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Deterministic Mathematical Model of Tuberculosis Disease with Treatment and Recovered Groups

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ABSTRACT: *In this paper we formulated the model. We proved the basic properties of the model which are Positivity and boundedness and also determined the Reproduction number which helped us to determine the local asymptotic stability (LAS) of the DFE. We went further to prove the global asymptotic stability (GAS) of DFE and Endemic Equilibrium using lyapunov function. Finally, a simulation study of the model was carried out to help gain more insight into the formulated model. The simulations of the deterministic model shows (a) susceptible population which decreases over time as people interact with infected individuals and move to the Exposed class (b) Exposed population which increases with time when susceptible individuals get the disease but cannot infect it (c) Infected population which increases with time (d) Treated population which increases with respect to time. The simulation of the deterministic model of Recovered class which increases over time and the Treated class .We noticed from the graph that as R0 ≤ 1 the Treated class decreases over time which will eventually die out while when R0 ≥ 1 the disease persists and becomes endemic.*

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I. INTRODUCTION

Tuberculosis (TB), an airborne-transmitted bacterial disease caused by Mycobacterium Tuberculosis, remains one of the most important global public health challenges for decades. Numerous mathematical modeling studies have been carried out to gain insight into the transmission dynamics and control of TB spread in human population. The first mathematical model specifically linked to TB that we are aware of is in the form of a linear discrete system. It was introduced by Waaler in 1962. Waaler's model includes three epidemiological classes: Susceptible, Latent (TB), and Infectious (active TB), Carlos et al. (2015). Tuberculosis is an ancient and complex infectious disease on which a large number of theoretical studies have been carried out. MTB's infection can remain latent, become active, or it can progress from latent TB to active TB either by endogenous re-activation and/or exogenous re-infection. Active TB is most of the time acquired through co-infection of MTB with other diseases (diabetes, (Human Immunodeficiency Virus Acquired Immuno deficiency Syndrome) HIV/AIDS) or some substance abuse such as alcohol and tobacco. The mathematical analysis of biomedical and disease transmission models can significantly contribute to the understanding of the mechanisms of these processes and to the design of potential therapies. Many researchers have worked on models of Tuberculosis epidemics in the past. Song et al. (2004) considered dynamical models of Tuberculosis and applications. The dynamical model that incorporates close and contacts (as if there were two epidemiological contact units) was developed and analyzed in order to address the role of heterogeneous contacts on TB transmission using three compartments: Susceptible, Exposed (Latent), Infected (SEI). The population was partitioned into TB-active and TB-inactive clusters. And the term generalized household was used to describe a group of persons (friends or relatives or coworkers) who have frequent contact with each other. They observed that the eventually eradication of Tuberculosis, it is not necessary that transmission be immediately and completely prevented. It is necessary only that the rate of transmission be held permanently below the level at which a given number of infection spreading (i.e. open) cases succeed in establishing an equivalence number to carry on the succession. If in successive periods of time, the number of infectious host is continuously reduced, the end result of this diminishing ratio, if continued long enough, must be extermination of Tubercle bacillus is losing ground and that the eventual eradication of Tuberculosis requires that the present balance against it be maintained. It was examined mathematical models of Tuberculosis with exogenous re-infection. Four compartments was used Susceptible, Exposed, Infected, Treated (SEIT). They showed that re-activation or re-infection mechanisms are capable of supporting qualitative changes in TB dynamics. Specifically, these mechanisms could be responsible for supporting multiple endemic states and bi-stability. The impact of these mechanisms is likely to increase due

to factors that include increases in HIV prevalence and deteriorating economic conditions (famine and the likes). Hence, the eradication or effective

Control of TB becomes a challenging and critical enterprise. They looked at policies that bring

R0 to value less than one may no longer sufficient if re-activation or re-infection is strong. They also examined simple models deliberately ignoring a large number of epidemiological factors, social and socio-economic, host's heterogeneity, population structure and movement patterns. They also neglected new and critically important activation mechanisms that include co-infections (HIV) or DR-TB (drug resistance) or XDR-TB. However, they believed that the addition of these additional levels of complexity will strengthen their results. That is, that reactivation or re-infection mechanisms are more likely to play an important role in the context of complex social environment and highly heterogeneous communities. Another worked on agent-based simulation (ABS) of a Tuberculosis epidemic: understanding the timing of transmission to study TB transmission dynamics and the role of various contact networks. Their model simulates the course of a TB epidemic across a single population and uses a hierarchical network of contacts in three levels, typical to the transmission of airborne diseases,). Parameters are chosen from the literatures, and the model is calibrated to a setting of high TB incidence the used their model to study the transmission dynamics at an individual level with regard to the timing and distribution of secondary infection from single sources. The average time for disease diffusion to reach 50% of infections at an individual level is estimated, and the timing patterns are compared among different networks. They performed sensitivity analysis of results with regard to multiple parameter values, and discussed the implications for TB control policy. They considered a model of transmission involving three contact networks (referred to as close, casual and random contacts) that represent the main social relationships in transmission of an airborne disease. Their model simulates the stochastic contact events at an individual level and enables us to study patterns of transmission across different network. Close contacts, at the first level, represent the most frequent contact type among household members. On the second level, casual contacts model social relationships such as those among friends at a bar, neighbours at a store, or children at school. These contacts are less frequent and intimate than close contacts, and restricted to a specific network of related individuals including friends, coworkers, etc. Rafalli et al. (1996); Classen et al.(1999). They restricted the domain of casual contacts to each neighborhood's residents, and assume a limited period of one year for the duration of contacts. Finally random contacts are used to model encounters of people at places such as bus stops, museums, etc. such contacts have the shortest duration (one month), and account for potential risk of transmission among non-related people in the whole community. They derived that ABS provides a exible yet powerful platform to model the population heterogeneity with regard to personal characteristics and different contact networks. Moreover, the ABS ability to represent the course of an epidemic at a micro (individual) level (as well as at a macro population level) enables us to estimate the timing of TB transmissions in our model. They used an ABS approach to study the emergence of drug-resistant TB due to treatment with antibiotics. They assume a lattice structure for spatial presentation of their population and model TB transmission through local and global interactions across the lattice. The lattice structure, however, does not provide a realistic representation of social settings and cannot be used to study transmission dynamics at the individual level. He evaluated stability of a two-strain Tuberculosis model with general contact rate which allows Tuberculosis patients with drug-sensitive mycobacterium Tuberculosis strain to be treated. They subdivided the population according to the transmitted features of TB, into susceptible individuals (S), those exposed to drug-sensitive (E1), individual with symptoms of TB and drug-sensitive (I1), those exposed to drug-resistant TB (E2), those displaying the symptoms of TB and drug-resistant (I2) by using Lyapunov stability theory, La Selle's invariant set theorem and Dulac's criterion, the global stability of equilibrium of the proposed model is proved. Another author examined mathematical model for vaccinated tuberculosis disease with VEIT model. They used four populations in this model, the Vaccinated, Exposed, Infected, and Treated. The type of TB spreading in this model is exogenous re-infection. They also explained equilibrium point, and analyzing of stability endemic model. They observed that the model of vaccinated Tuberculosis with exogenous re-infection have two equilibrium points, there is disease free and endemic. Eigen value of disease free is always negative so the stability of system is stable asymptotic at disease free points. By contrast, the impact of enhanced diagnostics on TB incidence is likely to be smaller, with < 10% of new cases averted. The modeled impact depends strongly on the quality of existing diagnostic services and the population's existing level of access to diagnostic services, but is robust across a wide range of population parameters including HIV and TB. Dodd (2015) presented a framework that uses notification, prevalence and mortality data to inform TB burden estimates in a single rigorously defined statistical framework. He handled temporal correlations by introducing a simple stochastic compartmental model of TB transmission that builds on current modeling assumptions used in WHO estimates, and that includes demographic trends in ages and sexes of populations. He used 12 parameters to characterize the model and is treated as uncertain and Monte Carlo methods are used to perform inference and prediction in a Bayesian framework for 9 countries with prevalence survey data available. He concluded by saying that a

variety of statistical and transmission models to relate the incidence at one time to other times should be formally assessed against each other. Transmission models have the potential to leverage additional population data, including LTBI (latent Tuberculosis Infection) surveys, and use information on natural history to extrapolate reasonably to groups where direct data may be particularly unreliable (for example, children). Availability as a package for the R statistical framework would facilitate installation and use, and encourage additional contributions and analyses. Dodd (2015) worked on the economic impact of Tuberculosis. He found that Adult mortality has a significant effect on national economies, through both the direct loss of productivity among those of working age and by altering fertility, incentives for risk-taking behavior, and investment in human and physical capital. TB is the most important cause of adult death due to infectious disease after HIV/AIDS. TB has its greatest impact on adults between the ages of 15 and 59. So, the social and economic burden of TB is great because the most economically productive persons in society, parents on whom development and survival of children depend are affected. TB places an extraordinary burden on those affected by the disease, their families, communities and on government budgets. According to him, the greatest burden of TB falls on productive adults who, once infected, are weakened and often unable to work. The burden of taking care of sick individuals usually falls on other family members and, besides putting at greatest risk of infection, can lower their productivity. Diagnosed individuals with TB are often medically quarantined for a period of time, which can affect their financial well-being. The infected populations have an economic impact on their families and in turn their countries national economies through their inability to contribute financially, as they are often unable to be productive workers. Okuonghae (2017) analyzed the epidemiological models of infectious diseases. He formulated an SEIR model, where he used Tuberculosis as a case study. He proved the basic properties of the model which are Positivity and boundedness and also determined the Reproduction number which helped him to determine the local asymptotic stability (LAS) of the DFE. He finally proved the global asymptotic stability (GAS) of DFE and EE using lyapunov function.

II. MODEL FORMULATION

2.1 Flow Diagram

Some modifications made on the model:

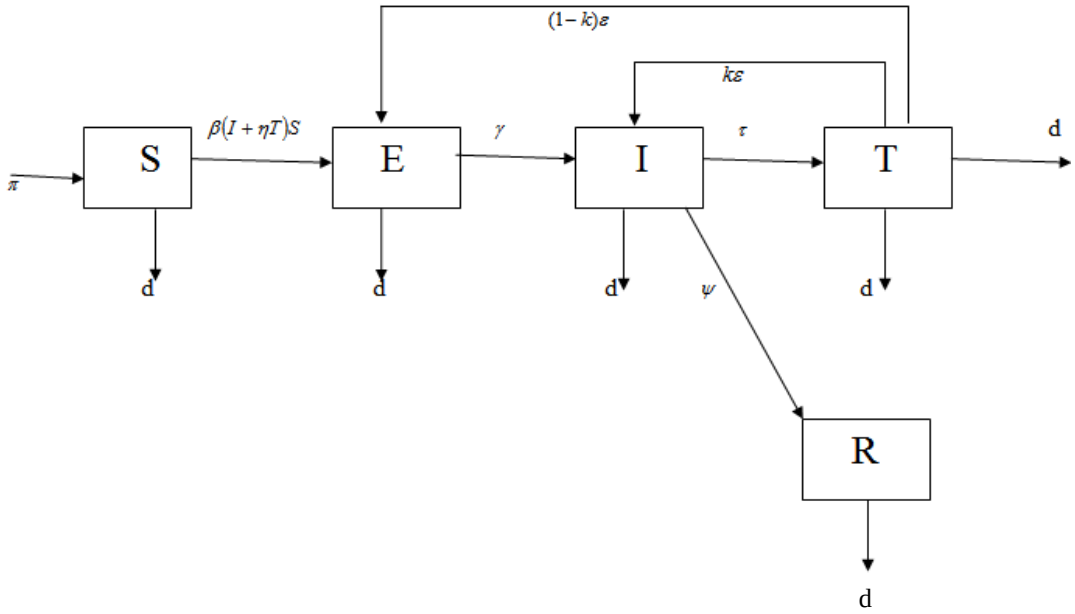


Figure 3.1: Schematic diagram of the compartments of the model

2.2 Assumptions of our mode

1. Infected individuals who are receiving treatment can transfer the disease
2. There is a Recovered class.
3. Our Model involves both deterministic and stochastic
4. The population is heterogeneous; hence, the individuals that make the population can be grouped into different compartments or groups according to their epidemiological states.
5. That the population size in a compartment is differentiable with respect to time.

6. That the population mixes homogeneously, that is, all susceptible individuals are equally likely to be infected by infectious individuals in case of contact.
7. Those in each compartment can die as a result of natural death.
8. Only those in infectious class recovers
9. The susceptible individuals can get Exposed by interacting with those in infectious andTreated class
10. We assume that the infectious class transmits a high percentage of the disease than the treated class.

2.3 Symbols and Parameters

Table 2.1

Symbols	Description
S	Population of susceptible Compartment
E	Population of exposed compartment
I	Population of Infected and infectious compartment
T	Population of the treated compartment
R	Population of the Recovered compartment
π	Recruitment rate into the susceptible compartment
d	Natural death rate
β	The rate at which exposed gets infected
ψ	Recovery rate
τ	The Treatment rate
δ_1	Additional induced rate for infected class
δ_2	Additional induced rate for treated class
ε	Rate of treatment failure
η	Rate which treated class transmits the disease
k	Fraction of those whose treatment failed and proceeds to infectious class
(1-k)	Fraction of those whose treatment failed and proceeds to exposed class

2.4 Model Equation

Applying the symbols and parameters, assumptions and the above flow diagram, we write the model equations as follows:

$$\left.\begin{aligned}
\frac{dS}{dt} &= \pi - \beta(I+\eta T)S - dS \\
\frac{dE}{dt} &= \beta(I+\eta T)S + (1-k)\varepsilon T - (d+\gamma)E \\
\frac{dI}{dt} &= \gamma E + k\varepsilon T - (\tau + \psi + d + \delta_1)I \\
\frac{dT}{dt} &= \tau I - (\varepsilon + d + \delta_2)T \\
\frac{dR}{dt} &= \psi I - dR
\end{aligned}\right\} \qquad (2.1)$$

III. MODEL ANALYSIS

3.1 Basic Properties of the Model

3.1.1 Positivity and Boundedness of solutions

For the model (3.10) to be epidemiologically meaningful, it is important to prove that all its state variables are non-negative for all time (t). In other words, solutions of the model system (2.1) with positive initial data will remain positive for all time t > 0.

Theorem 3.1: Let the initial data for the model (2.1) be S(0) > 0;E(0) > 0; I(0) > 0; T(0) >0;R(0) > 0.Then the Solutions $\{S(t), E(t), I(t), T(t), R(t)\}$ of the model (2.1), with positive initial data, will remain positive for all time t > 0.

Proof: Let $t_1 = Supt > 0 : S(t), E(t), I(t), T(t), R(t) > 0 \in [0\ 1]$.

Thus, t1 > 0, it follows, from the first equation of the system (2.1) that

$$\frac{dS}{dt} = \pi - \beta(I + \eta T)S - dS = \frac{dS}{dt} = \pi - \lambda S - dS \text{ where } \lambda = \beta(I + \eta T)$$

$$\Rightarrow \frac{dS}{dt} + (\lambda + d)S = \pi \qquad (2.1)$$

Integrating factor is $\exp(\int(\lambda + d)dt) = \exp((\lambda + d)t) = e^{(\lambda+d)t}$

Integrating (3.1) we have

$$d\left(Se^{(\lambda+d)t}\right) = \pi\left(e^{(\lambda+d)t}\right)dt \Rightarrow \left(Se^{(\lambda+d)t}\right)\Big|_0^{t_1} = \frac{\pi}{(\lambda+d)}e^{(\lambda+d)t}\Big|_0^{t_1}$$

$$\Rightarrow Se^{(\lambda+d)t_1} - S(0) = \frac{\pi}{(\lambda+d)}e^{(\lambda+d)t_1} - \frac{\pi}{(\lambda+d)}$$

$$\therefore \quad S(t) = S(0)e^{-(\lambda+d)t_1} + \frac{\pi}{(\lambda+d)} - \frac{\pi}{(\lambda+d)}e^{-(\lambda+d)t_1}$$

As $t_1 \to \infty$, $S(t) \to \frac{\pi}{(\lambda+d)} > 0$

$\therefore\ S(t) \geq 0$ *for all* $t > 0$

Considering the second equation of (2.1)

$$\frac{dE}{dt} = \beta(I + \eta T)S + (1-k)\varepsilon T - (d + \gamma) \Rightarrow E \geq -(d + \gamma)E \qquad (2.2)$$

$$\Rightarrow \frac{dE}{dt} \geq -(d + \gamma)E \Rightarrow \frac{dE}{E} \geq -(d + \gamma)dt$$

Integrating both sides we have,

$$\ln E \geq -(d + \gamma)t + k \Rightarrow E(t) \geq e^{-(d+\gamma)t+k} = e^{-(d+\gamma)t}e^k$$

$$\therefore \quad E(t) \geq E_0 e^{-(d+\gamma)t} \quad \text{where } E_0 = e^k$$

$$As\ t \to \infty,\ E(t) \geq 0$$

Hence, $E(t) \geq 0$ *for all* $t > 0$

Following the same way we can easily prove that $I(t) \geq 0, T(t) \geq 0$ *and* $R(t) \geq 0$. Hence, we conclude the proof.

3.1.2 Boundedness (invariant set)

Invariant set also called invariant manifold; if a solution of a differential equations starts on a given space, surface or curve (manifold or set) and remains within it for all time, then the manifold or set is said to be invariant. Hence a positively manifold or set will have solutions that are positive for all time.

Theorem 3.2: The closed set $D = \left\{(S(t), E(t), I(t), T(t), R(t)) \in \Re_+^5 : N \leq \frac{\pi}{d}\right\}$ is positively invariant and attracts all positive solutions of the model.

Proof: Recall that $N(t) = S(t) + E(t) + I(t) + T(t) + R(t) \Rightarrow \frac{dN(t)}{dt} = \frac{dS(t)}{dt} + \frac{dE(t)}{dt} + \frac{dI(t)}{dt} + \frac{dT(t)}{dt} + \frac{dR(t)}{dt}$

$$\Rightarrow \frac{dN}{dt} = \pi - \beta(I + \eta T)S - dS + \beta(I + \eta T)S + (1-k)\varepsilon T - (d+\gamma)E + \gamma E + k\varepsilon T - (\tau + \psi + d + \delta_1)I + \tau I - (\varepsilon + d + \delta_2)T + \psi I - dR$$

$$= \pi - dS - dE - dI - \delta_1 I - dT - \delta_2 T - dR = \pi - d(S + E + I + T + R) - \delta_1 I - \delta_2 T = \pi - dN - \delta_1 I - \delta_2 T$$

In the absence of the disease, $\delta_1 = \delta_2 = 0$, hence, we have

$$\frac{dN}{dt} \le \pi - dN \Rightarrow \frac{dN}{dt} + dN \le \pi \qquad (2.3)$$

Solving (2.3) using integrating factor, $I = \exp\{\int d dt\} = e^{dt}$, we have

$$d\left(Ne^{dt}\right) \le \pi e^{dt} dt \Rightarrow \left(Ne^{dt}\right)_0^{\infty} \le \frac{\pi}{d} e^{dt}\Big|_0^{\infty}$$

$$\Rightarrow Ne^{dt} - N(0) \le \frac{\pi}{d} e^{dt} - \frac{\pi}{d} \Rightarrow N(t) \le \frac{\pi}{d} + (N_0 - \frac{\pi}{d})e^{-dt}$$

$$\therefore \ N(t) \le \frac{\pi}{d} \ \ as\ t \to \infty$$

In particular, if $N(t) \le \frac{\pi}{d}$, hence D is positively-invariant and an attractor so that no solution path leaves through any boundary of D

3.2 Existence of steady states of the Model

The steady states of the model (2.1) exists at $\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dT}{dt} = \frac{dR}{dt} = 0$

This implies,

$$\left.\begin{aligned} &\pi - \beta(I + \eta T)S - dS = 0 \\ &\beta(I + \eta T)S + (1-k)\varepsilon T - (d+\gamma)E = 0 \\ &\gamma E + k\varepsilon T - (\tau + \psi + d + \delta_1)I = 0 \\ &\tau I - (\varepsilon + d + \delta_2)T = 0 \\ &\psi I - dR = 0 \end{aligned}\right\} \qquad (3.1)$$

We now Solving (3.1)

Considering the first equation of (3.1) we have

$$\pi - \beta(I + \eta T)S - dS = 0 \Rightarrow [\beta(I + \eta T) + d]S = \pi \Rightarrow S^* = \frac{\pi}{[\beta(I^* + \eta T^*) + d]}$$

Considering the second equation of (3.1) we have

$$\beta(I + \eta T)S + (1-k)\varepsilon T - (d+\gamma)E = 0 \Rightarrow (d+\gamma)E = \beta(I + \eta T)S + (1-k)\varepsilon T$$

$$\Rightarrow E^* = \frac{\beta(I^* + \eta T^*)S^* + (1-k)\varepsilon T^*}{(d+\gamma)}$$

Considering the third equation of (3.1) we have,

$$\gamma E + k\varepsilon T - (\tau + \psi + d + \delta_1)I = 0 \Rightarrow (\tau + \psi + d + \delta_1)I = \gamma E + k\varepsilon T$$

$$\therefore\ I^* = \frac{\gamma E^* + k\varepsilon T^*}{(\tau + \psi + d + \delta_1)}$$

Considering the fourth equation of (3.1) we have,

$$\tau I - (\varepsilon + d + \delta_2)T = 0 \Rightarrow \tau I = (\varepsilon + d + \delta_2)T$$

$$\Rightarrow T^* = \frac{\tau I^*}{\tau I - (\varepsilon + d + \delta_2)}$$

Considering the fifth equation of (3.1) we have

$$\psi I - dR = 0 \Rightarrow \psi I = dR \Rightarrow R^* = \frac{\psi I^*}{d}$$

Hence, the steady state of the model is

$$\left.\begin{aligned} S^* &= \frac{\pi}{[\beta(I^* + \eta T^*) + d]} \\ E^* &= \frac{\beta(I^* + \eta T^*)S^* + (1-k)\varepsilon T^*}{(d+\gamma)} \\ I^* &= \frac{\gamma E^* + k\varepsilon T^*}{(\tau + \psi + d + \delta_1)} \\ T^* &= \frac{\tau I^*}{\tau I - (\varepsilon + d + \delta_2)} \\ R^* &= \frac{\psi I^*}{d} \end{aligned}\right\} \qquad (3.2)$$

The disease-free steady state is $\xi^0(S^*,0,0,0,0) = \xi^0\left(\frac{\pi}{d}, 0, 0, 0, 0\right)$ and endemic steady state is $\xi^E(0, E^*, I^*, T^*, R^*) = \xi^E\left(0, \frac{(1-k)\varepsilon T^*}{(d+\gamma)}, \frac{\gamma E^* + k\varepsilon T^*}{(\tau + \psi + d + \delta_1)}, \frac{\tau I^*}{\tau I - (\varepsilon + d + \delta_2)}, \frac{\psi I^*}{d}\right)$

3.3 Basic Reproduction Number R_0

Using the next generation method approach, we obtain

$$f_i = \begin{pmatrix} \beta S(I + \eta T) \\ 0 \\ 0 \end{pmatrix}$$

$$v_i^- = \begin{pmatrix} (d+\gamma)E \\ (\tau + \psi + d + \delta_1)I \\ (k\varepsilon + (1-k\varepsilon) + d + \delta_2)T \end{pmatrix}$$

$$v_i^+ = \begin{pmatrix} (1-k)\varepsilon T \\ \gamma E + k\varepsilon T \\ \tau I \end{pmatrix}$$

To find F we solve the Jacobian of f_i

$$F = \begin{pmatrix} 0 & \beta S^0 & \beta\eta S^0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} = \begin{pmatrix} 0 & \frac{\beta\pi}{d} & \frac{\beta\eta\pi}{d} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

To find V we note that

$v_i = v_i^- - v_i^+$

$$v_i = v_i^- - v_i^+ = v_i^+ = \begin{pmatrix} (d+\gamma)E \\ (\tau+\psi+d+\delta_1)I \\ (k\varepsilon+(1-k\varepsilon)+d+\delta_2)T \end{pmatrix} - \begin{pmatrix} (1-k)\varepsilon T \\ \gamma E + k\varepsilon T \\ \tau I \end{pmatrix} = \begin{pmatrix} (d+\gamma)E-(1-k)\varepsilon \\ (\tau+\psi+d+\delta_1)I - \gamma E - k\varepsilon T \\ (k\varepsilon+(1-k\varepsilon)+d+\delta_2)T - \tau I \end{pmatrix}$$

We now solve the Jacobian of v_i to get V

$$V = \begin{pmatrix} (d+\gamma) & 0 & -(1-k)\varepsilon \\ -\gamma & (\tau+\psi+d+\delta_1) & -k\varepsilon \\ 0 & -\tau & (\varepsilon+d+\delta_2) \end{pmatrix}$$

Let $K_1 = (d+\gamma),\ K_2 = (1-k)\varepsilon, K_3 = (\tau+\psi+d+\delta_1)$ *and* $K_4 = (\varepsilon+d+\delta_2)$

Therefore,

$$V = \begin{pmatrix} K_1 & 0 & -K_2 \\ -\gamma & K_3 & -k\varepsilon \\ 0 & -\tau & K_4 \end{pmatrix}$$

Therefore,

$$V^{-1} = \frac{1}{K_1K_3K_4 - k\varepsilon\tau - K_2\gamma\tau}\begin{pmatrix} K_3K_4 - k\varepsilon\tau & K_2\tau & \gamma\tau \\ \gamma K_4 & K_1K_4 & K_1k\varepsilon - \gamma K_2 \\ \gamma\tau & K_1\tau & K_1K_3 \end{pmatrix}$$

Therefore,

$$FV^{-1} = \begin{pmatrix} 0 & \frac{\beta\pi}{d} & \frac{\beta\eta\pi}{d} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \bullet \frac{1}{K_1K_3K_4 - k\varepsilon\tau - K_2\gamma\tau}\begin{pmatrix} K_3K_4 - k\varepsilon\tau & K_2\tau & \gamma\tau \\ \gamma K_4 & K_1K_4 & K_1k\varepsilon - \gamma K_2 \\ \gamma\tau & K_1\tau & K_1K_3 \end{pmatrix}$$

$$\therefore\ FV^{-1} = \frac{\beta\pi}{d\left[K_1K_3K_4 - k\varepsilon\tau - K_2\gamma\tau\right]}\begin{pmatrix} \gamma K_4 + \eta\tau\gamma & K_1K_4 + \eta K_1\tau & K_1k\varepsilon - K_2\gamma + K_1K_3 \\ 0 & 0 & 0 \\ 9 & 0 & 0 \end{pmatrix}$$

We find the eigenvalues of FV^{-1} and then the spectral radius of FV^{-1}, that is, $\rho\left(FV^{-1}\right)$ which is the maximum eigen-value, that is,

$$\left[\frac{\beta\pi\gamma}{d\left[K_1K_3K_4 - k\varepsilon\tau - K_2\gamma\tau\right]} - \lambda\right]\left[\lambda^2 - 0\right] = 0$$

$$\lambda = 0 \quad or \quad \lambda = \frac{\beta\pi\gamma\left(K_4 + \eta\tau\right)}{d\left[K_1K_3K_4 - k\varepsilon\tau - K_2\gamma\tau\right]}$$

Therefore, the basic reproduction number $\mathrm{R}_0 = \dfrac{\beta\pi\gamma\left(K_4 + \eta\tau\right)}{d\left[K_1K_3K_4 - k\varepsilon\tau - K_2\gamma\tau\right]}$

Hence, this theorem

Theorem 3.3: (Theorem 2 in Van den Driessche and Watmough (2002))
Consider the disease transmission model given as (2.1) with f(x) satisfying the necessary conditions. If ξ^0 is DFE of the model, then ξ^0 is locally asymptotically stable if $\mathrm{R}_0 < 1$, but unstable if $\mathrm{R}_0 > 1$.

Proof: From R_0 obtained above we have the proof of the theorem (see Van den Driessche and Watmough (2002))
Epidemiologically, this implies that TB will be eliminated from the population whenever R0 < 1 if the initial size of the sub-population is in the basin of attraction of the DFE, that is,. a small influx of TB infectious individuals into the community will not generate a large TB outbreak, and the disease dies out in time.

3.4 Global Stability of Disease-free Steady (Equilibrium) State
Here we construction a Lyapunov function to prove the global stability of the disease-free steady (Equilibrium) (DFE). We first state this as a theorem.

Theorem 3.4: The disease-free equilibrium (steady state) (DFE), ξ^0, of the model (2.1) is Global Asymptotically stable in D whenever $\mathrm{R}_0 < 1$.

Proof: We shall first construct a Lyapunov function which shall enable us to prove the global stability of the DFE. Recall the Basic Reproduction number which is given as; $\mathrm{R}_0 = \dfrac{\beta\pi\gamma\left(K_4 + \eta\tau\right)}{d\left[K_1K_3K_4 - k\varepsilon\tau - K_3\gamma\tau\right]}$

The eigenvector is given by $\left(\omega_1 \quad \omega_2 \quad \omega_3\right)$.

$$\mathrm{V}^{-1}F = \frac{1}{dK_1(K_3K_4) - k\varepsilon\tau}\begin{bmatrix} 0 & \dfrac{\beta\pi(K_3K_4 - k\varepsilon\tau)}{d} & \dfrac{\beta\eta\pi(K_3K_4 - k\varepsilon\tau)}{d} \\ 0 & \dfrac{\beta\pi(\gamma K_4)}{d} & \dfrac{\beta\pi\eta(\gamma K_4)}{d} \\ 0 & \dfrac{\beta\pi\tau\gamma}{d} & \dfrac{\beta\pi\tau\gamma\eta}{d} \end{bmatrix}$$

$$WV^{-1}F = \frac{\beta\pi}{d\left[K_1(K_3K_4) - k\varepsilon\tau) - K_2\gamma\tau\right]}\left[0 \quad (K_3K_4) - k\varepsilon\tau)\omega_1 + \gamma K_1\omega_2 + \gamma\tau\omega_3 \quad (K_3K_4) - k\varepsilon\tau)\eta\omega_1 + \gamma K_4\eta\omega_2 + \gamma\eta\tau\omega_3\right]$$

$$R_0W = \frac{\beta\gamma\pi(K_4 + \eta\tau)}{d\left[K_1(K_3K_4) - k\varepsilon\tau) - K_3\gamma\tau\right]}\left(\omega_1 \quad \omega_2 \quad \omega_3\right)$$

Since $WV^{-1}F = R_0W$, then, $\omega_1 = 0, \quad \omega_2 = 1 \; and \; \omega_3 = \eta$

$\therefore\ W = \left[0 \quad 1 \quad \eta\right]$

Hence,

$$WV^{-1} = \begin{bmatrix} 0 & 1 & \eta \end{bmatrix} \frac{1}{d\left[K_1(K_3K_4) - k\varepsilon\tau) - K_3\gamma\tau\right]} \begin{bmatrix} K_3K_4 - k\varepsilon\tau & K_2\tau & \gamma\tau \\ \gamma K_4 & K_1K_4 & K_1k\varepsilon - K_2\gamma \\ \gamma\tau & \tau K_1 & K_1K_3 \end{bmatrix}$$

$$= \frac{1}{d\left[K_1(K_3K_4) - k\varepsilon\tau) - K_3\gamma\tau\right]} \begin{bmatrix} \gamma K_4 + \eta\gamma\tau & K_1K_4 + \eta K_1\tau & K_1k\varepsilon - K_2\gamma + K_1K_2\eta \end{bmatrix}$$

Now a suitable lyapunov function would be

$$L = c_1E + c_2I + c_3T \qquad (3.3)$$

Where $c_1 = \frac{\gamma K_4 + \eta\gamma\tau}{K_1(K_3 - k\varepsilon\tau) - K_2\gamma\tau}, c_2 = \frac{K_1K_4 + \eta K_1\tau}{K_1(K_3 - k\varepsilon\tau) - K_2\gamma\tau}, c_3 = \frac{K_1K_2k\varepsilon - K_2}{K_1(K_3 - k\varepsilon\tau) - K_2\gamma\tau}$

Differentiating (3.3) we have

$$\dot{L} = c_1\dot{E} + c_2\dot{I} + c_3\dot{T} \qquad (3.4)$$

where $\dot{L} = \frac{dL}{dt}$, $\dot{E} = \frac{dE}{dt}$, $\dot{I} = \frac{dI}{dt}$ *and* $\dot{T} = \frac{dT}{dt}$

$\frac{dE}{dt} = \beta IS + \beta\eta TS + k_2T - k_1E$, $\frac{dI}{dt} = \gamma E + K\epsilon T - K_3I$, $\frac{dT}{dt} = \tau I - k_4T$

$\dot{L} = \frac{\gamma k_4+\eta\gamma\tau}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau}\left[\beta IS + \beta\eta ST + k_{2T-k_1E}\right] + \frac{k_1k_4+\eta k_1\tau}{k_1(k_3k_4-k\epsilon\tau)-k_2\tau}\left[\gamma E + k\epsilon T - k_3I\right]$

$+ \frac{k_1k\epsilon-k_2\gamma+k_1k_3\eta}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau}\left[\tau I - k_4T\right]$

$\dot{L} = \frac{(\gamma k_4+o\eta\gamma\tau)\beta IS}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau} + \frac{(\gamma k_4+\eta\gamma\tau)\beta\eta ST}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau} + \frac{(\gamma k_4+\eta\gamma\tau)k_2T}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau} - \frac{(\gamma k_4+\eta\gamma\tau)k_1E}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau} + \frac{(k_1k_4+\eta\eta k_1\tau)\gamma E}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau} +$

$\frac{(k_1k_4+\eta k_1\tau)k\epsilon T}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau} - \frac{(k_1k_4+\eta k_1\tau)k_3I}{K_1(K_3K_4-K\epsilon\tau)-K_2\gamma\tau} + \frac{(k_1k\epsilon-k_2\gamma+k_1k_3\eta)\tau I}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau} - \frac{(k_1k\epsilon-k_2\gamma+k_1k_3\eta)k_4T}{K_1(K_3K_4-K\epsilon\tau)-K_2\gamma\tau}$

Collecting like terms we have

$\dot{L} = \frac{[(\gamma k_4+\eta\gamma\tau)\beta S-(k_1k_4+\eta k_1\tau)k_3+(k_1k\epsilon-k_2\gamma+k_1k_3\eta)\tau]I}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau} + \frac{[(k_1k_4+\eta k_1\tau)\gamma-(\gamma k_4+\eta\gamma\tau)k_1]E}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau}$

$+ \frac{[(\gamma k_4+\eta\gamma\tau)\beta\eta ST+(\gamma k_4+\eta\gamma\tau)k_2+(k_1k_4+\eta k_1\tau)k\epsilon-(k_1k\epsilon-k_2\gamma+k_1k_3\eta)k_4]T}{K_1(K_3K_4-K\epsilon\tau)-K_2\tau}$

$\dot{L} \leq \frac{[(\gamma k_4+\eta\gamma\tau)\beta S-(k_1k_4+\eta k_1\tau)k_3+(k_1k\epsilon-k_2\gamma+k_1k_3\eta)\tau]I}{K_1(K_3K_4-K\epsilon\tau)-K_2\gamma\tau}$

$\dot{L} \leq \frac{[\beta S\gamma(k_4+\eta\tau)-k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau]I}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau}$

$= [\frac{\beta\gamma S(k_4+\eta\tau)}{k_1(k_3k_4-k\varepsilon\tau)-k_2\gamma\tau} - \frac{k_1(k_3k_4-k\epsilon\tau\tau)-k_2\gamma\tau}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau}]I$

$= \frac{\beta\gamma S^0(k_4+\eta\tau)I}{k_1(k_3k_4-k\epsilon\tau)-k_2\gamma\tau} - I$ (3.5)

But recall that $S^* = \frac{\pi}{d}$ *and* $R_0 = \frac{\beta\pi\gamma(K_4 + \eta\tau)}{d\left[K_1(K_3K_4 - k\varepsilon\tau) - K_2\gamma\tau\right]}$ (3.6)

Substituting (3.6) in (3.5) we have

$$\dot{L} = \frac{dL}{dt} = \frac{\beta\pi\gamma(K_4 + \eta\tau)I}{d\left[K_1(K_3K_4 - k\varepsilon\tau) - K_2\gamma\tau\right]} - I$$

$$= R_0I - I = (R_0 - 1)I$$

Since all the model parameters and variables are non-negative, it follows $\dot{L} \leq 0$ *for* $R_0 < 1$ with $\dot{L} = 0$ If and only if

E = I = T = O.

Hence, L is a Lyapunov function on D. Thus, using the Lassalle Invariance Principle (La Selle and O. Lefschetz (1976)), $E \to 0, I \to 0, T \to 0$

3.4 Global Asymptotic Stability of the Endemic Equilibrium (EE) of the Model

Consider the system of (2.1). For the sake of convenience, we shall construct lyapunov function to prove the GAS of the treatment free equilibrium, that is, T = 0.

Theorem 3.5: Let X = 0 be an equilibrium point of $X = f(X)$, $f : D \to X$. Let $L : D \to \Re^n$ be a continuously differentiable function such that;

(i) L(X = 0)

(ii) L(X) >0, in D − {O}

(iii) L(X) is "radically unbounded".

(iv) $\dot{L}(X) < 0, \; in \; D - \{0\}$

Then X = 0 is "globally asymptotically stable".

Proof: GOH-Volterra type of lyapunov /quadratic lyapunov

$$L = S - S^{**} - S^{**} \ln\left(\frac{S}{S^{**}}\right) + E - E^{**} - E^{**} \ln\left(\frac{E}{E^{**}}\right) + K_1\left[I - I^{**} - \ln\left(\frac{I}{I^{**}}\right)\right] \tag{3.7}$$

Finding the lyapunov derivative we have

$$\dot{L} = S - S^{**}\frac{\dot{S}}{S} + E^{**} - E^{**}\frac{\dot{E}}{E} + K_1\left(\dot{I} - I^{**}\frac{\dot{I}}{I}\right)$$

$$\dot{L} = \left(1 - \frac{S^{**}}{S}\right)\dot{S} + \left(1 - \frac{E^{**}}{E}\right)\dot{E} + K_1\left(1 - \frac{I^{**}}{I}\right)\dot{I}$$

$$\dot{L} = \left(1 - \frac{S^{**}}{S}\right)[\pi - \beta IS - dS] + \left(1 - \frac{E^{**}}{E}\right)[\beta IS - K_3E] + K_1\left(1 - \frac{I^{**}}{I}\right)[\gamma E - K_3E] \tag{3.8}$$

At steady state, $\pi = \beta I^{**}S^{**} + dS^{**}$, $\beta I^{**}S^{**} = K_3E^{**}$, $\gamma E^{**} = K_3I^{**}$ and substituting this into (3.8), we have

$$\dot{L} = [1 - \tfrac{\dot{S}}{S}][\beta I^{**}S^{**} + dS^{**} - \beta IS - dS] + [1 - \tfrac{E^{**}}{E}][\beta IS - k_3E] + k_1[1 - \tfrac{I^{**}}{I}][\gamma E - k_3I]$$

$$\dot{L} = \beta I^{**}S^{**} + dS^{**} - \beta IS - dS - \beta I^{**}\tfrac{(S^{**})^2}{S} - \tfrac{d(S^{**})^2}{S} + \beta IS^{**} + dS^{**} + \beta IS - k_3E - \beta IS\tfrac{E^{**}}{E} + k_3E^{**} + k_1\gamma E - k_1k_3I - k_1\gamma E\tfrac{I^{**}}{I} - k_1k_3I^{**}$$

$$\dot{L} = 2dS^{**} - dS - \tfrac{d(S^{**})^2}{S} + \beta I^{**}S^{**} - \beta I^{**}\tfrac{(S^{**})^2}{S} + \beta IS^{**} - \tfrac{\beta I^{**}S^{**}E}{E^{**}} - \tfrac{\beta ISE^{**}}{E} + \beta I^{**}S^{**} + \tfrac{k_1k_3I^{**}E}{E^{**}} -$$

$$k_1K_3I - \tfrac{k_1\gamma EI^{**}}{I} + k_1k_3I^{**}$$

Collect terms with ** in the infected classes and equate to zero to solve for the coefficient k_1

$$\dot{L} = \mu S^{**}[2 - \tfrac{S}{S^{**}} - \tfrac{S^{**}}{S}] + \beta I^{**}S^{**} - \beta I^{**}(S^{**}) + \beta IS^{**} - \tfrac{\beta I^{**}S^{**}E}{E^{**}} - \tfrac{\beta ISE^{**}}{E} + \beta I^{**}S^{**} + \tfrac{S^{**}I^{**}E}{E^{**}} +$$

$$\beta S^{**}I - \tfrac{\beta S^{**}E(I^{**})^2E^{**}I}{+}\beta S^{**}I^{**}$$

$$\dot{L} = dS^{**}[2 - \tfrac{S}{S^{**}} - \tfrac{S^{**}}{S}] + 3\beta I^{**}S^{**} - \tfrac{\beta I^{**}(S^{**})^2}{S} - \tfrac{\beta ISE^{**}}{E} - \tfrac{\beta S^{**}E(I^{**})^2}{E^{**}I}$$

$$\dot{L} - dS^{**}[2 - \tfrac{S}{S^{**}} - \tfrac{S^{**}}{S}] + \beta I^{**}S^{**}[3 - \tfrac{S^{**}}{S} - \tfrac{\beta ISE^{**}}{S^{**}I^{**}E} - \tfrac{EI^{**}}{E^{**}I}]$$

$$A.M \to \tfrac{n_1+n_2+n_3}{2}, \; G.M \to \sqrt[3]{n_1n_2n_3}$$

$$\text{Geometric mean (G.M)} \le \text{Arithmetic mean (A.M)} \Rightarrow \text{GM - AM} \le 0$$

$$2 - \tfrac{S}{S^{**}} - \tfrac{S^{**}}{S} \le 0$$

$$3 - \tfrac{S^{**}}{S} - \tfrac{SIE^{**}}{S^{**}I^{**}E} - \tfrac{EI^{**}}{E^{**}I} \le 0$$

Therefore, since $\dot{L}(X) < 0$, *in* $D - \{0\}$, then $\dot{L}(X) < 0$ *for* $R_0 > 0$ with $\dot{L}(X) = 0$ if and only if S =R = 0. Hence, L is a Lyapunov function on D. Thus, using the Lassalle Invariance Principle La Selle and Lefschetz (1976), $S \to 0$, $R \to 0$

IV. NUMERICAL SOLUTION (SIMULATION)

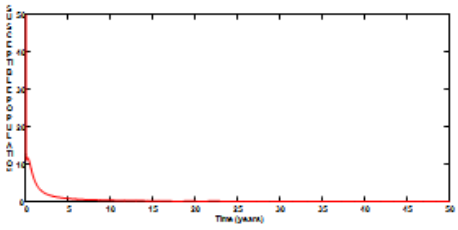
First look at parameter values as follow (as contained in Table 4.1 below)

Table 4.1: Parameter values

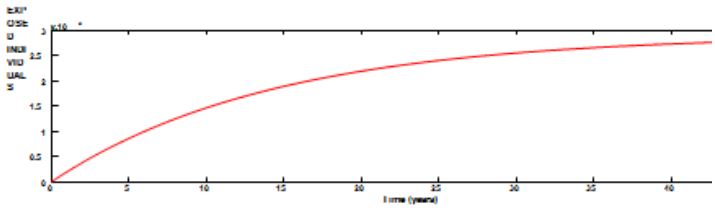
parameter	**Baseline values**	Reference
d	0.02041	UNIAIDS-WHO(2004)
π	$dx10^5$	Song et al(2002)
β	8.557	Okuonghae and Aihie(2008)
γ	0.05	Blower et al (1995)
ψ	1.5	Feng et al (2001)
δ_1	0.365	Borgdorff (2004)
δ_2	0.365	Borgdorff(2004)
τ	0.2	Borgdorff(2004)
	0.05	Assumed
η	0.8	Assumed
k	0.5	Assumed
S	50	Assumed
E	10	Assumed
I	10	Assumed
T	15	Assumed
R	20	Assumed
Total population	105	Assumed

4.1 Graphs of the Simulation

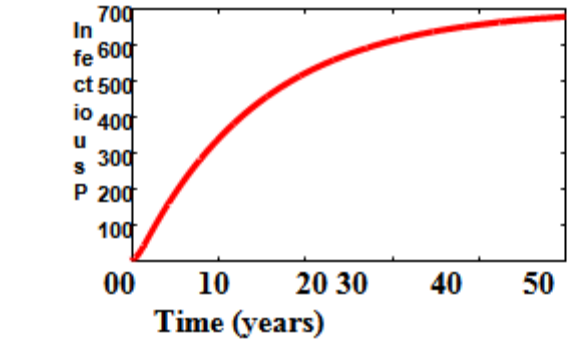
Here we present the graphs of our simulation study which gives a good analysis of the model.



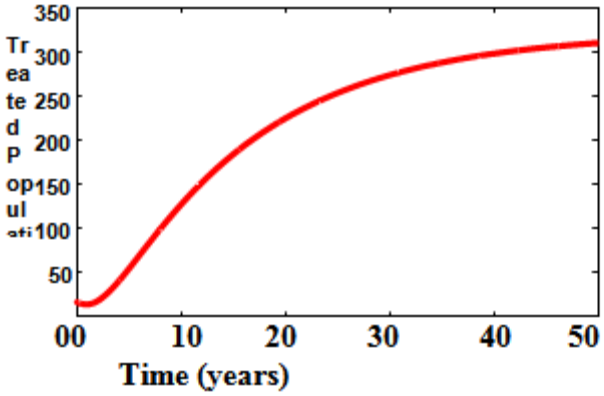
(a) Deterministic simulation of the susceptible class with time



(b) Deterministic simulation of the Exposed class With time



(c) Deterministic simulation of the Infectious class



(d) Deterministic simulation of the Treated class

Figure 4.3: Graph of R(t) when $R_0 < 1$ and when $R_0 > 1$ against time (t)

4.3 Discussion of Results

Figure 4.1 shows the simulations of the deterministic model showing (a) susceptible population which decreases over time as people interact with infected individuals and move to the Exposed class.(b)Exposed population which increases with time when susceptible individuals get the disease but cannot infect it (c)Infected population which increases with time (d)Treated population which increases with respect to time.

Figure 4.2 shows the simulation of the deterministic model of Recovered class which increases over time. Figure 4.3 shows the simulation of deterministic model of the Treated class .We noticed from the graph that as $R0 \leq 1$ the Treated class decreases over time which will eventually die out while when $R0 \geq 1$ the disease persists and becomes endemic.

V. SUMMARY, CONCLUSION AND RECOMMENDATION

In this work we considered the Deterministic Mathematical model of Tuberculosis. The survey result in Okuonghae (2008) and partly reported in Okuonghae and Omosigho (2010) had identified the following key parameters necessary for an effective management of Tuberculosis: awareness rate of TB programmes, associated cost factor for testing and treating TB, use of chronic cough as a marker for identifying a potential TB cases and effective treatment rate. A model incorporating the key parameter was developed. Analysis of the model showed that Tuberculosis cannot be eliminated if the authorities are only concerned with those receiving treatment. A sufficient effective combination of making Tuberculosis medical test and treatment free, high awareness rate, high active cough identification rate to improve notification rate and an effective and high treatment rate will eventually lead to eradication of Tuberculosis.

Also those receiving treatment should be kept in some form of isolation to reduce their infectiousness. In all, this study has shown, from the associated mathematical model, that the prospect of effectively controlling the spread of Tuberculosis in a community and improving case detection is very bright. Emphasis should be shift to preventive strategies by the pragmatic use of Tuberculosis awareness programmes in both the electronic and print media in enlightening the public on the disease, how TB spreads, how TB can be controlled and the Federal government policy on the treatment and management of Tuberculosis in Nigeria. This should include helping the public make use of simple markers for the quick identification of a 'potential' TB case. A good example is the use of chronic cough as a marker. This will not only hasten up the treatment of the TB case, it

also minimizes the likelihood of transmission as the persons infectious period is reduced, more so, when the index case is living amongst susceptible (and even latent) persons.

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