rate at which individuals recovered from primary infection due to treatment	0.625	Assumed
b_1	Progression rate for individuals who develops temporary deformities from tertiary infection	0.0291	Assumed

b_2	Recovery rate from tertiary yaws infection	0.0291	Assumed
b_3	Progression rate for secondary yaws infection to tertiary infection	0.102	Assumed
ζ	Secondary yaws infected individuals who develops temporary deformities	0.21	Assumed
ς	Rate at which individuals recovered from secondary infection due to treatment	1.05	Assumed
φ_1	Rate at which individuals recovered from temporary scarred and infectious due to treatment	0.0193	Assumed
φ_2	Rate at which individuals becomes permanently deformed	0.085	Assumed
n	Rate at which individuals recovered from yaws infection but with deformities	0.009	Assumed
φ_Y	Discount Rate	0.03	Momoh, *et, al.,* (2021)

Table 2: Variable Values for the Yaws model

Variables	Description	Values	Sources
$S(t)$	Susceptible individuals at time t	2500	Assumed
$E(t)$	Exposed (Latent) individuals at time t	1500	Assumed
$M_Y(t)$	Primary yaws infected individuals at time t	900	Assumed
$D_Y(t)$	Secondary yaws infected individuals at time t	1150	Assumed
$T_Y(t)$	Tertiary yaws infected individuals at time t	500	Assumed
$D_S(t)$	Temporary scarred individuals at time t	120	Assumed
$I_S(t)$	Permanent scarred individuals at time t	50	Assumed
$R_S(t)$	Recovered individuals with permanent scarred at time t	150	Assumed
$R_Y(t)$	Recovered individuals without scar at time t	250	Assumed

The following control strategies were used to run the Yaws model simulation;

Strategy W: use of personal hygiene and treatment of infections

Strategy X: use of personal hygiene and treatment and surgery for reversible disfigurements

Strategy Y: use of treatment of infections and treatment and surgery for reversible disfigurements

Strategy Z: use of personal hygiene, treatment of infections and treatment and surgery for reversible disfigurements

To find the best strategy out of all the strategies, the optimality system (2.12) – (2.14) was solved. To solve the optimality system, an iterative technique was employed. ODE45 in the Matlab scheme solves the adjoint equations utilizing the iterative solutions of the state equations due to the transversality conditions (4.189)..

4.1 Strategy W: Use of Personal Hygiene (u_1) and Treatment of Infections (u_2) Only

This strategy, combines the controls on personal hygiene (u_1) and treatment of infections (u_2) as the first strategy to be implemented in optimizing the cost objective functional (J) while we set the treatment and surgery for reversible disfigurements (u_3) to zero. When the method is implemented as opposed to when there is no control, the numbers indicated a notable increase in the populations of those who have recovered without scars. However, when comparing the infected population with control to the infected population without a control plan, the figure showed notable disparities. On the other hand, the control profile displays the effects of both settings over time.

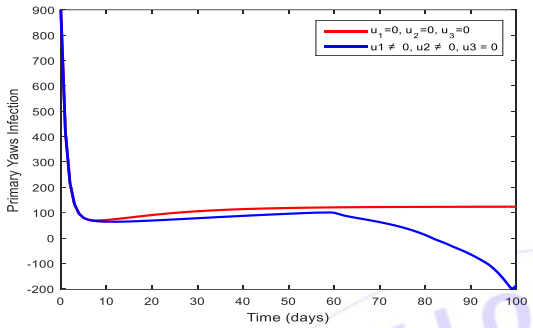


Figure 1(a)

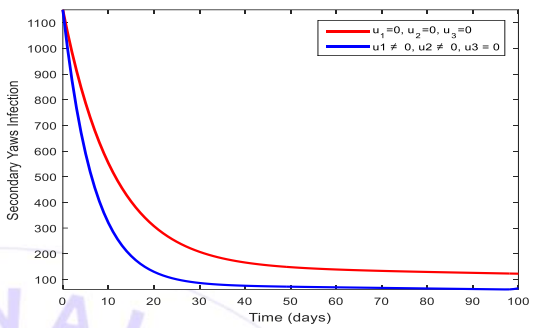


Figure 1(b)

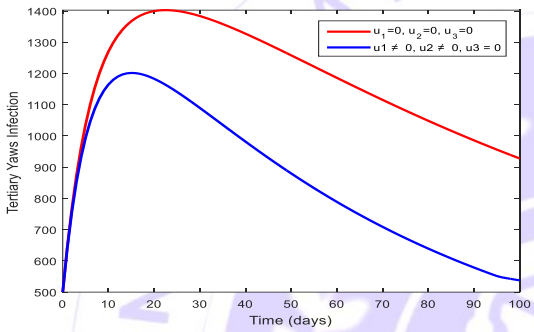


Figure 1(c)

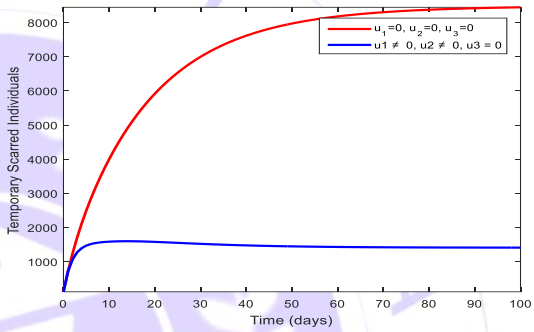


Figure 1(d)

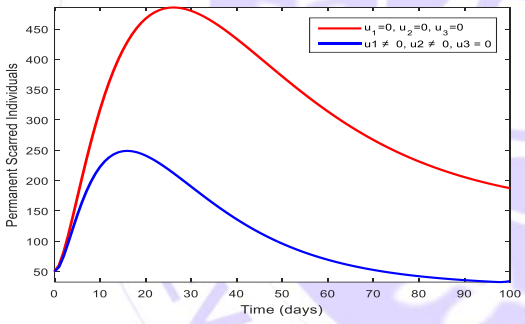


Figure 1(e)

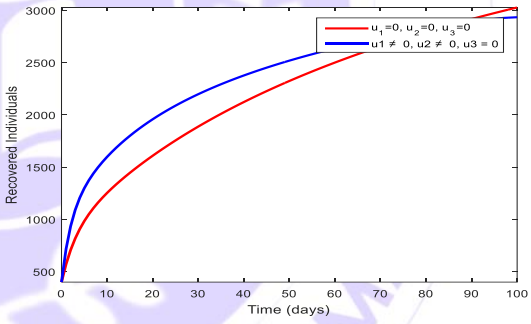


Figure 1(f)

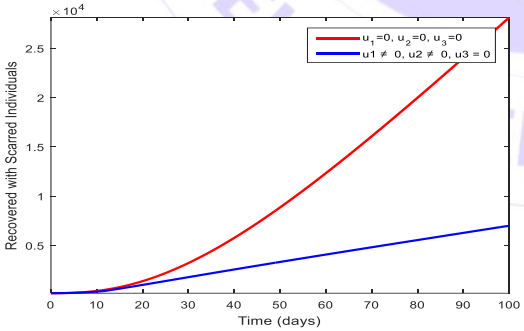


Figure 1(g)

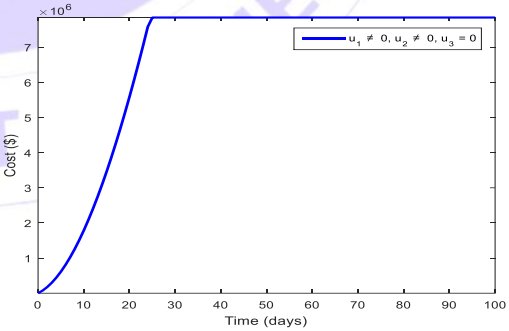


Figure 1(h)

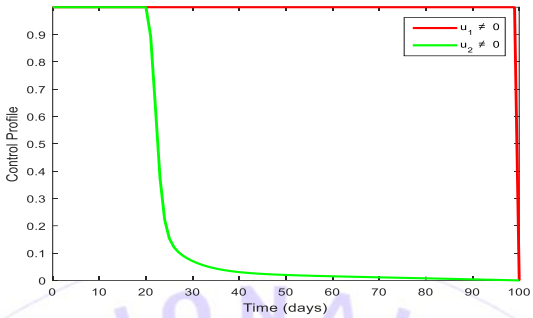


Figure 1(i)

Figure 1: Strategy W (when (u_1) and (u_2) are used as a single startegy)

4.2 Strategy X: Use of Personal Hygiene (u_1) and Treatment and Surgery for Reversible Disfigurements (u_3) Only

This strategy, combines the controls on personal hygiene (u_1) and treatment and surgery for reversible disfigurements (u_3) as the second control strategy to be implemented in optimizing the cost objective functional (J) while we set the treatment of infections (u_2) to zero. The populations of those who healed without scars when it wasn't indicated a noteworthy increase in either case. However, when comparing the infected population with control to the infected population without control, the figure showed notable variances. While the control profile displays the two controls' combined effects over time.

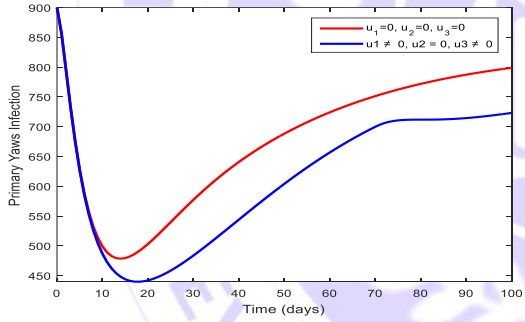


Figure 2(a)

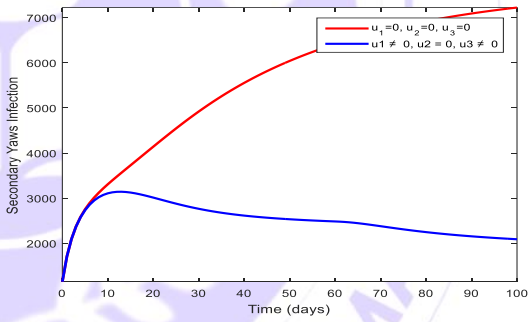


Figure 2(b)

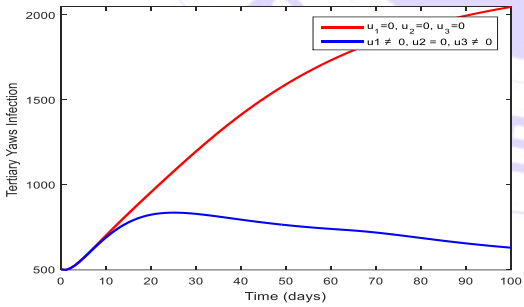


Figure 2(c)

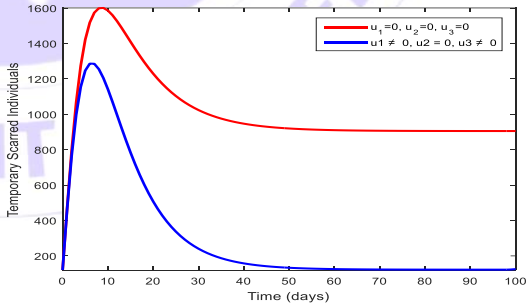


Figure 2(d)

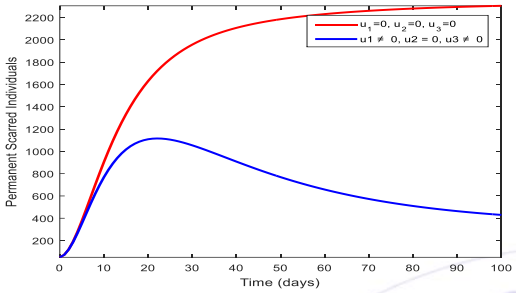


Figure 2(e)

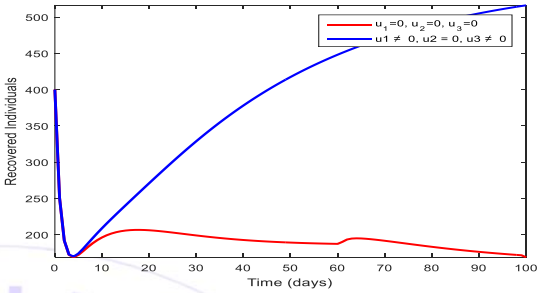


Figure 2(f)

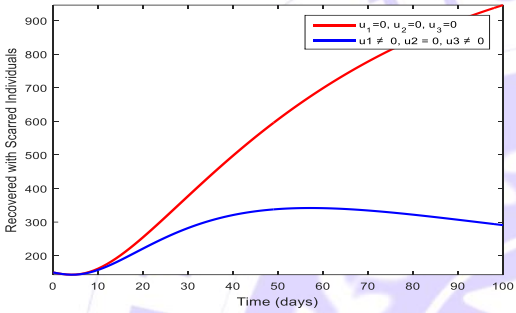


Figure 2(g)

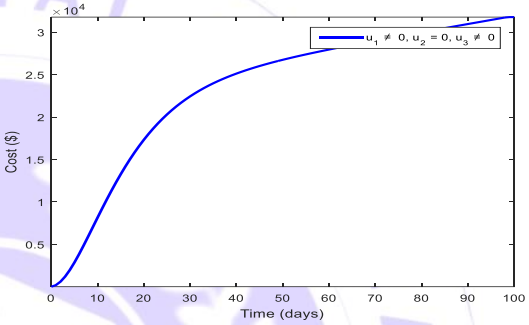


Figure 2(h)

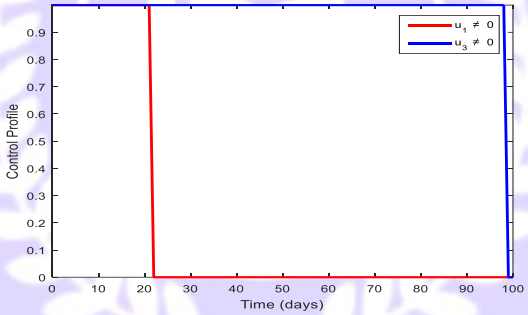


Figure 2(i)

Figure 2: Strategy X (when (u_1) and (u_3) are used as a single startegy)

4.3 Strategy Y: Use of Treatment of Infections (u_2) and Treatment and Surgery for Reversible Disfigurements (u_3) Only

This strategy, combines the controls on treatment of infections (u_2) and treatment and surgery for reversible disfigurements (u_3) as the third control strategy to be implemented in optimizing the cost objective functional (J) while we set the personal hygiene (u_1) to zero. When the method is implemented as opposed to when there is no control, the numbers indicated a notable increase in the populations of those who have recovered without scars. However, when compared to the infected population without control, the figure showed notable differences in the infected population with control. Although the control profile shows the effects of the two controls during certain times.

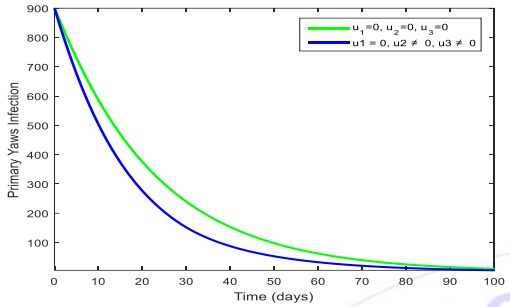


Figure 3(a)

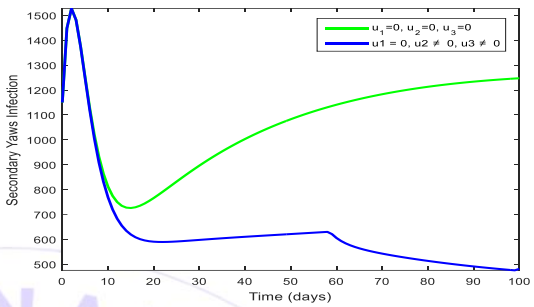


Figure 3(b)

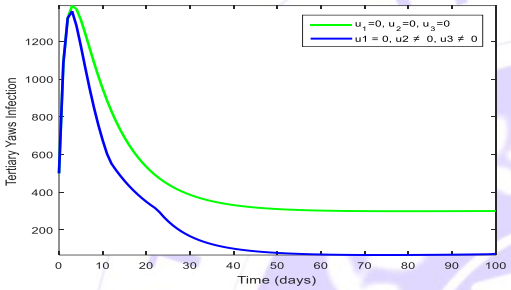


Figure 3(c)

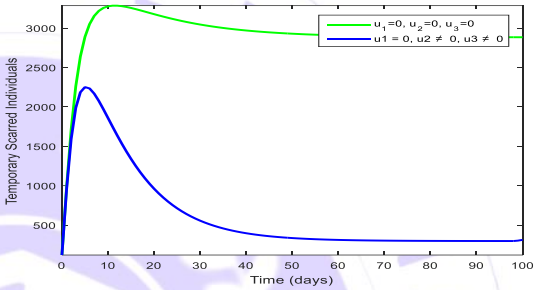


Figure 3(d)

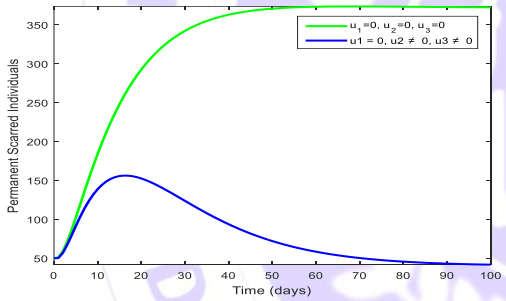


Figure 3(e)

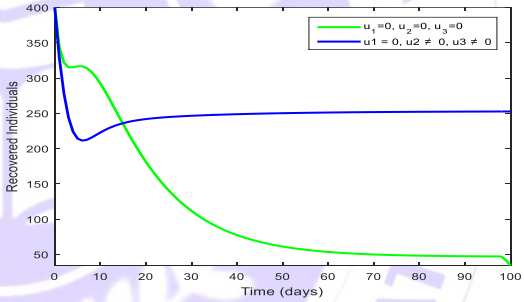


Figure 3(f)

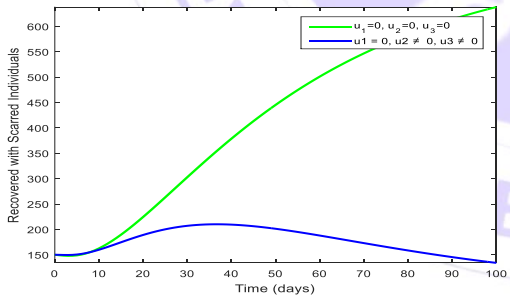


Figure 3(g)

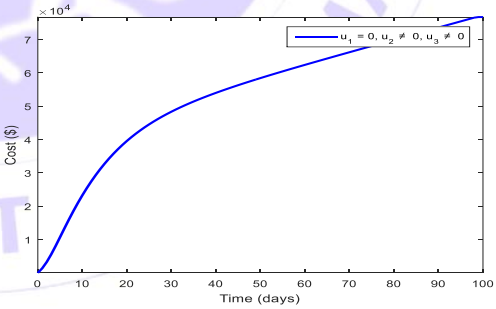


Figure 3(h)

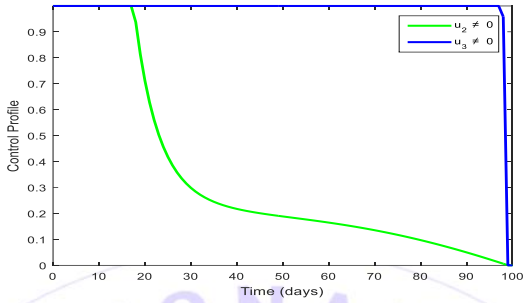


Figure 3(i)

Figure 3: Strategy Y (when (u_2) and (u_3) are used as a single startegy)

4.4 Strategy Z: Use of Personal Hygiene (u_1), Treatment of Infections (u_2) and Treatment and Surgery for Reversible Disfigurements (u_3)

In an attempt to identify the most effective method for containing the illness in the population, this technique applies all three controls as a unified control strategy to optimize the cost objective functional (J). When the method is implemented as opposed to when there is no control, the numbers indicated a notable increase in the populations of those who have recovered without scars. However, when compared to the infected population without control, the figure showed notable differences in the infected population with control. Although the control profile shows how the three controls affect things for a while.

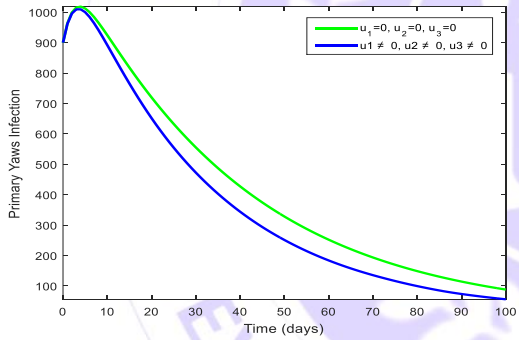


Figure 4(a)

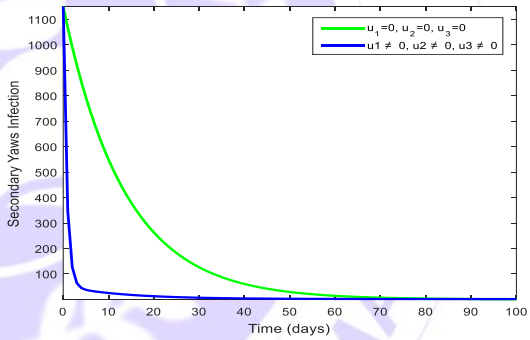


Figure 4(b)

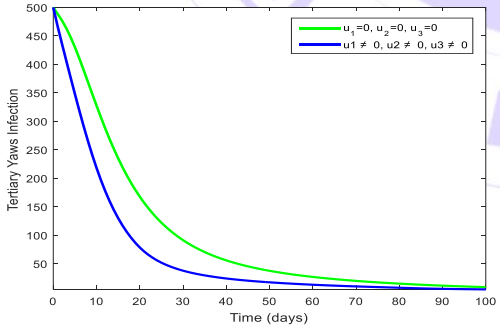


Figure 4(c)

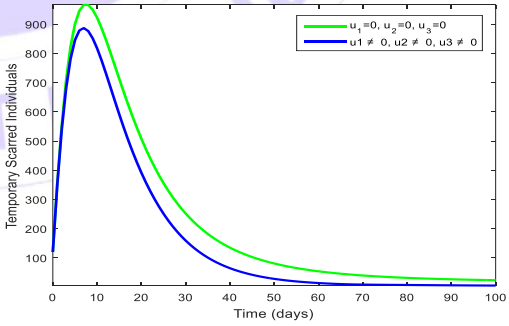


Figure 4(d)

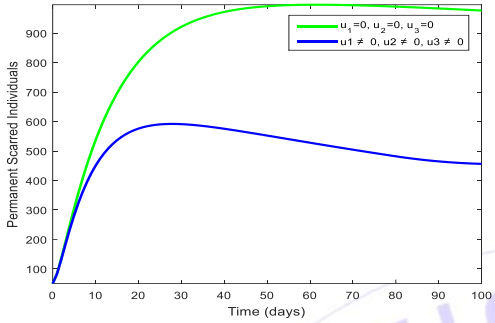
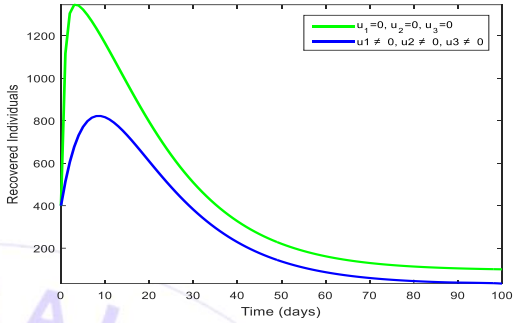


Figure 4(e)



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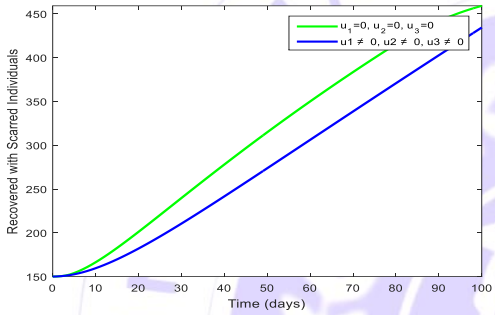

Figure 4(g)

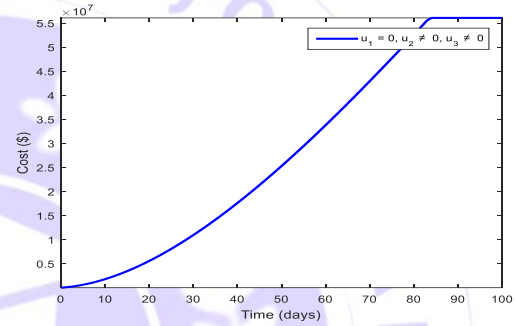

Figure 4(i)

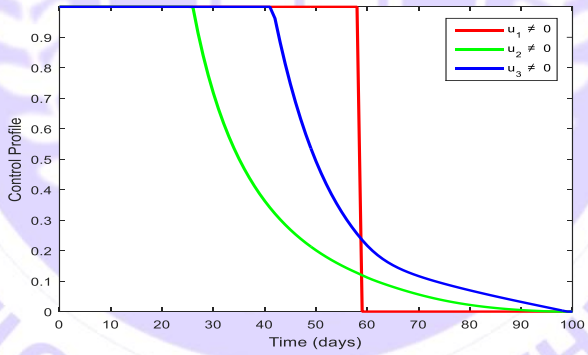

Figure 4(j)

Figure 4: Strategy Z (when (u_1), (u_2) and (u_3) are used as a single startegy)

5. Cost-Effectiveness Analysis

We want to measure the cost effectiveness of the control strategies for the purpose of the study by adopting the method of ICER as used by Seidu, Makinde, and Daabo (2016);

$$ICER = \frac{Cost_a - Cost_b}{Effect_a - Effect_b} = \frac{\Delta Cost}{\Delta Effect}$$

5.1 Incremental Cost-Effective Ratio (ICER) for Yaws

The incremental cost-effectiveness ratio (ICER) is calculated by dividing the difference in costs between two options by the difference in their respective effects. In the case of yaws the controls, ICER enables us to compare the cost-effectiveness of combinations of at least two or three control factor: personal hygiene, treatment

and treatment and surgery. The table below presents the control strategies along with the corresponding total infections prevented and total expenses based on the model numerical simulation results obtained;

Table 3: Total Infections Averted and Total Costs Averted without ICER

Strategies	Total infection averted	Total cost ($)	*ICER*
W	3827.9825	7844285	
X	3737.9021	8850885	
Y	5034.3624	22130	
Z	31589.0230	4948785	

Table 3: Arrangement of Strategies in Order of Increasing Effectiveness and $ICER$ Which was Obtained Using (3.89)

Table 4: Ranked Total Infections Averted and Total Costs Averted with ICER

Strategies	Total infection averted	Total cost ($)	*ICER*
No strategy	0	0	-
X	3737.9021	8850885	2367.8750
W	3827.9825	7844285	–11174.4619
Y	5034.3624	22130	–6483.9898
Z	31589.0230	4948785	–185.5288

Table 5: ICER when X is Eliminated after W and X are Compared

Strategies	Total infection averted	Total cost ($)	*ICER*
W	3827.9825	7844285	–11174.4619
Y	5034.3624	22130	–6483.9898
Z	31589.0230	4948785	–185.5288

Table 6: ICER when Y is Eliminated after W and Y are Compare

Strategies	Total infection averted	Total cost ($)	*ICER*
W	3827.9825	7844285	–11174.4619
Z	31589.0230	4948785	–185.5288

We found that strategy W is the most cost-effective option out of all of the strategies after running the ICER for each strategy. As such, it is selected for use in combating the spread of disease.

6. Discussion of the Results

6.1 Discussion Economic Evaluation for the Control Parameters

The economic evaluation for controlling yaws infection was performed on personal hygiene (u_1) as the only control parameter; the result shows $\frac{\chi\left(P_Y + x_1 A_Y + x_2 T_S\right)S_Y^*}{N}\left(\lambda_{S_Y} - \lambda_L\right)$ as the total marginal benefit for the use of personal hygiene while $C_{hy} S_Y^* \lambda_{C_Y} e^{-\varphi_Y t}$ as the marginal cost. So if the marginal cost is greater than the marginal benefit as shown by (2.4) when $u_1(t) = 0$, the personal hygiene is not effective for use. Similarly, if the marginal cost is equals to the marginal benefit; where $u_1(t) \in (0,1)$ in (2.4), then personal hygiene could be used as a control parameter over a period of time. Prevention using personal hygiene would be optimal only when the expected marginal benefit is superior than the marginal cost of using personal hygiene where $u_1(t) = 1$. Therefore, the use of personal hygiene reduces the number of exposed. We also performed the cost evaluation for treatment for infected populations (u_2) as control parameter, the results show that

$C_{tt}\left(mz_1P_Y^* + z_2b_2T_Y^* + z_3f_2A_Y^* + z_5nP_S\right)e^{-\varphi_Y t}$ and $mz_1P_Y^*\left(\lambda_{R_Y} - \lambda_{P_Y}\right) + b_2z_2T_Y^*\left(\lambda_{R_Y} - \lambda_{T_Y}\right) + \varsigma z_3A_Y^*\left(\lambda_{R_Y} - \lambda_{A_Y}\right) + z_5nP_S^*\left(\lambda_{R_S} - \lambda_{P_S}\right)$ are the respective marginal cost and marginal benefit for treatment for infected populations. If the marginal cost is greater than the marginal benefit as shown in (2.6) when $u_2(t) = 0$, then the treatment for infected populations is not effective. Similarly, if the marginal cost is equal to the marginal benefit where $u_2(t) \in (0,1)$ in (2.6), then treatment for infected populations could be considered over a finite time. While, treatment for infected populations would be optimal only when the projected marginal benefit is superior than the marginal cost of using treatment for infected populations where $u_2(t) = 1$. Therefore, treatment for infected populations could the best control strategy for the infected human. The marginal cost for treatment and surgery for temporary scarred u_3 against the infected individuals who developed temporary scarred is given as $C_{ts}f_5\upsilon_1T_D^*e^{-\varphi_L t}$ being the marginal cost for implementing the control, while $f_5\upsilon_1T_D^*\left(\lambda_{T_D} - \lambda_R\right)$ is the marginal benefit for implementing the control as shown by (2.8). If the marginal cost is greater than the marginal benefit as shown in (2.8) when $u_3(t) = 0$, then the treatment and surgery for temporary scarred is not effective. Likewise, if the marginal cost is equal to the marginal benefit $u_3(t) \in (0,1)$ in (2.8), then treatment and surgery for temporary scarred could be considered over a predetermined time. While, treatment and surgery for temporary scarred would be optimal only when the anticipated marginal benefit is better than the marginal cost of using treatment and surgery for temporary scarred where $u_3(t) = 1.$ Therefore, treatment and surgery for temporary scarred could the best control parameter for eradicating scars.

6.2 Discussion on Incremental Cost Effectiveness Ratios

Based on the model simulation results, the Table 3 shows the strategies and their respective total infections averted and total costs averted for the strategies while, Table 4 shows the ranking of the strategies based on their effectiveness incrementally. The comparison of the strategies indicates that strategy W is dominant over strategy X, Table 5. Therefore, strategy X is costlier and less effective than strategy W. Therefore, strategy X is eliminated as set of alternatives. $ICER$ is recalculated in Table 6 and carry out comparison between strategies W and Y shows that strategy Y is costlier and less effective than strategy W. So strategy Y is eliminated. With the remaining result; it is concluded that strategy Z dominates in higher cost and less effectiveness than strategy W. Therefore, we recommend strategy W (combination of personal hygiene and treatment for infected populations as the most cost-effective strategy for controlling yaws transmission.

7. Conclusion

The economic evaluation for the model was carried-out in order to determine the marginal benefits against the marginal costs for model. It is found that if the marginal cost is greater than the marginal benefit the parameter(s) could not be effective and could not be considered in controlling yaws transmissions. Similarly, if the marginal cost is equal to the marginal benefit, the parameter(s) could be considered over a finite time as transmission control. Furthermore, whenever the marginal benefit of the control parameter(s) is larger than the marginal cost, then the parameter could be considered as the best prevention strategy for controlling the transmission. Optimal control was applied to investigate and analyze the most optimal strategies for controlling the transmission of yaws infection using personal hygiene, treatment for infected populations, treatment and surgery for temporary scarred as control parameters. The results show significantly, how the transmission would be controlled whenever a control(s) is used. The numerical simulation using ode45 in MatLab was performed, the results showed how the transmissions could be reduced or eliminated whenever a control or combination(s) of the controls is/are applied. The incremental cost effectiveness ratio (ICER) for yaws infection was computed for the implementation of various combinations of the controls to determine the most cost effective strategy that can control the disease transmissions. The ICER for the control strategy shows that the most cost-effective strategy for

yaws infection control is the combination of personal hygiene and treatment for infected populations as the most cost-effective strategy for controlling yaws transmission.

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