International Journal of Development Mathematics Vol 3 Issue 2 Page No. 202 - 220

INTERNATIONAL JOURNAL OF DEVELOPMENT MATHEMATICS

ISSN: 3026-8656 (Print) | 3026-8699 (Online)

journal homepage: https://ijdm.org.ng/index.php/Journals

Modeling the Transmission of Tuberculosis Meningitis Disease with Optimal Control Strategy

Muritala A. Afolabi[a], Musibau A. Omoloye[b,*], Saheed O. Ajao[c] and Moses O. Adeyemi[a]

[a]Department of Mathematics, University of Ilesa, Ilesa, Osun State, Nigeria
[b]Department of Mathematical Sciences, Nigerian Defence Academy, Kaduna State
[c]Department of Mathematics, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria

ARTICLE INFO

Article history:
Received 02 March 2026
Received in revised form 10 May 2026
Accepted 30 May 2026

Keywords:
Basic reproduction number, sensitivity analysis, incremental cost-effectiveness ratio, optimal control

MSC 2020 Subject classification:
34D20

ABSTRACT

Mycobacterium tuberculosis causes Tuberculosis Meningitis (TBM) which is a life-threatening infectious disease that leads to inflammation of the membranes surrounding the brain and the spinal cord. It remains a major public health challenge due to its high rates of mortality and long-term neurological disability. Though various clinical studies have been done to alleviate its burden, little focus has been put on deterministic mathematical modelling and optimum cost-effectiveness analysis of its transmission dynamics. This paper presented a deterministic mathematical model of the transmission dynamic of tuberculosis meningitis to explore optimal control methods and cost-efficiency of control. The model has been developed as a set of ordinary differential equations. The autonomous version of the model was subjected to qualitative analysis. Next Generation Matrix method was used to calculate the basic reproduction number and sensitivity analysis carried out to find out how important model parameters affect reproduction number. Moreover, Pontryagin's Maximum Principle was used to perform a detailed analysis of the non-autonomous optimal control model with three control interventions. Incremental Cost-Effectiveness Ratio was calculated in order to assess the economic efficiency of the suggested control strategies. Analytical results were illustrated using numerical simulations to determine the most cost-effective strategy of preventing and controlling tuberculosis meningitis.

1. Introduction

Mycobacterium tuberculosis causes tuberculosis meningitis (TBM) which is a life-threatening infectious disease that leads to inflammation of the membranes surrounding the brain and the spinal cord. TBM is the most destructive strain of tuberculosis (TB) that has over 100,000 new cases annually (Huyuh et al., 2022). This bacterium is mostly infected by affecting the lung and spreading through the blood to the meninges that cover the brain against injury and infection resulting in tuberculosis meningitis (Daniel et al., 2019). The development of tuberculosis meningitis is usually slow and can have faint symptoms such as aches and pains, loss of appetite, fatigue and constant headache during some weeks before the more specific symptoms of meningitis such as severe headache, aversion to bright light, stiffening of the neck can appear (CDC, 2019). Early diagnosis and treatment of TBM particularly in children is crucial in order to minimize mortality and morbidity (WHO, 2025; CDC,2019). TBM is a common disease that often has non-specific symptoms during the early stages of the disease and is diagnosed during the later stages of the disease when the brain has already been damaged (WHO, 2025). The disease has a slow onset and is thus hard to identify and is in many cases at an advanced stage too late to be treated. Bacillus

* Corresponding author. Tel.: +2347082876059
E-mail address: *muritala_afolabi@unilesa.edu.ng* (Afolabi, M. A.)
https://doi.org/10.62054/ijdm/0302.14

Calmette–Guérin (BCG) vaccines are vaccine used to prevent TB in infants and young children against the more serious forms of this disease including TBM (Pontryagin,1962; Anggriani et al., 2016; Daniel et al., 2019; WHO, 2025) but what happened once this vaccine expires or wanes away. It is treated by admitting the patient into the hospital and with close observations to check the development of the disease. Several types of investigations like lumber puncture and procedures are going to be necessary. When treatment among the individuals is timely, the majority will recover well as long as the treatment regimen is followed to the end as a result of which some individuals do not experience the after-effects over the long-run (WHO, 2025; Hethcole, 2000; Du et al., 2022).

Mathematical models have proved useful in the process of affecting decision-making process about intervention and control of TB. Nevertheless, the only work on TBM is a mathematical approach to the management of hydrocephalus of tuberculosis meningitis. In study the work of (Sharomi et al., 2008; Hethcole, 2000), their work was dependent on dichotomous nature that is either to conduct surgery or not through logistic regression model. Others like (Sanusi et al.,2025; Huyuh et al., 2022) carried out clinical management and control of TBM where (Lenhart& Workman, 2007; Afolabi et al., 2021) was on public health emergency and burden reduction of death and disability in tuberculosis meningitis. This paper has extensively covered mathematical transmission model to optimal cost-effective strategy to prevent and control the tuberculosis meningitis. Six compartmental model has been organized in the following way in this paper. In section 2, the non-autonomous tuberculosis meningitis is formulated and the qualitative properties of solutions of the autonomous versions determined. Section 3 has made some assumptions and analysis of autonomous model is carried out further in section4. In section 5 optimal controls on non-autonomous model was implemented. Numerical simulations of optimality system and cost-effectiveness analysis are conducted in section 6 with graphical profile. Section 7 contains the conclusion.

2. Method

2.1. Model formulation

Total homogeneous population at time t, denoted by $\mathrm{N(t)}$ where $\mathrm{N(t)}$ is human population partitioned into sub-populations: $S_H(t)$ susceptible individuals, $V_T(t)$ vaccinated individuals, $L(t)$ Latent individuals, $C_U(t)$ Carrier-undetected individuals, $C_D(t)$ Carrier-detected individuals and $R_T(t)$ recovered individuals.

It is assumed that susceptible human population is increased by the recruitment of individuals assumed to be susceptible at rate π except those that have been vaccinated against TBM at the rate ρ and vaccine wanes-off rate at ω. The transmission rate for TBM is given as:

$$\lambda_T = \frac{\beta_T (C_U + \eta C_D)}{N} \tag{1}$$

where β_T represents the effective contact rate capable of leading to tuberculosis meningitis (TBM) infection while" η " is modification parameter which accounts for the risk of infectiousness of individuals in C_D class. This population is decreased by natural death rate and disease-induced death rate. This class is later increased by natural immunity rate "σ "as well as treatment rate "τ ". Latent TBM individuals $L(t)$ progress to active TBM at rate "κ_T". Exogenous re-infection of Latent individuals occurred at the rate $(1-P_2)\psi_e\gamma_T$ and recovered individuals at the rate $(1-P_3)\psi_a\gamma_T$. The population of TBM vaccinated class $V_T(t)$ is increased by recruiting the vaccinated individuals into the vaccinated class at the rate" $\rho\pi$ ". This is decrease by the rate at which vaccine expired or wanes-off "ω" and natural death rate of vaccinated individuals.

A fraction θ of the newly TBM infected individuals known as Fast progressor are moved to the carrier undetected class C_U (t) while the remaining fraction $(1-\theta)$ called Slow progressor are moved to latent class $\mathrm{L(t)}$. The population of the latent individuals is decreased by the progression of latent individuals to active individuals at the rate "κ_T ", natural death rate and exogenous re-infection at the rate $\psi_e\gamma_T$. The population of carrier undetected individuals $C_U(t)$ is increased by infection of fast progressor $\theta\lambda_T$. It is further increased by the progression of latent individuals that have the probability of developing it at the rate $(1-\upsilon)$, exogenous re-infection of Latent individual at the rate $(1-P_2)\psi_e\gamma_T$ and by recovered individuals at the rate $(1-P_3)\psi_a\gamma_T$. This population is decreased by natural death rate and disease-induced death rate.

* Corresponding author. Tel.: +2347082876059
E-mail address: *muritala_afolabi@unilesa.edu.ng* (Afolabi, M. A.)
https://doi.org/10.62054/ijdm/0302.14

The population of carrier detected individuals $C_D(t)$ increased by progression of fraction of the latent individuals that have the probability of developing infectious TBM at the rate "υ". It is further increased by exogenous re-infection of latent and recovered individuals at $P_2\psi_e\gamma_T$ and $P_3\psi_a\gamma_T$ respectively. This later decreased by both natural death and induced death rate. It further reduced by treatment rate "τ "of infected detected individuals and natural immunity at the rate "σ". The population of recovered individuals $R_T(t)$ is increased by treatment rate "τ " of carrier detected individuals, natural immunity rate and by exogenous re-infection at $\psi_a\gamma_T$. This population is finally reduced by natural death rate"μ " of the recovered individual.
Thus,

2.2. The optimal control model for tuberculosis meningitis is given as

$$\frac{dS_H}{dt} = (1-\rho)\pi_H - (1-u_1)\lambda_T S_H - \mu S_H + u_2\,\omega V_T$$
$$\frac{dV_T}{dt} = \rho\pi_H - (\mu + u_2\omega)V_T$$
$$\frac{dL}{dt} = (1-u_1)(1-\theta)\lambda_T S_H - (\mu+\kappa_T)L - (1-u_1)\psi_e\lambda_T L$$
$$\frac{dC_U}{dt} = (1-u_1)\theta\lambda_T S_H + (1-u_1)(1-P_2)\psi_e\lambda_T L + (1-u_1)(1-P_3)\psi_a\lambda_T R_T - (\mu+\delta)C_U + (1-\upsilon)\kappa_T L \quad (2)$$
$$\frac{dC_D}{dt} = \upsilon\kappa_T L + (1-u_1)P_2\psi_e\lambda_T L - (\mu+\delta+u_3\tau+\sigma)C_D + (1-u_1)P_3\psi_a\lambda_T R_T$$
$$\frac{dR_T}{dt} = (u_3\tau+\sigma)C_D - \mu R_T - (1-u_1)\psi_a\lambda_T R_T$$

Where $\lambda_T = \dfrac{\beta_T(C_U + \eta C_D)}{N}$

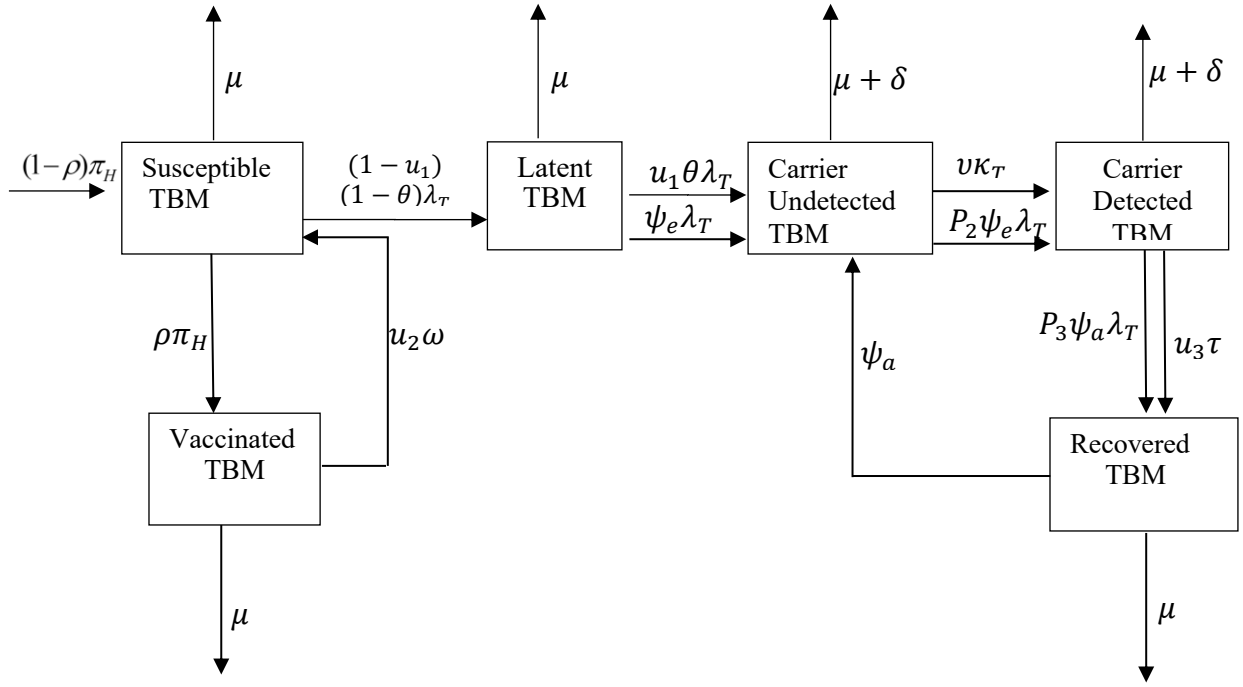

Figure 1. Tuberculosis Meningitis Transmission Model

* Corresponding author. Tel.: +2347082876059
E-mail address: *muritala_afolabi@unilesa.edu.ng* (Afolabi, M. A.)
https://doi.org/10.62054/ijdm/0302.14

2.3. Autonomous Version of the model

By inputting the three control variables u_1, u_2 and u_3 to zero, the autonomous version of equation (2) can be obtained because it is time dependent.

$$\frac{dS_H}{dt} = (1-\rho)\pi_H - \lambda_T S_H - \mu S_H$$
$$\frac{dV_T}{dt} = \rho\pi_H - \mu V_T$$
$$\frac{dL}{dt} = (1-\theta)\lambda_T S_H - (\mu+\kappa_T)L - \psi_e \lambda_T L$$
$$\frac{dC_U}{dt} = \theta\lambda_T S_H + (1-P_2)\psi_e \lambda_T L + (1-P_3)\psi_a \lambda_T R_T - (\mu+\delta)C_U + (1-\upsilon)\kappa_T L \quad (3)$$
$$\frac{dC_D}{dt} = \upsilon\kappa_T L + P_2\psi_e \lambda_T L - (\mu+\delta+\sigma)C_D + P_3\psi_a \lambda_T R_T$$
$$\frac{dR_T}{dt} = \sigma C_D - \mu R_T - \psi_a \lambda_T R_T$$

It is necessary to prove the non-negativity of the state variables of equation (3) for all times, given that all parameters are non-negative in the feasible region.

3. The assumptions that were made in this paper included:

(i) The tuberculosis meningitis (TBM) is the most devastating type of tuberculosis caused by same Mycobacterium tuberculosis.

(ii) Few parameters use for TB is also applicable to tuberculosis meningitis (TBM) in numerical simulation.

(iii) That carrier population is sub-divided into carrier-undetected and carrier-detected due to slow progression of tuberculosis meningitis.

4. Qualitative properties of solutions

4.1. Positivity of solutions

Theorem 1: The closed set $D = \{(S_H, V_T, L, C_U, C_D, R_T)\}$ is positive for all $t > 0$ with respect to autonomous version of model equation (3) above.

Proof:

To prove, sub-equations of system (3) were considered. Thus, the first equation of autonomous version of model equation (3) gives rise to:

$$\frac{dS_H}{dt} + (\mu+\lambda_T)S_H \geq 0 \quad (4)$$

(which is the first order homogeneous differential equation and upon on integration yields)

$$d(S_H e^{(\mu+\lambda_T)t}) \geq 0\, dt \quad (5)$$

Integrate both sides with respect to t

* Corresponding author. Tel.: +2347082876059
E-mail address: *muritala_afolabi@unilesa.edu.ng* (Afolabi, M. A.)
https://doi.org/10.62054/ijdm/0302.14

Hence,

$$S_H(t) \geq S_H(0)e^{-(\mu+\lambda_T)t} \tag{6}$$

Since $\mu + \lambda_T \geq 0$ and $S_H(0) \geq 0$ then

$S_H(t) \geq 0$ if $t = 0$ *and* $t \to \infty$. Therefore, $S_H(t) \geq 0 \quad \forall\ t \geq 0$.

It can be shown, using similar method, that the remaining state variables, $V_T(t)$; $L(t)$; $C_U(t)$; $C_D(t)$; $R_T(t)$ are non-negative for all the time t>0

4.2. Invariant region

Theorem 2 The biologically feasible region Ω of TBM model (3) is positively invariant.

The solutions of the model (3) are feasible for all $t > 0$ if they enter the invariant region $\Omega = \Omega \subset \mathrm{R}_+^6$

Where $\Omega = (S_H, V_T, L, C_U, C_D, R_T) \in R_+^6$

Proof:

It is clear from the first six equations of the model that in absence of the TBM,

that is when $C_D = 0$, gives the below equation:

$$\frac{dN(t)}{dt} = \pi - \mu N(t) \tag{7}$$

After solving the equation (7) and evaluating it as time t tends to infinity, then

$$\mathrm{N} \leq \frac{\pi}{\mu} + \left(\mathrm{N}_0 - \frac{\pi}{\mu}\right)\mathrm{e}^{-\mu t} \tag{8}$$

Applying the theorem of differential inequality by (Birkhoff & Rota, 1988), gives

$$0 \leq \mathrm{N} \leq \frac{\pi}{\mu} \text{ as } t \to \infty. \tag{9}$$

Hence, all feasible solution set of the human population of the TBM model enters the region

$$\Omega = \left\{ \begin{array}{l} \left(\{S_H, V_T, L, C_U, C_D, R_T\}\right) \in R_+^6 : S_H \geq 0, V_T \geq 0 \ \ L \geq 0, \ C_U \geq 0, \\ C_D \geq 0, R_T \geq 0, N \leq \dfrac{\pi}{\mu} \end{array} \right\} \tag{10}$$

Therefore, the region Ω is positively invariant i.e. solution remains positive for all temporal values. Thus, the model (3) is biologically meaningful and mathematical well-posed in the domain Ω.

4.3. Tuberculosis meningitis free equilibrium

At critical point, $\frac{dS_H}{dt} = \frac{dV_T}{dt} = \frac{dL}{dt} = \frac{dC_U}{dt} = \frac{dC_D}{dt} = \frac{dR_T}{dt} = 0$

Let disease free equilibrium (DFE) be denoted by ε_0, then, at DFE,

$$L = C_U = C_D = R_T = 0 \tag{11}$$

Then, the set of the uninfected classes of the model presented as:

$$\varepsilon_0 = \left(S_0, V_{T0}, L_0, C_{U0}, C_{D0}, R_{T0}\right) = \left\{ \frac{\pi(\mu + \omega - \rho\pi)}{\mu(\mu + \omega)}, \frac{\rho\pi}{\mu + \omega}, 0, 0, 0, 0 \right\} \tag{12}$$

* Corresponding author. Tel.: +2347082876059
E-mail address: *muritala_afolabi@unilesa.edu.ng* (Afolabi, M. A.)
https://doi.org/10.62054/ijdm/0302.14

4.4. Basic reproduction number (R_{0T}) for tuberculosis meningitis

The basic reproduction number for this model was calculated using the next generation matrix method as described by (Driessche & Watmought, 2002). Consider the next generation matrix which made up of two parts F and V^{-1}, where $F = \left[\frac{\partial F_i(x_i)}{\partial x_i}\right]$ and $V = \left[\frac{\partial V_i(x_i)}{\partial x_i}\right]$. The non-negative matrix F are the new infection terms and the non-singular matrix V shows the transfer of infections terms from one compartment to another are derived by expressing the six-sub equations in equation (3) as a vector differential equation. It shows that

$$F = \begin{pmatrix} 0 & (1-\theta)\beta_T & (1-\theta)\beta_T\eta \\ 0 & \theta\beta_T & \theta\beta_T\eta \\ 0 & 0 & 0 \end{pmatrix} \quad and \quad V = \begin{pmatrix} K_2 & 0 & 0 \\ -(1-\upsilon)\kappa_T & K_3 & 0 \\ -\upsilon\kappa_T & 0 & K_4 \end{pmatrix} \tag{13}$$

where

$$K_2 = (\mu + \kappa_T), \qquad K_3 = (\mu + \delta) \qquad K_3 = (\mu + \delta + \tau + \sigma)$$

It finally gives

$$R_{OT} = \begin{pmatrix} 0 \\ 0 \\ \left(\frac{\beta_T}{K_2K_3K_4}\right)(G_1 + \eta G_2) \end{pmatrix} \tag{14}$$

Where

$$G_1 = \{\eta\theta K_2K_3K_4 - \eta K_3K_4 - \theta K_4\kappa_T - K_4\kappa_T\} \; and$$
$$G_2 = \{\theta K_4\kappa_T - \theta K_2K_4 - K_4\kappa_T\}$$

Upon substituting the values of parameters in Table 1 in equation (14), the basic reproduction number $R_{0T} = 0.6698$

Table 1. Parameters Definitions and values used for the numerical simulation

Parameters	Definition	Values	Sources
π	Human Recruitment rate	2000	Afolabi et al., 2021
μ	Natural death rate	0.02, 0.12	Adewale et al., 2009, Assumed
β_T	Contact rate for TB\TBM	0.1	Assumed
δ	Induced mortality rate for TB\TBM	0.001	Hethcole, 2000
θ	Fast progressor rate for TB\TBM	0.7	Assumed
ρ	Vaccination rate for TB\TBM	0.2	Nainggolan et al., 2013
κ_T	Progression rate from L to C_U	0.2522	Adewale et al., 2009
τ	Treatment rate	0.3	Adewale et al., 2009
σ	Natural immunity rate for carrier detected	0.2	Du et al., 2022
ω	Vaccine wanes-off in V_T	0.1	Assumed
P_2, P_3	Fraction of re-infected in Latent and recovered	0.7 , 0.7	Adewale et al., 2009

* Corresponding author. Tel.: +2347082876059
E-mail address: *muritala_afolabi@unilesa.edu.ng* (Afolabi, M. A.)
https://doi.org/10.62054/ijdm/0302.14

ψ_e, ψ_a	Exogenous re-infection of TBM in Latent and recovered	0.35, 0.35	Adewale et al., 2009
η	Modification parameters	0.001	Saranza et al., 2017

5. Sensitivity analysis for tuberculosis meningitis

The relative significance of the various factors that bring about the transmission of Tuberculosis Meningitis should be known in order to determine the most effective mode of control and reduction of human morbidity and mortality. Sensitivity enables us to determine the relative change in state variable with change in parameter. Such indices inform us of the importance of each parameter to the transmission of diseases (Afolabi et al., 2022). By definition, the normalized forward sensitivity index "ξ" of a variable "u" that depends differentiably on a parameter "p" is defined as:

$$\xi_p^u = \frac{\partial u}{\partial p} \times \frac{p}{u} \tag{15}$$

Calculation of sensitivity indices of R_{0T} for TBM model

The explicit formula in equation (15) can be derived analytically. The sensitivity of basic reproduction number (R_{0T} = 0.6698) to each of the parameters described in Table 1 with respect to equation (14) gives the result

Table 2. Values of numerical sensitivity for tuberculosis meningitis model

Parameters	**Sensitivity values**
β_T	1.00000000
σ	0.000122818
μ	-0.02282657
θ	0.16621869
υ	-0.024572485
δ	-0.011413286
κ_T	0.049300654
η	-0.071326697
τ	-0.0004191753

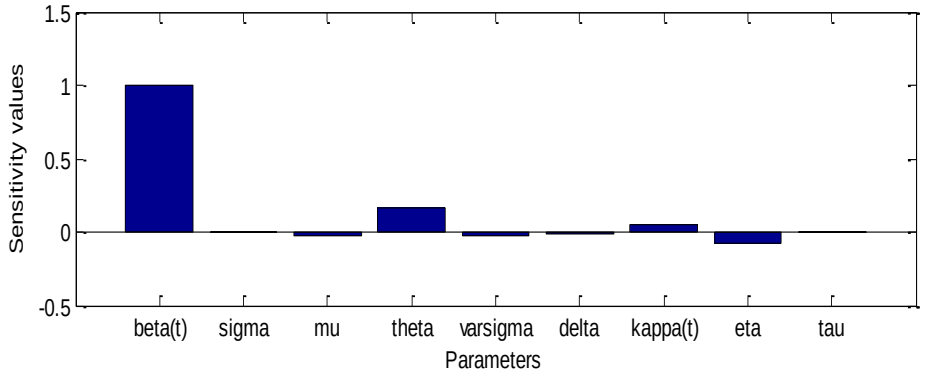

Figure 2: Chart showing the positive and negative Sensitive parameters

* **Corresponding author. Tel.**: +2347082876059
E-mail address: *muritala_afolabi@unilesa.edu.ng* (Afolabi, M. A.)
https://doi.org/10.62054/ijdm/0302.14

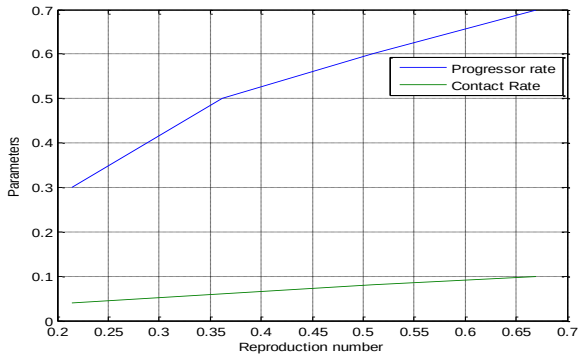

Figure 3**a.**

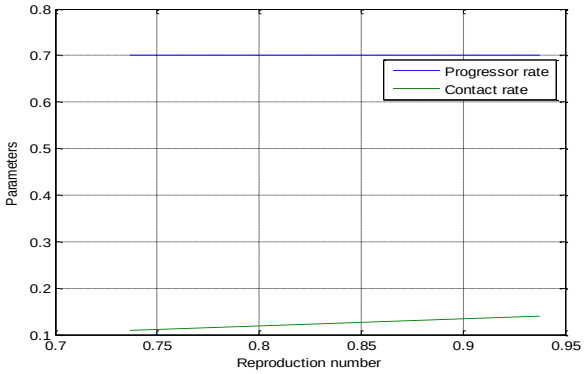

Figure 3**c**

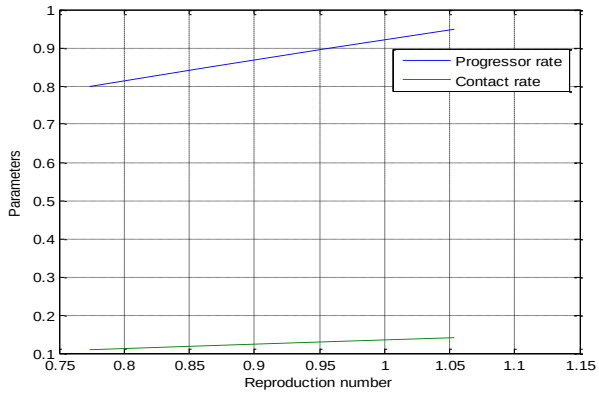

Figure 3b**.**

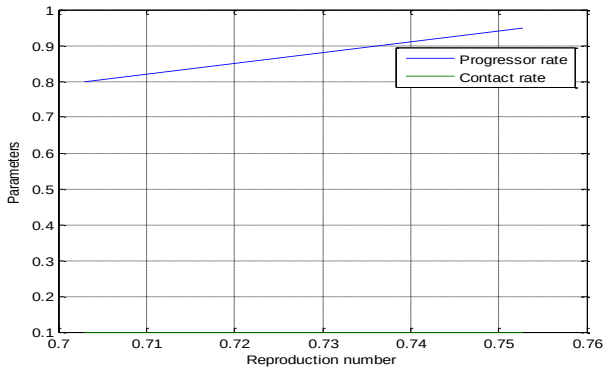

Figure 3d

Figure 3. Sensitivity values against the parameters of reproduction number R_{0T}

* **Corresponding author. Tel.**: +2347082876059
E-mail address: *muritala_afolabi@unilesa.edu.ng* (Afolabi, M. A.)
https://doi.org/10.62054/ijdm/0302.14

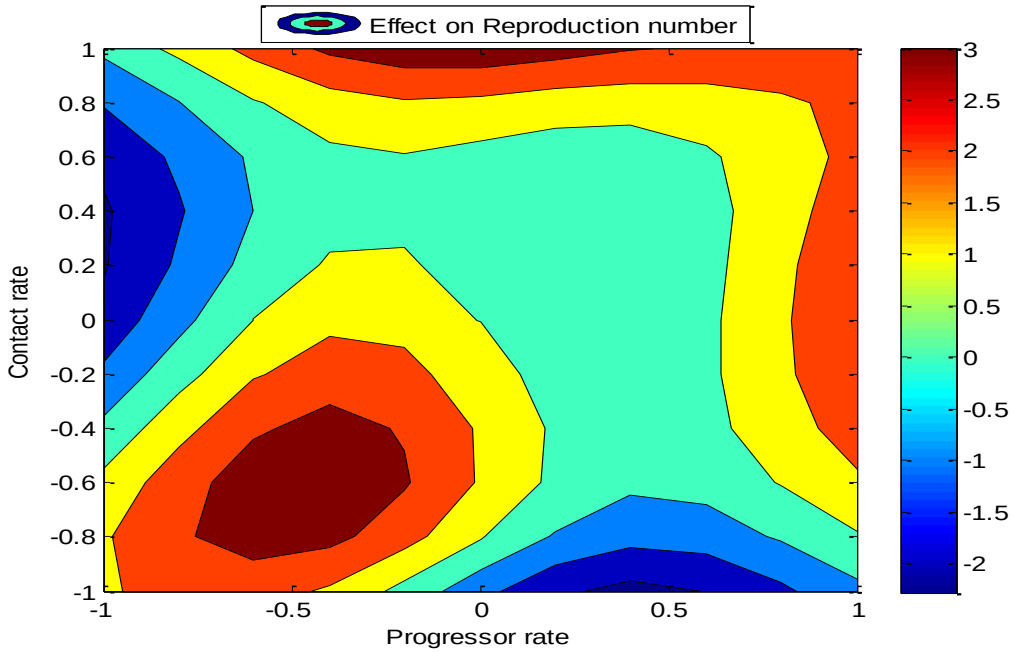

Figure 4: Contour plot between progressor rate and contact rate against R_{0T}

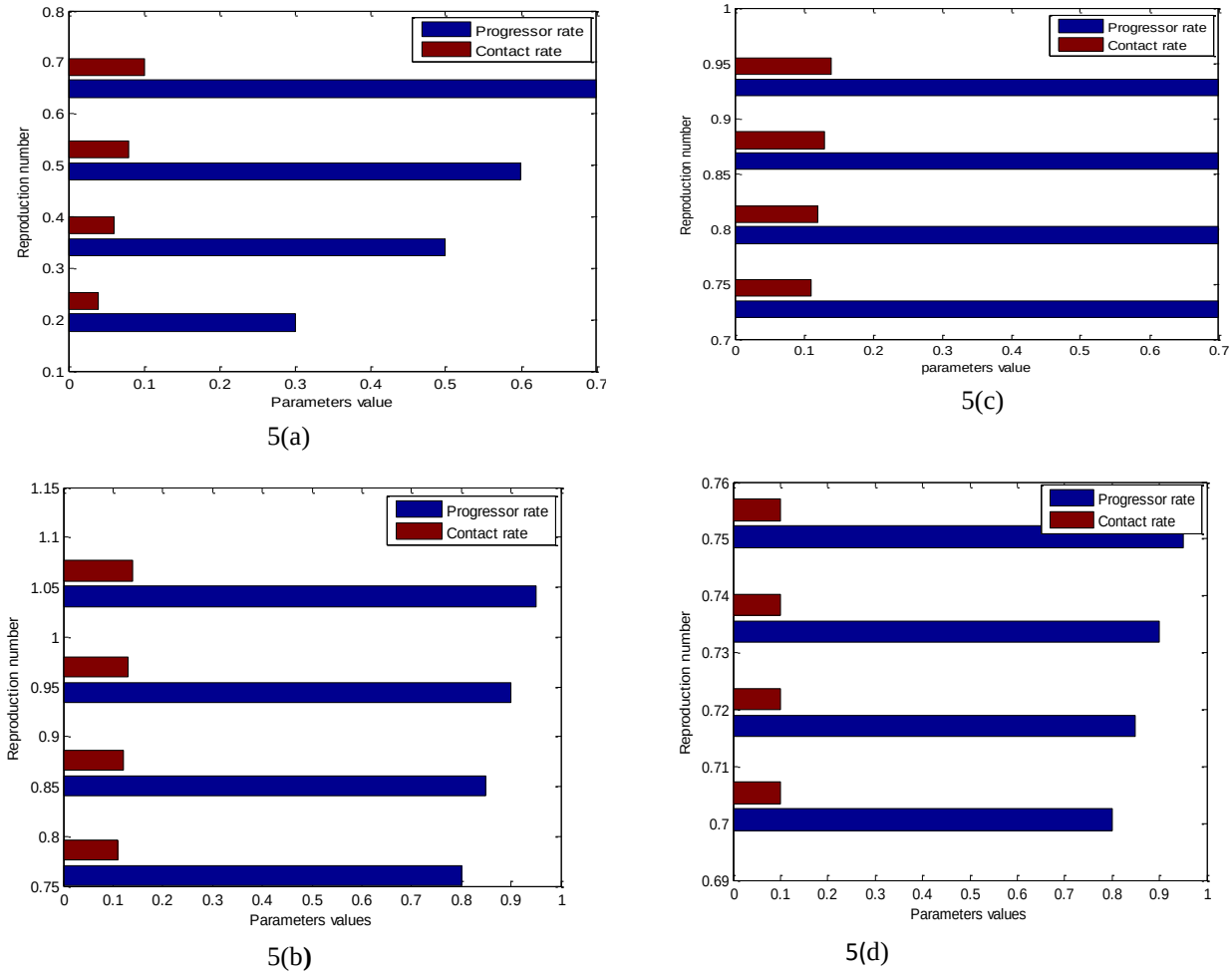

Figure 5. The effect of contact rate and progressor rate against R_{0T}

6. Optimal Control

Optimal control problem is formulated to minimize the number of humans that are exposed and infected with tuberculosis meningitis and the cost of implementing the TBM infected humans (Afolabi et al., 2022). The objectives function J is constructed to minimize the number of people infected and the cost involved in applying the control u_1, u_2 and u_3. The objectives function J is given as:

$$J(u_1,u_2,u_3)=\int_0^{t_f} B_1C_U+B_2C_D+B_3L+\frac{1}{2}(A_1u_1^2+A_2u_2^2+A_3u_3^2))dt \qquad (16)$$

where t_f is the final time, B_1, B_2, and B_3 are positive weights to balance the factors of Latent, carrier undetected and carrier detected. A_1, A_2 and A_3 are the positive weight constants for public awareness on preventing the menace of TBM, administering of TB\TBM vaccine and treatment for TBM.

The terms B_1C_U, B_2C_D *and* B_3L were the cost incurred by TBM latent, carrier undetected and carrier detected individuals. The terms $\frac{A_1u_1^2}{2}, \frac{A_2u_2^2}{2}$ and $\frac{A_3u_3^2}{2}$ represent the cost of implementing the control.

6.1. Characterization of optimal control

The optimal control u_1^*, u_2^* and u_3^*, is sought such that ;

$$J(u_1^*, u_2^*, u_3^*) = \min_{u_1^*, u_2^*, u_3^*} \{J(u_1, u_2, u_3) / (u_1, u_2, u_3) \in U\} \tag{17}$$

where $U = \{(u_1, u_2, u_3)\}$ such that u_1, u_2, u_3 are measurable with

$0 \le u_1 \le 1, \quad 0 \le u_2 \le g_2, \quad 0 \le u_3 \le g_3$ for $t \in [0, t_f] \to [0,1]$ is the control set.

The necessary conditions that an optimal control must satisfy come from Pontryagin`s Maximum Principle (Pontryagin, 1962). The principle converts equations (2) and (17) into a problem of minimizing poitwise a Hamiltonian function H with respect to the controls as shown in Equation (18)

$$\begin{aligned} H \quad &= B_1C_U + B_2C_D + B_3L + \frac{1}{2}(A_1u_1^2, A_2u_2^2, A_3u_3^2) \\ &+ M_{S_h}[(1-\rho)\pi_H - (1-u_1)\lambda_T S_H - \mu S_H + u_2 \omega V_T] \\ &+ M_{V_T}[\rho\pi_H - (\mu + u_2\omega)] + M_{E_T}[(1-u_1)(1-\theta)\lambda_T S_H - (\mu+\kappa_T)L - (1-u_1)\psi_e\lambda_T L] \\ &+ M_{C_U}[(1-u_1)\theta\lambda_T S_H + (1-u_1)(1-P_2)\psi_e\lambda_T L + (1-u_1)(1-P_3)\psi_a\lambda_T R_T - (\mu+\delta)C_U + (1-\upsilon)\kappa_T L] \\ &+ M_{C_D}[\upsilon\kappa_T L + (1-u_1)P_2\psi_e\lambda_T L - (\mu+\delta+u_3\tau+\sigma)C_D + (1-u_1)P_3\psi_a\lambda_T R_T] \\ &+ M_{R_T}[(u_3\tau+\sigma_T)C_D - \mu R_T - (1-u_1)\psi_a\lambda_T R_T] \end{aligned} \tag{18}$$

Where; $M_{S_H}, M_{V_T}, M_{E_T}, M_{C_U}, M_{C_D}, M_{R_T}$ are the adjoint variables or co-state variables

Theorem 3: Given an optimal control u_1^*, u_2^*, u_3^* and solutions $S_H^*, V_T^*, L^*, C_U^*, C_D^*, R_T^*$ of the corresponding state system (17) that minimizes $J(u_1, u_2, u_3)$ over U. Then, there exists adjoint variables M_{S_H}, M_{V_T}, M_L, M_{C_U}, M_{C_D}, M_{R_T}, which must be satisfied alongside with transversality conditions.

Proof:The differential equations governing the adjoint variables are gotten by differentiating the Hamiltonian function H with respect to the state variables, so that

$$\frac{dM_{S_H}}{dt} = -\frac{\partial H}{\partial S_H}, \quad \frac{dM_{V_T}}{dt} = -\frac{\partial H}{\partial V_T}, \quad \frac{dM_L}{dt} = -\frac{\partial H}{\partial L}, \quad \frac{dM_{C_U}}{dt} = -\frac{\partial H}{\partial C_U}, \tag{19}$$

$$\frac{dM_{C_D}}{dt} = -\frac{\partial H}{\partial C_D}, \quad \frac{dM_{R_T}}{dt} = -\frac{\partial H}{\partial R_T}$$

and with transversality conditions;

$$\frac{\partial H}{\partial u_1} = 0 \quad for \quad u_1^*; \qquad \frac{\partial H}{\partial u_2} = 0 \quad for \quad u_2^*; \qquad \frac{\partial H}{\partial u_3} = 0 \quad for \quad u_3^* \tag{20}$$

$$M_{S_H}(t_f) = 0,\ M_{V_T}(t_f) = 0,\ M_L(t_f) = 0,\ M_{C_{UT}}(t_f) = 0,\ M_{C_D}(t_f) = 0,\ M_{R_T}(t_f) = 0 \tag{21}$$

By standard control arguments involving bounds control, then

$$u_1^* = \begin{cases} \xi_1^* \ if \ \ 0 < \xi_1^* < 1 \\ 0 \ if \ \ \xi_1^* \le 0 \\ 1 \ if \ \ \xi_1^* \ge 1 \end{cases} \qquad u_2^* = \begin{cases} \xi_2^* \ if \ \ 0 < \xi_2^* < 1 \\ 0 \ if \ \ \xi_2^* \le 0 \\ 1 \ if \ \ \xi_2^* \ge 1 \end{cases} \quad and \quad u_3^* = \begin{cases} \xi_3^* \ if \ \ 0 < \xi_3^* < 1 \\ 0 \ if \ \ \xi_3^* \le 0 \\ 1 \ if \ \ \xi_3^* \ge 1 \end{cases} \tag{22}$$

Where;

$$\xi_1^* = \max\left\{0, \min\left[1, \frac{((1-\theta)M_L + \theta M_{C_U} - M_{S_H})\lambda_T S_H}{A_1}\right]\right\}$$

$$\xi_2^* = \max\left\{0, \min\left[1, \frac{(M_{V_T} - M_{S_H})\omega V_T}{A_2}\right]\right\} \tag{23}$$

$$\xi_3^* = \max\left\{0, \min\left[1, \frac{(M_{C_D} - M_{R_T})\tau_T C_D}{A_3}\right]\right\}$$

7. Numerical Simulation

The optimality system consists of the state equations (2) coupled with the adjoint equation (18) with initial conditions at t =0, the terminal condition (21) and the characterization of the optimal control equation (23) (Daniel et al., 2019). To illustrate the impact of at least two combinations of the three control intervention strategies on the transmission dynamics of TBM in the population, the parameter values as shown in Table 1 were used such that $R_{0T} = 2.1116$ with the initial conditions $S_H(0) = 500$, $V_T(0) = 180$, $E_T(0) = 120$, $C_U(0) = 90$, $C_D(0) = 50$, $R_T(0) = 30$. The weight constants values are chosen as A_1=50, A_2=50, A_3=50, B_1=120, B_2=120 and B_3=120. The control strategy U_1 is for public awareness, U_2 is for administering of TB\TBM vaccine and U_3 if for the treatment of TBM. The cost of implementing U_1 = \$8.76 [15], U_2 = \$2.5 (WHO, 2025) and U_3 = \$34.6 (https://bmcinfectdis.biomecntra.com, 2025)

Graphical profiles of control intervention strategies using Data Cursor were as follows:

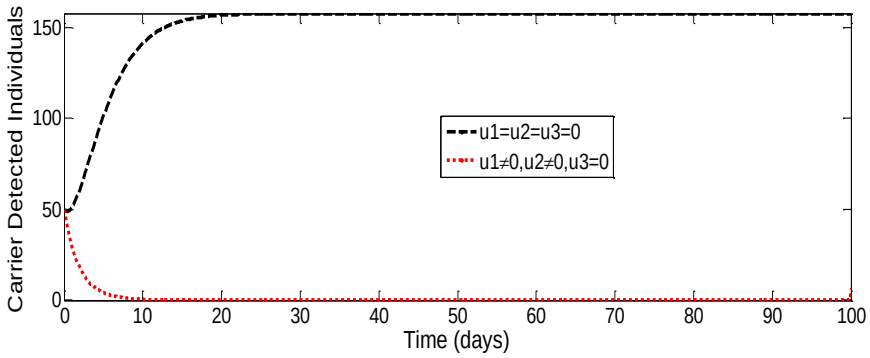

Figure 6. Simulations graph showing the control strategy A that combines TBM Public awareness and vaccination.

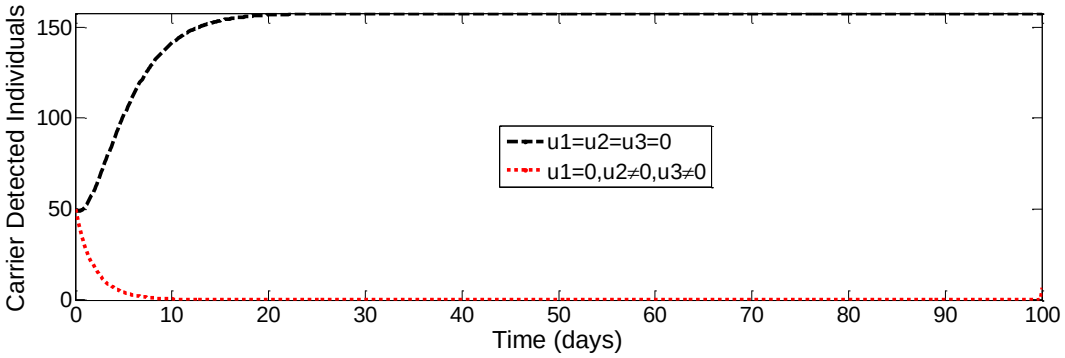

Figure7. Simulations graph showing the control strategy B that combines TBM Vaccination and treatment.

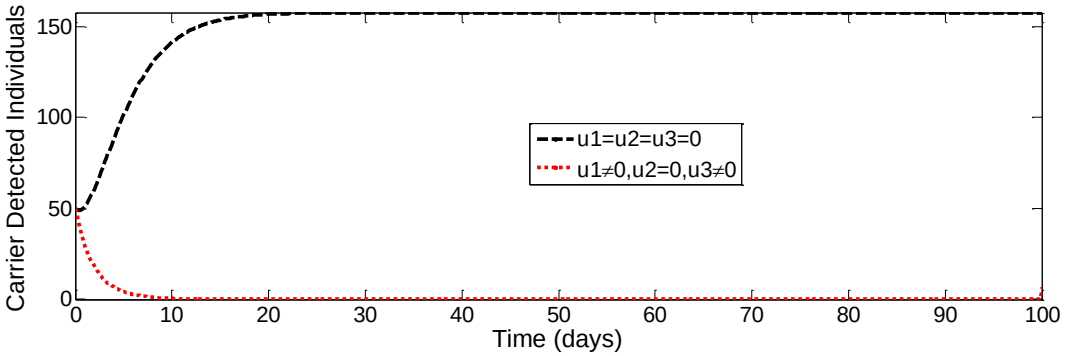

Figure 8. Simulations graph showing the control strategy C that combines TBM Public awareness and treatment.

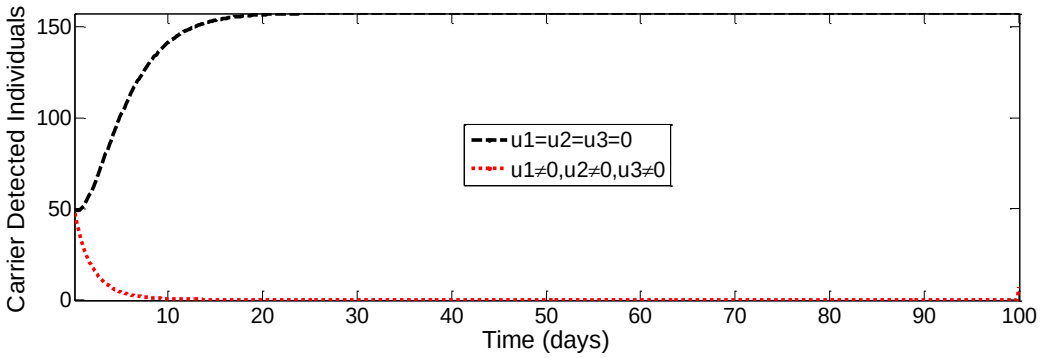

Figure 9. Simulations graph showing control strategy D that combines TBM Public awareness, vaccination and treatment.

7.1 Cost- effectiveness analysis

Cost-effectiveness analysis (CEA) is an economic evaluation method used to compare the relative costs and outcomes of two or more competing control strategies implemented under limited resources (Olaniyi et al., 2020), Akanni et al., 2019; Lenhart& Workman, 2007; Daniel et al., 2019). It assesses which intervention provides greater benefit for a given cost. Mathematically, it is defined as the ratio of the difference in total costs to the difference in total control benefits between strategies.

Mathematically, ICER = $\dfrac{\text{Difference in total cost in strategies i and j}}{\text{Difference in total infected averted in strategies i and j}}$

Table 3: Increasing order of infection averted with their ICER

Strategies	Total Infection Averted	Total Cost ($)	ICER
Strategy C	148.2	43.36	0.29
Strategy B	149.4	37.1	-5.22
Strategy A	149.8	11.26	-64.6
Strategy D	150.7	45.86	38.44

Calculation of ICER for:

$$\begin{aligned} Strategy C: \quad & \frac{43.36}{148.2} = && 0.29 \\ Strategy B: \quad & \frac{37.1-43.36}{148.4-148.2} = && -5.22 \\ Strategy A: \quad & \frac{11.26-37.1}{149.8-149.4} = && -64.6 \\ Strategy D: \quad & \frac{45.86-11.26}{150.7-149.8} = && 38.44 \end{aligned} \tag{25}$$

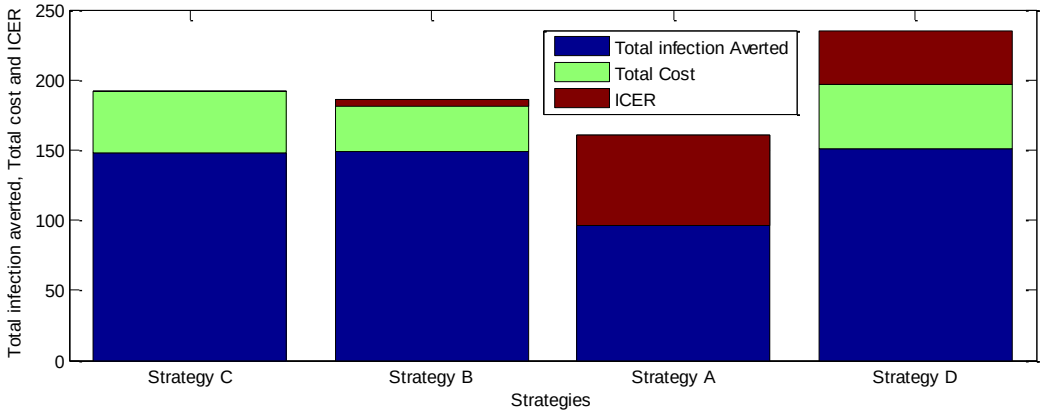

Figure 10. Bar chart of increasing order of infection averted with ICER

Table 4: New ICER when strategy C is eliminated

Strategies	Total Infection Averted	Total Cost ($)	ICER
Strategy B	149.4	37.1	0.25
Strategy A	149.8	11.26	-72.1
Strategy D	150.7	45.86	38.4

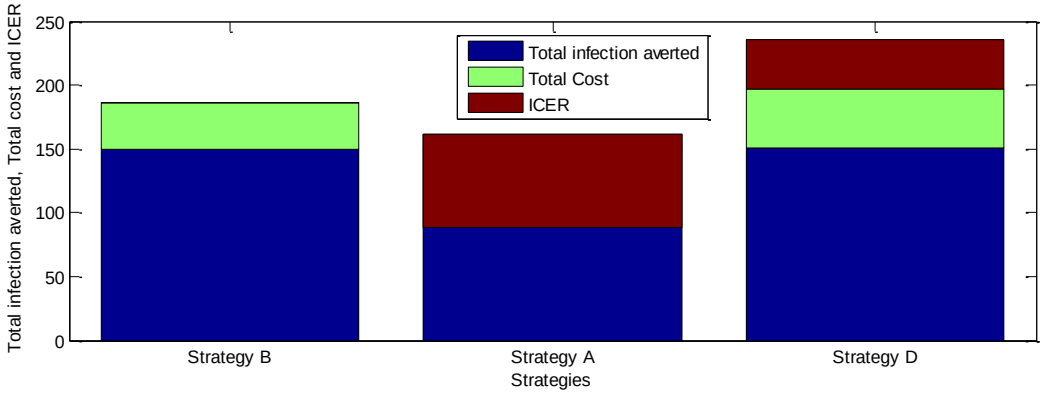

Figure 11. Bar chart of new ICER when strategy C is eliminated

Table 5: New ICER when strategy B is eliminated

Strategies	Total Infection Averted	Total Cost ($)	ICER
Strategy A	149.8	11.26	0.08
Strategy D	150.7	45.86	38.4

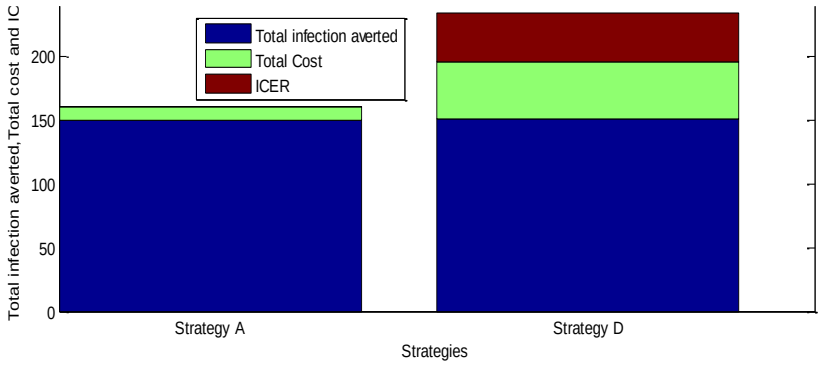

Figure 12. Barchart of new ICER when strategy B is eliminated

In the comparison of strategy A and strategy D, strategy A has lower ICER hence indicating that strategy D is highly dominant over strategy A implying that strategy D is more expensive and less effective than strategy A. We can therefore conclude that the strategy that is the best among all the strategies in the control of TBM infection is strategy A that involves both; public awareness and vaccines.

7.2 Discussion of Results

Figure2 indicated the parameters that have either positive or negative number. Figure3 indicates sensitivity values for contact rate and progressor rate against the reproduction number. In Figure 3(a), the progressor rate and contact rate were reducing subject to base line value 0.7 to 0.3. and from base line 0.1 to 0.05 respectively. This has positive effect on reproduction number which starts reducing from 0.65 to 0.25 for both progressor rate and contact rate. This indicates that reducing both parameters has a significant positive impact in lowering the reproduction number. In figure 3(b), both progressor rate and contact rate were increasing subject to base line value 0.7 and 0.1 respectively which in-turn increasing reproduction number at higher rate. This can be seen when progressor rate was 0.95 and contact rate was 0.14 and reproduction number was 1.0537. The reproduction number increased to 1.0537, indicating possible disease persistence. In figure 3(c), the progressor rate was fixed to 0.7 while the contact rate was increasing as 0.11, 0.12, 0.13 and 0.14. These demonstrating that variations in contact rate significantly influence transmission dynamics. In figure 3(d), the contact rate was fixed at 0.1, while the progressor rate increased from 0.8 to 0.85, 0.9, and 0.95. The reproduction number increased at a rate of 0.0166. Despite the fact that the progressor rate affects the reproduction number, its impact is less pronounced compared to the contact rate. Figure4 resents a contour plot illustrating the combined effects of the progressor rate and contact rate on the reproduction number. The contour levels clearly show regions where the reproduction number exceeds unity, indicating high transmission potential. Figure5, in continuation of the values applied in figure 3(a-d), Figure5(a-d) further indicates the joint influence of the contact rate and progressor rate on the reproduction number as well as their interaction with each other. Figure6 demonstrates the implement of Control Strategy A in the best way possible for the carrier-detected population, which was analyzed with the help of the Data Cursor tool on MATLAB. When a combination of this control was applied the maximum value was 156.3 and the maximum value in the absence of control was 6.5. The cost of the overall treatment was $11.26 and the aversion of infection 149.8. Figure8 gives the best implementation of Control Strategy B to the carrier-detected population. In the case of this combination of control the maximum value was 156.9 and the maximum value of no control was 7.5. The infection aversion was 149.4 and the overall price of treatment of this strategy B was $37.1. The Figure8 shows that Control Strategy C of carrier-detected population is best implemented. The highest value of this mixture of control was 156.9 and highest value of no control was 8.7. The infection aversion for this strategy C was 148.2 and the overall cost of the treatment was $43.36. Figure9 illustrates that Strategy D of Control Strategy of carrier-detected population is ideal in implementation. In the event of applying this mixture of control the highest value was 157.2 and the highest value was 6.49 in the absence of a control. Aversion of infection to this strategy D was 150.7 and the total cost of treatment was $45.86. Figure10 shows the increasing order of control strategies in relating with their cost of

implementation. Figure11 shows the remaining control strategies after the elimination of less effective strategy. Figure12 shows the strongly dominant strategy of the last two control strategies and determined the best between them.

8. Conclusion

This work entails modeling the transmission of tuberculosis meningitis (TBM) diseases and optimal control. The autonomous version of the model was shown to be mathematically well-posed and epidemiologically feasible, ensuring that the solutions remain positive and bounded within a biologically meaningful region. Optimal control analysis was performed to investigate effective strategies for reducing TBM transmission. The control measures considered include public awareness campaigns for TBM prevention, administration of TB/TBM vaccines, and treatment of TBM-infected individuals. On sensitivity analysis of the parameters on reproduction number, the values for contact rate and progressor rate were the most sensitive against the reproduction number. As shown in this work, the progressor rate and contact rate were reducing subject to base line value 0.7 to 0.3. and from base line 0.1 to 0.05 respectively. This has positive effect on reproduction number which starts reducing from 0.65 to 0.25 for both progressor rate and contact rate. This indicates that reducing both parameters has a significant positive impact in lowering the reproduction number. Simulation results revealed that: Strategy A resulted in a total cost of $11.26 with 149.8 infections averted. Strategy B incurred a total cost of $37.10 with 149.4 infections averted. Strategy C required $43.36 and averted 149.8 infections while Strategy D had a total cost of $45.86 and averted 150.7 infections. Based on the incremental cost-effectiveness analysis, the study demonstrates that preventive control strategies, particularly the optimal combination of public awareness and vaccination are the most cost-effective interventions for controlling TBM transmission. Overall, the findings emphasize the importance of preventive measures over treatment approaches in reducing the burden of TBM. The conclusion also going in line with the work of (Huyuh et al., 2022) that carried out reducing the burden of death and disability of TBM and the work of (Daniel et al., 2019) which worked on clinical management and outcome of tuberculosis meningitis.

References

Adewale, S.O., Podder, C.N. and Gummel A.B. (2009), Mathematical Analysis of a TB transmission model with DOTS, *Canadian Applied Mathematical Quarterly*. 17(1) Spring.

Adewale, S. O., Omoloye, M. A., Olopade, I. A. & Adeniran, G. A.(2017). Mathematical Analysis for dynamic al spread of Malaria in the Population. *International Journal of Innovation and Scientific Research, 31(2):225-233.*

Afolabi, M. A, Adewoye, K.S, Folorunso, A. I & Omoloye, M. A.(2021). A Mathematical model on transmission dynamics of Meningococcal Meningitis. *Iconic Research and Engineering Journal 4(10).*

Afolabi, M. A., Adewale, S. O. & Omoloye, M. A.(2022) Optimal control analysis for transmission dynamics of Tuberculosis-Malaria co-infection. Strad research, 9(2) 2,183-193.

Akanni, J.O, Akinpelu, F.O. Olaniyi, S., Oladipo, A.T. and Ogunsola, A.W. (2019): Modelling financial Population Dynamics: Optimal Control and Cost-Effectiveness Analysis. *International Journal of Dynamics and Control*. Doi.10.1007/s40435-019-00572-3

Anggriani, N., Wicaksosn, B.C. and Supriatna, A.K. (2016). Optimal Control for TB disease with Vaccination Assuming Endogeneous Reactivation and Exogenous Re-infection. *Journal of Physics: Conference Series*

725 (2016) 012011. Doi:10.1088/1742-6596/727/1/012011.

Birkhoff, G. and Rota, G.C. (1988). Ordinary Differential Equations, 4th Edition, John Wiley and Sons, Inc., New York

Centre for Disease Control and Prevention (CDC) (2019), On emergence of mycobacterium tuberculosis with extensive resistance to second line drugs-worldwide, http://www.cdc.gov/tb/topic/basics/default.htm

Daniel, B.D., Grace, G.A. and Natrajan, M. (2019). Tuberculosis meningitis in children: Clinical management & outcome. Indian J Med Res 150. DOI:10.4103/ijmr.IJMR_786_17.

Du Preez, K., Jenkins, H.E., Donald, P.R., Solomons, R.S.,Graham, S.M., Schaaf, H.S., Starke, J.R., Hesseling, A.C. and Seddon, J.A. (2022), Tuberculosis Meningitis in Children: A Forgotten Public Health Emergency.

Driessche, P. V. and Watmought, J. (2002): Reproduction Numbers and Sub-Threshold Endemic Equlibria for Compartmental Models of Disease Transmission. *Math. Biosciences,*180, 29-48. https://doi.org/1o.1016/S0025-5564(02)00108-6

Huyuh, J., Abo, Y-N., du Preez, K., Solomons, R., Dooley, K.E. and Seddon, J.A. (2022). Tuberculosis Meningitis in Children: Reducing the Burden of Death and Disability. *Pathogens 2022*, 11,38. Doi.org/10.3390/pathogens11010038

Hethcole, H.W. (2000), The mathematics of infectious diseases. Society for industrial and applied mathematics (SIAM) 42(4);599-653

Lenhart, S, and Workman, I.T. (2007) Optimal Control Applied to Biological Models, London. Chapman & Hall, 2007.

Nainggolan, J., Sudradjat Supian, Supriatna A.K. and Anggrian N. (2013), Mathematical Model of Tuberculosis Transmission with Recurrent Infection and Vaccination, *Journal of Physics: Conference Series***423:** 012059.

Okuonghae, D and Korobeinikov A. (2007), Dynamics of tuberculosis: The effect of Direct Observation Therapy Strategy (DOTS) in Nigeria*, Math. Modeling Natural Phenomena***2**(1); 101-113

Olaniyi, S., Okosun, O.K., Adesanya, S.O., Lebelo, R.S., (2020). Modeling Malaria Dynamics with Partial Immunity and Protected Travelers: Optimal Control and Cost Effectiveness Analysis. *Journal of Biological Dynamics* http://doi.org/10.1080/17313758.2020.1722265

Pontryagin, L .S.,Boltyanski, V .G., Gamkrelidze, R. V. and Mishchenko, E. F.(1962): The Mathematical theory of optimal processes. Wiley, New York.

Saranza, G. R. M., Sumalapao, D. E. P., Batara, J.M.F. and Arceo, S.P. (2017). A mathematical approach in the management of hydrocephalus from tuberculosis meningitis. National Journal of Physiology, Pharmacy and Pharmacology. 7(11); 1195-1200

Sanusi, A. O., Omoloye, M. A, Emiola, O.K.S., Shaba, W.M. (2025). Evaluating predictive factors impacting

tuberculosis treatment outcomes. *International Journal of Advances in Engineering and Management (IJAEM) 7(05),178-195.*

World Health Organization (2025). Accessed on 17th February. https://www.who.inf/vaccines

https://bmcinfectdis.biomecntra.com., (2025). Accessed on 16th October,