Vol. 2 No. 2, Dec. 2022

FUAM Journal of Pure and Applied Science

Available online at
www.fuamjpas.org.ng

An official Publication of
College of Science
Joseph Sarwuan Tarka University,
Makurdi.

FUAM Journal of Pure and Applied Science
© College of Science, Joseph Sarwuan Tarka University, Makurdi
https://fuamjpas.org.ng/
Vol.2. No. 2. December, 2022

Estimation of Variables and Parameters in an Infection-age-structured Mathematical Model for Tuberculosis Disease Transmission Dynamics

T. T. Ashezua
Department of Mathematics, Joseph Sarwuan Tarka University, Makurdi, Nigeria
Correspondence E-mail: ttashezua@gmail.com

Received: 21/07/2022 **Accepted**: 14/08/2022 **Published online**: 02/09/2022

Abstract

In this paper, a guide on how the variables and parameters of an infection-age-structured mathematical model for tuberculosis disease transmission dynamics were estimated is provided. In the model, both the latent and infectious classes are structured according to time and age-of-infection. The total population size considered in this paper is that of Nigeria. The estimation of these variables and parameters will be found useful when performing sensitivity analysis and numerical simulations. The estimations provided in this paper will serve as a guide in the estimating variables and parameters of other developed epidemiological models of both infectious and non-infectious diseases.

Keywords: Variable and parameter estimation, tuberculosis, mathematical model, Infection-age-structure.

Introduction

Tuberculosis (TB) remains a major public health challenge. It is caused by the bacteria, *mycobacterium tuberculosis* and currently ranks one of the top 10 causes of illness and death. Globally, 10 million people were infected with TB and about 1.4 million died in 2019 according to the World Health Organization (WHO), [1]. In 2020, 86% of the new TB cases occurred in the 30 high TB burden countries. Eight countries accounted for two thirds of the new cases: India, China, Indonesia, Philippians, Pakistan, Nigeria, Bangladesh and South-Africa [Centers for Disease Control and Prevention (CDC), [2]]. Epidemiological models play a vital role in understanding the spread and severity of a pandemic (or epidemic) of an infectious diseases [3]. Epidemiology by definition is the branch of science that explores the spread of diseases, with an ultimate goal of understanding the factors that contribute to their occurrence [4]. During the outbreak of an infectious disease, it is crucial to simulate the potential growth for planning the outbreak control measures in order to provide useful insights into measurable outcome of existing interventions, predictions of subsequent growth and guiding alternative interventions ([5] and [6]). The estimation of variables and parameters are essential for modelling epidemiological models. This is a process used in calculating the model variables and parameters based on a data set [7]. Hence, estimating the exact variables and parameters associated with each constructed epidemiological model will help in guiding health workers and other critical stakeholders in the health sector in taking the right decision aimed at curbing further spread of an infectious disease. Some authors have attempted to estimate variables and parameters associated with their constructed model, (see for example, [7], [8], [9] and [10]). Most epidemiological models when successfully constructed are qualitatively analyzed to obtain conditions that will provide an insight in the prevention and possibly eradication of such disease (s) under study. After computing the basic reproduction number or control (effective) reproduction number as the case may be, sensitivity analysis is often carried out in order to determine parameters of the model that are most sensitive and targeted by way of intervention strategies. Thereafter, many researchers often conduct numerical simulations in order to gain a better insight of such disease(s) under consideration over a specified period of time. Now, the values of these variables and parameters associated with the developed models are most a time lifted from other papers without actually estimating them with respect to the formulated model, (see for example, [11], [12], [13], [14] and [15]). When variables and parameters are properly estimated with respect to a model, they help in taking the right decision especially after conducting numerical simulations in the case of epidemiological models as to whether there will be a potential growth or reduction of a pandemic (or an epidemic) in a population.

In Ashezua [16], qualitative analysis of the model was carried out without showing how the variables and parameters of the model were estimated. In this paper, a careful guide is provided on how the variables and parameters of an infection-age-structured model developed in Ashezua [16] is estimated from the available information obtained from the WHO, CDC, Central Intelligence Agency (CIA) and the works of other authors cited in this paper. This will go a long way in helping most researchers estimate variables and parameters of their constructed models.

Model description

The infection-age-structured model considered in this paper sub-divides the total population size at time t, denoted by $N(t)$, into the following sub-populations of the Vaccinated individuals $(V(t))$;this is the class in which members are vaccinated against TB infection; the second class is the Susceptible individuals $(S(t))$; this is the class in which members are free from TB but are open to infection as they interact with those who have active TB; the third class is the Latent individuals $(L(t))$; this is the class that have contracted TB but are not infectious; the fourth class is the Infectious individuals $(I(t))$; this is the class that have contracted the disease and are infectious. The fifth class is made up of the Treated individuals $(T(t))$; this is the classes that have recovered from both latent and active TB infections due to effective treatment.

The latent $L(t)$ and Infectious class $I(t)$ as earlier stated are structured by the infection age with the density functions $l(t,\tau)$ and $i(t,\tau)$ where t the time parameter and τ is the infection age. T stands for a maximum infection age at which a member of the infectious class $I(t)$ must leave the compartment through death; and so $0 \le \tau \le T$. Similarly, there is a maximum infection age, T at which the latently infected must reach and hence move to the actively infected compartment. The infection-age-structured model formulated in Ashezua [16] is reproduced in this paper as follows:

$$\frac{dS(t)}{dt} = (1-\upsilon)\Lambda - \alpha(1-\theta)S(t)I(t) - \alpha\theta(1-\psi_e)S(t)I(t) + \omega V(t) + \phi T(t) - \mu S(t) \quad (1)$$

$$\frac{dV(t)}{dt} = \upsilon\Lambda - (\mu+\omega)V(t) \quad (2)$$

$$\frac{\partial l(t,\tau)}{\partial t} + \frac{\partial l(t,\tau)}{\partial \tau} + (\mu+\gamma+\rho_2)l(t,\tau) = 0 \quad (3)$$

$$\frac{\partial i(t,\tau)}{\partial t} + \frac{\partial i(t,\tau)}{\partial \tau} + (\mu+\delta+\rho_1)i(t,\tau) = 0 \quad (4)$$

$$\frac{dT(t)}{dt} = \rho_2 L(t) + \rho_1 I(t) - (\mu+\phi)T(t) \quad (5)$$

$$l(t,0) = B_1(t) = \alpha(1-\theta)S(t)I(t) \quad (6)$$

$$i(t,0) = B_2(t) = \alpha\theta(1-\psi_e)S(t)I(t) + \gamma L(t) \quad (7)$$

$$L(t) = \int_0^T l(t,\tau)d\tau \quad (8)$$

$$I(t) = \int_0^T i(t,\tau)d\tau \quad (9)$$

$$S(0) = S_0,\ L(0) = L_0,\ I(0) = I_0,\ N(0) = N_0\ \ V(0) = V_0, \quad (10)$$

$$l(0,\tau) = \phi_1(\tau) \quad (11)$$

$$i(0,\tau) = \phi_2(\tau) \quad (12)$$

The total population size at time, t is represented by:

$$N(t) = S(t) + V(t) + L(t) + I(t) + T(t) \quad (13)$$

The variables and parameters of the infection-age-structured model equations are summarized on Tables 1 and 2 respectively.

Table 1: Variables of the model

S/No.	Variable	Interpretation
1	$V(t)$	Vaccinated individuals at time, t
2	$S(t)$	Susceptible individuals at time, t
3	$L(t)$	Latently infected individuals at time, t
4	$I(t)$	Actively infected individuals at time, t
5	$T(t)$	Treated individuals at time, t

Table 2: Parameters of the model

S/No.	Parameter	Interpretation
1	τ	Age-of-infection
2	T	Maximum infection age
3	α	Infection rate
4	μ	Natural death rate for the population
5	ω	Waning rate of the BCG vaccine
6	θ	Probability of the susceptible individuals acquiring active TB Infection
7	$(1-\theta)$	Probability of the susceptible individuals acquiring latent TB Infection
8	γ	Breakdown rate of individuals from the latent TB to the infectious TB
9	Λ	Recruitment number due to birth
10	$\upsilon\Lambda$	Proportion of the susceptible new births vaccinated against TB infection
11	$(1-\upsilon)\Lambda$	Proportion of the susceptible new births not vaccinated against TB infection
12	$\alpha\theta$	Proportion of the susceptible individuals acquiring active TB infection
13	$\alpha(1-\theta)$	Proportion of the susceptible individuals acquiring latent TB infection
14	υ	Effective vaccination rate
15	δ	Death rate due to TB infection
16	ρ_1	Treatment rate for the actively infected individuals
17	ρ_2	Treatment rate for the latently infected individuals
18	ψ_e	Public health education campaign

Materials and Methods

As a result of the non-availability of primary data, the estimation of variable and parameter values are based on the available information obtained from the (CIA), (CDC), (WHO) and the published works of other authors cited in this work.

Results

Estimation of variables and parameters

A guide is provided below on how the variables and parameters of the infection-age-structured mathematical model for tuberculosis disease transmission dynamics developed in Ashezua [16] are estimated.

The total population of Nigeria

According to the Central Intelligence Agency (CIA), [17], Nigerian population stands at 214,028,302.

Vaccinated children at birth in Nigeria

The total number of new-borns vaccinated at birth in Nigeria from the year 2008 to 2017 is thus summarized in Table 3:

Table 3: Total number of vaccinated (Nigerians) at birth from 2008 to 2017

Year	Total Population	Birth rate per 1000	Number of new births	Percentage of vaccinated new births	Number of vaccinated new birth
2008	146,255,300	37.23	5,445,085	65	3,539,305
2009	149,229,100	36.65	5,469,247	76	4,156,628
2010	152,217,300	36.07	5,490,478	62	3,404,096
2011	155,215,600	35.51	5,511,706	46	2,535,385
2012	170,123,700	39.23	6,673,953	73	4,871,986
2013	174,507,500	38.78	6,767,401	80	5,413,921
2014	177,155,800	38.03	6,737,235	74	4,985,554
2015	181,181,744	39.37	7,133,125	71	5,064,519
2016	185,989,640	38.90	7,234,700	75	5,426,025
2017	190,886,311	36.90	7,043,705	79	5,564,527

Sources: 1. WHO, [1] 2. CIA, [17]

From Table 3, the total number of vaccinated new birth stands at 44,961,946.

TB incidence and prevalence rate

TB incidence and prevalence rate are central to the transmission dynamics of tuberculosis. TB incidence is defined as the estimated number of new pulmonary, smear positive and extra-pulmonary TB cases per unit time and TB prevalence is defined as the proportion of infected individuals at one point in time or over a short period of time [18].

As recorded by WHO [1], tuberculosis incidence rate per 100,000 people in Nigeria was last estimated (measured) at 418 in 2017. Also, the average prevalence rate of TB between the years 2008 to 2017 is given as 380/100,000 which is equivalent to 0.380. This implies that 0.380 of Nigerians are infected with TB. Thus, we have the total number of infected individuals with TB as:

$$L + I = 0.380 \times 214{,}028{,}302 = 81{,}330{,}755. \quad (14)$$

So the total number of individuals infected with *mycobacterium tuberculosis* in Nigeria is 81,330,755.

Total number of latent individuals in Nigeria

The latency period of an individual may be for a life time if the person's immune system has not been compromised with other opportunistic infections like HIV/AIDS. People who are infected with HIV/AIDS are more prone to be infected with tuberculosis when they interact or come into close contact with individuals infected with TB and progress easily to active TB when their immune system is compromised. Generally speaking 90% of individuals infected with TB remain latent [1]. So from equation (14), we see that out of the 81,330,755 infected with TB, 90% remain latent [1] and this is calculated as follows:

$$L = 90\% \times 81{,}330{,}755 = 73{,}197{,}680 \quad (15)$$

Total number of actively infected individuals

Here, note that 90% out of the 75,177,419 infected with TB are latent cases. So the remaining 10% are actively infected with TB and is calculated as follows:

$$I = 10\% \times 81{,}330{,}755 = 8{,}133{,}076 \quad (16)$$

Total number of treated individuals in Nigeria

According to WHO [1], 24% of the individuals infected with TB are successfully treated for TB. Therefore, the total population of Nigeria according to CIA [17] stands at 214,028,302. So 24% of the treated individuals are:

$$T = 24\% \times 214{,}028{,}302 = 51{,}366{,}792 \quad (17)$$

Total number of susceptible individuals in Nigeria

Here, to get the total number of susceptible individuals in Nigeria, the values obtained from Table 3, equations (15), (16) and (17) are substituted into (18). The estimated total population of Nigeria is provided, we therefore, obtain the total number of susceptible individuals in Nigeria as follows:

$$S = N - (V + L + I + T) = 36{,}368{,}808 \quad (18)$$

Natural death rate in Nigeria

The death rate is defined as the inverse of the life expectancy at birth [19]. The life expectancy at birth for Nigeria as at the year 2020 is 60.4 years [17]. The gives the natural death rate for Nigeria to be $\mu = \frac{1}{60.4} = 0.0166$ per year.

The Recruitment Number due to Birth (Λ).

According to CIA [17], the birth rate for Nigeria as at the year 2020 is 34.60 births per year per 1000 people. This gives the birth rate as $\frac{34.60}{1000} yr^{-1} = 0.0346.$ However, the average population of new birth in Nigeria is gotten from:

$$N = \frac{\Lambda}{\mu},$$

where N is the total population size of Nigeria and μ is the natural death rate. Thus the recruitment number of new birth (Λ) in Nigeria is estimated as:

$$\Lambda = N \times \mu = 214{,}028{,}302 \times 0.0346 = 7{,}405{,}379 \quad (19)$$

Waning rate of BCG vaccine

As outlined in the works of Enagi and Ibrahim [20], the BCG vaccine is a vaccine that prevents young children from getting TB. The BCG vaccine is at best 80% effective in preventing tuberculosis for a period of 15 years [1]. Therefore, the 15 years immunity of period of the vaccine is used. This gives $\omega = \frac{1}{15} = 0.067 yr^{-1}$.

Infection rate

On the average, the estimated annual risk of TB infection in Nigeria is put at 1.9% [1]. The prevalence rate of TB in Nigeria as stated earlier is 0.380. The infection rate of TB is thus calculated as follows:

$$\alpha = 0.380 \times 1.9/100 = 0.0000722\ yr^{-1}. \quad (20)$$

Breakdown rate from latent TB to active TB

According to CDC [2], approximately 5% of individuals with latent TB infection will progress to active TB within two year of contracting the disease. From this fact, we compute the breakdown rate from latent TB to active TB as follows:

$$\gamma = \frac{1}{2} yr^{-1} = 0.5 yr^{-1}. \quad (21)$$

Proportion of the susceptible acquiring active TB infection

As noted in WHO [1], 90% of individuals have latent TB and the remaining 10% have active TB. So we get the proportion of those acquiring active TB has follows

$$\theta = 0.1 yr^{-1}.$$

Varying parameters $(\tau, \upsilon, \psi_e, \rho_1, \rho_2)$.

The control parameters $(\tau, \upsilon, \psi_e, \rho_1, \rho_2)$ which represents the age-of-infection, effective vaccination rate, public health education campaign, treatment rate for the actively infected and the latently infected individuals respectively are varied to see their impact in the transmission dynamics of TB.

The summary of the estimation of variables and parameters for the model (1) - (5) are presented in Tables 4 and 5.

Table 4: Values for population-dependent parameters of the model

S/NO	Variable/Parameter	Value	Source
1	S	36,215,472	Estimated
2	V	44,961,946	Estimated
3	L	73,197,680	Estimated
4	I	73,197,680	Estimated
5	T	51,366,792	Estimated
6	N	214,028,302	Estimated
7	μ	0.0346 yr^{-1}	Estimated
8	Λ	3,873,912	Estimated

Table 5: Values for population-independent parameters of the model

S/NO	Parameter	Value	Source
1	α	0.0000722 yr^{-1}	Estimated
2	ω	0.067 yr^{-1}	Estimated
3	γ	0.5 yr^{-1}	Estimated
4	θ	0.1 yr^{-1}	Estimated
5	$\rho_1, \rho_2, \tau, \upsilon, \psi_e$	(0-1) yr^{-1}	Assumed

Conclusion

In this paper, a careful guide on how the variables and parameters are estimated for an infection-age-structured model for tuberculosis disease dynamics developed by Ashezua [16] is shown. This guide will help researchers estimate variables and parameters of epidemiological models constructed to study the transmission dynamics, prevention and control of both infectious and non-infectious diseases.

Declaration of conflicting interests

The author declared no potential conflicts of interest

Acknowledgement:

I sincerely appreciate the Tertiary Education Trust Fund (Tetfund) for making available grants under the Institution Based Research (IBR) grant which enabled me to carry out this research work. My special appreciation also goes to the Department of Mathematics, Joseph Sarwuan Tarka University, Makurdi, Nigeria for providing a conducive research environment.

References

[1] World Health Organization, 2020. Global tuberculosis report fact sheet, stop TB department, Geneva, Switzerland. https://www.who.int/teams/global.pdf. *Accessed 18th March, 2021*. Accessed 18th March, 2021.

[2] Centres for Disease Control and Prevention, 2020. Tuberculosis: saving lives and protecting people. Retrieved from https://www.cdc.gov/

[3] Thompson, R. N. 2020. Epidemiological models are important tools for guiding COVID19 interventions. *Journal of BioMed Central*, 18:152.

[4] Diekmann, O. and Heesterbeek, J. A. P. 2000. Mathematical epidemiology of infectious diseases. John Wiley and Sons Ltd.

[5] Viboud, C., Sun, K., Gaffey, R., Ajelli, M., Fumanelli, L., Merler, S., Zhang, Q., Chowell, G., Simonsen, L., Vespignani, A., et al. 2018. The RAPIDD ebola forecasting challenge: synthesis and lessons learnt. *Journal of Epidemics*, 22: 13-21.

[6] Kucharski, A. J., Camacho, A., Checchi, F., Waldman, R., Grais, R. F., Cabrol, J. C., Briand, S., Baguelin, M., Flasche, S., Funk, S., et al. 2015. Evaluation of the benefits and risks of introducing ebola community care centers, Sierra Leone. Journal of *Emerging Infectious Diseases,* 21:393-399.

[7] Canto, B., Coll, C. and Sanchez, E. 2017. Estimation of parameters in a structured SIR model. *Advances in Difference Equations,* 33. https://doi10.1186/s13662-017-1078-5.

[8] Omale, D., Atokolo, W. and Akpa, M. 2019. Mathematical modelling of the transmission dynamics of tuberculosis and its control (A case study of Ika General Hospital, Ankpa, Kogi State). *IOSR Journal of Mathematics,* 15(16) : 37 - 57.

[9] Gopal, K., Lee, L. S. and Seow, H. V. 2021. Parameter estimation of compartmental epidemiological model using Harmony Search Algorithm and its variants. *Journal of Applied Sciences*, 11: 1138, https://10.3390/app11031138.

[10] Zhang, H., Zhao, X., Yin, K., Yan, Y., Qian, W., Chen, B. and Fang, X. 2021. Dynamic estimation of epidemiological parameters of COVID-19 outbreak and effects of interventions on its spread. *Journal of Public Health Research,* 10:1906.

[11] Usman, S. and Adamu, I. I. 2017. Modelling the transmission dynamics of the Monkeypox virus infection with treatment and vaccination interventions. *Journal of Applied Mathematics and Physics,* 5: 2335-2353, https://doi.org/10.4236/jamp.2017.512191.

[12] Liu, S., Bi, Y. and Liu, Y. 2020. Modelling and dynamic analysis of tuberculosis in mainland China from 1998 to 2017: the effects of DOTS strategy and further control. *Journal of Theoretical Biology and Medical Modelling,* 17(6), https://doi.org/10.1186/s/2976-020-00124-9.

[13] Kabunga, S. K., Goufo, E. F. D. and Tuong, V. H. 2020. Analysis and simulation of a mathematical model of tuberculosis transmission in Democratic Republic of the Congo. *Advances in Difference Equations,* 642. https://doi.org/10.1186/s13662-020-03091-0.

[14] Mengistu, A. K. and Witbooi, P. J. 2022. Tuberculosis in Ethiopia: Optimal intervention strategies and cost-effectiveness analysis. *Axioms,* 11, 343, https://doi.org/10.3390/axioms11070343.

[15] Goudiaby, M. S., Gning, L. D., Diagne, M. L., Dia, B. M., Rwezaura, H. and Tchuenche, J. M. 2022. Optimal control analysis of a COVID-19 and tuberculosis co-dynamics model. *Informatics in Medicine Unlocked,* 28: 100849, https://doi.org/10.1016/j.imu.2022.100849.

[16] Ashezua, T. T. 2021. Mathematical Analysis of an infection-age-structured model for tuberculosis disease dynamics incorporating control measures. *FUAM Journal of Pure and Applied Science,* 1(1), 52-70.

[17] Central Intelligence Agency 2020. World fact book. Retrieved from www.cia.gov/library/publication/the-world-factbook/geos/ni.html.

[18] Ozcaglar, C. Shabbeer, A. Vandenberg, S. L. Yener, B. and Bennett, K. P. 2012. Epidemiological models of mycobacterium tuberculosis complex infections. *Mathematical Biosciences*, 236, 77-96.

[19] Moualeu, D. P. Roblitz, S. Ehrig, R. and Deuflhard, P. 2013. Parameter Identification for a tuberculosis model in Cameroon. *ZIB-report*, 13-72.

[20] Enagi, A. I. and Ibrahim, M. O. 2011. Preventing mother to child transmission of tuberculosis using Bacillus Calmette-Guerin vaccine: A deterministic modelling approach. *Research Journal of Mathematics and Statistics,* 3(2), 67-71.

Cite this article

Ashezua T.T. (2022). Estimation of Variables and Parameters in an Infection-age-structured Mathematical Model for Tuberculosis Disease Transmission Dynamics. FUAM Journal of Pure and Applied Science, **2**(**2**):4-10