# EPIDEMIOLOGICAL BENEFITS OF MORE EFFECTIVE TUBERCULOSIS VACCINES, DRUGS, AND DIAGNOSTICS
## TECHNICAL DOCUMENTATION

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# I. DOCUMENT OVERVIEW:

This document constitutes the technical documentation of our tuberculosis (TB) model. Included is a schematic of the full model with interventions (Figure 1), a schematic of the model including only TB natural history and current treatment (Figure 2), a graphical representation of the diagnostics model, mathematical equations and narrative description of the modeled dynamics, and the parameter descriptions (Table 1). In an effort to explore the relative impact of the introduction of several novel interventions on the global burden of tuberculosis between the present and 2050, this model of the disease natural history and epidemiological dynamics was developed with an emphasis on capturing the specific impact by age, disease-stage, and disease-form. The model takes the form of a system of differential equations. The model was programmed in Berkeley Madonna.

[Figure 1 extracted for submission]

# II. NARRATIVE DESCRIPTION OF MODEL:

### NATURAL HISTORY AND CURRENT TREATMENT:

Our model is an extension of models reported by Dye and colleagues (1, 2) and is informed by other approaches to modeling TB dynamics at the population level (3-14). The natural history in this age-structured model is described by the general epidemiological states of 1) susceptible, 2) latent infection, 3) early disease, 4) treated early disease, 5) disease, 6) treated disease, and 7) recovered (Figure 1). The population size is held stationary to allow the disentanglement of epidemiological from demographic effects in TB dynamics and the impact of novel interventions. The population is divided into distinct age groups where the flow from one age group to the next follows an exponential distribution.

All individuals are born susceptible and remain such until infected, which occurs at a rate of $\lambda(t)$, the force of infection. Newly infected individuals proceed to one of two latent states, slow or fast, which is determined by the proportion $p_F$. This proportion differs between children and adults. The parsing of the latent infection state into fast and slow categories captures the epidemiological observation that at the level of a population, a proportion of the latently infected individuals can remain infected for an extended period of time without proceeding to clinical disease, whereas others, here modeled as latent-fast individuals, proceed quickly to clinical disease. In addition, latent-slow infected individuals may at some stage of their latent infection be re-exposed to the infection and subsequently proceed to latent-fast infection; however, their prior exposure to TB reduces the force of infection acting upon them. The reduction in susceptibility to reinfection is parameterized by $q$, which denotes the fractional reduction in susceptibility due to prior exposure. Latently infected individuals remain in this state until they proceed to early disease, which occurs at a rate of $\omega_{L_F}$ and $\omega_{L_S}$, for latent-fast and latent-slow infected individuals respectively.

As a means to consider the potential effects of novel diagnostics, we introduce the epidemiological state of early disease, split into two categories by speed of disease progression. Because early disease is not necessarily a clinically defined state, rates for progression through this state are determined by considering the expected overall rates of movement from latent infection to active disease states, and selecting early disease parameters that preserve these rates. Individuals entering the first disease state, early disease, enter either as fast or slow early disease depending upon the preceding latent state. Individuals leave the early disease state by either tuberculosis-related mortality ($\vartheta$), spontaneous recovery ($\nu$), progression to TB disease ($\Pi$), or detection and treatment of early disease ($\chi * z$ where $\chi$ is the treatment rate and $z$ is the

proportion of treatments that are effective). These outgoing fluxes are modeled as separate rates for fast and slow early disease.

Individuals who are diagnosed and treated while in the early disease state proceed to the treated early disease state. There are two forms, fast and slow, and individuals proceeding from the fast early disease state enter the fast treated early disease state; individuals proceeding from the slow early disease state enter the slow treated early disease state. Individuals within these states may leave by either tuberculosis-related mortality ($\vartheta$), spontaneous recovery ($\nu$), successful completion of treatment ($\psi$), or re-infection ($\lambda(1-q)$). These movements out of the treated early disease states are modeled as separate rates for fast and slow states respectively.

The TB disease state is split into three clinically and epidemiologically relevant forms: smear-positive pulmonary, smear-negative pulmonary, and non-pulmonary disease. Only the pulmonary disease types are considered infectious for others, though to varying degrees. Proportions specific to the early disease category determine which type of disease a progressing individual will develop. Individuals with TB disease leave that state by either tuberculosis-related mortality ($\vartheta$), spontaneous recovery ($\nu$), or detection and effective treatment of disease ($\chi * z$). These movements out of the disease states are modeled as rates and are specific to each form of the disease.

There are also three forms of the treated disease state, which correspond to the three TB disease types. Movement from the disease to the treated disease state occurs only between equivalent forms of disease (for example, only between smear-positive disease and treated smear-positive disease). Individuals within the treated disease state may leave by either tuberculosis-related mortality ($\vartheta$), spontaneous recovery ($\nu$), successful completion of treatment ($\psi$), or through re-infection ($\lambda(1-q)$). These movements out of the treated disease state are modeled as form-specific rates.

All individuals who have experienced spontaneous recovery or have successfully completed treatment enter the recovered state. Apart from natural mortality, the only movement out of the recovered state is through re-infection, which proceeds at a rate of $\lambda(1-q)$.

## Force Of Infection

The force of infection ($\lambda(t)$) is a function of time, and is determined by the respiratory contact rate within a population ($\eta$), the probability of transmission per respiratory contact ($u$), relative infectivity of TB diseased persons with respect to the infectiousness of smear-positive pulmonary TB diseased persons ($h$), and TB disease and early disease prevalence. In this model, the respiratory contact rate is assumed to be region dependent and the mixing in the population is assumed to be random. The respiratory contact rate was one of two parameters obtained by fitting the model.

## Demographics And Disease Mortality

We model 14 5-year age groups, of which the first 3 are considered to be children (ages 1-15). The life expectancy ($Life_{Exp}$) is assumed to be 70 years, consistent with that of many developing and TB high burden countries (HBCs), such as China and India, where a large TB disease burden is present (2). Accordingly the annual natural mortality rate of all causes excluding TB ($\mu = 1/Life_{Exp}$) is 0.014 per year. Persons in early disease stages of TB experience no additional mortality due to TB. Smear-positive persons

of all ages experience an annual mortality rate due to TB of 0.25 per year (2); smear-negative persons of all ages experience an annual mortality rate due to TB of 0.10 per year (2); non-pulmonary persons of all ages experience an annual mortality rate due to TB of 0.10 per year (2). These values are broadly consistent with those found in the literature (1, 15-26), but are adjusted to maintain the relationship between TB cases and TB mortality (2) within this model. In all disease states, persons remain subject to natural mortality as well as TB-related mortality. These TB mortality rates apply to both vaccinated and unvaccinated persons.

### LATENCY

Of children infected, 5% enter fast breakdown , as do 15% of newly infected adults (1, 27-36). In contrast, of adults who are HIV+, 67% enter fast breakdown (37-39). We assume that the annual progression rate from the latent-fast to TB disease is 0.9 per year (2) and from the latent-slow to TB disease is 0.00075 per year. The latter value corresponds to a 5% lifetime risk of developing TB disease; values are broadly representative of those found in the literature (3-5, 26, 34, 40-44). Because our model includes an early disease state to examine the utility of diagnostics and treatment at early disease, we have adjusted these disease progression rates to account for the progression from latency to early disease, and early disease to TB disease, while still preserving the overall expected rate structure. Thus the progression rate from latency to early disease for fast progressors is 1.64 per year, while the annual progression rate from early disease to TB disease is 2.0 per year (assumes an early disease stage of 6 months; not an unreasonable assumption considering the outcome of a household study (45)). The progression rate from latency to early disease for slow progressors is 0.00075 while the annual progression rate from early disease to TB disease is also 2.0 per year. Note that the inclusion of early disease has virtually no impact on the rate of progression for the slow progressors since their rate of progression is very small. Persons who have been previously infected with tuberculosis experience a 65% reduction in susceptibility to reinfection (2, 34, 46).

### ACTIVE TB DISEASE

Upon progressing to active disease from either latent-slow or latent-fast, 10% of children (25, 47) and 50% of adults express smear-positive pulmonary tuberculosis. Similarly, 65% of children and 40% of adults express smear-negative tuberculosis and 25% of children (47-50) and 10% of adults express non-pulmonary tuberculosis. These values are representative of those used in the TB modeling literature (2, 8, 25, 40, 44, 51, 52). In all cases, the proportions of persons expressing each disease state are independent of latency state. Smear-positive persons are infectious, and smear-negative persons are 25% as infectious as smear-positive persons (53-56). Persons with early disease are assumed to be as infectious as smear-negative persons, but persons with non-pulmonary tuberculosis are assumed not to be infectious.

### RECOVERY

Once experiencing TB disease, persons can recover without medical intervention. Persons in smear-positive, smear-negative and non-pulmonary disease categories naturally recover at a rate of 0.1 per year (2). These spontaneous recovery rates apply to both vaccinated and unvaccinated persons and are broadly consistent with those found in the literature (1, 21-23, 57, 58), but are adjusted to maintain the relationship between TB cases and TB mortality (2). We assume that persons with early TB disease experience no spontaneous TB recovery.

## MODELING NOVEL INTERVENTIONS

### VACCINATION:

To incorporate potential novel vaccines into TB natural history dynamics, TB vaccination is assumed to generate distinct and separate TB natural histories for the proportion of infants successfully vaccinated ( $f_{Vac}$), as compared to those not receiving the vaccination (Figure 1). The vaccination design is based on one administered to infants and then boosted by an adolescent vaccination to extend the duration of the efficacy of the vaccine. In principle, all TB rate and proportion parameters can have distinct values for the vaccinated compared to the non-vaccinated population.

Mass vaccination of susceptible individuals with pre-exposure vaccine occurs at a rate of $\rho_S$ . After vaccination, the vaccine efficacy wanes and persons move to the waning susceptible category at a rate of $\gamma$ . Once there, persons may receive a vaccine boost to return to the vaccinated state at a rate of $\rho_{WS}$ , or they may become infected with TB at a rate of $\lambda(t)$, at which point they proceed to follow the TB natural history of non-vaccinated persons. Alternatively, vaccinated persons may become infected with TB before the vaccine wanes. If infected, vaccinated individuals proceed through disease stages that are analogous to those for non-vaccinated persons (described above).

In addition, we have included in the model the option to include the potential effects of a post-exposure vaccine. We assume that persons who are latent infected, either fast or slow, can receive a vaccine at a rate of $\rho_{PExp}$ that effectively moves them into the vaccinated latent fast or slow categories respectively at proportions defined by $a_{L_{\{F,S\}} \to VL_{\{F,S\}}}$ . Once in either vaccinated latent slow or fast, persons who received effective post-exposure vaccine experience the same vaccinated natural history as those who received a pre-exposure vaccine and became infected.

Vaccination simultaneously introduces several potential biological effects. First, it reduces the fraction of TB infected persons who are fast progressors to TB disease ( $p_F$ ) by $(1-VE_P)$, where $VE_P$ is the vaccine efficacy against this type of TB disease progression. $VE_P$ may take different values for adults and children. The second vaccine effect is to reduce the infectivity of those vaccinated persons who become infected and develop pulmonary TB disease by the fraction $(1-VE_I)$. The third vaccine effect is to reduce the rate of progression to TB disease of those who are latent-slow infected by the fraction $\left(1-VE_{P_{VLS}}\right)$. Lastly, vaccine immunity is assumed to wane with time at a rate of $\gamma = 1/D_{vp}$ where $D_{vp}$ is the duration of vaccine protection. We assume that the waning of vaccine immunity follows an exponential distribution. The nomenclature used to define these vaccine efficacies is based on the conventions introduced by Halloran and colleagues (59).

To consider the impact of novel vaccines administered to infants, we modeled the implementation of vaccine in 2015. We model two scenarios for the vaccine. We model a basic pre-exposure vaccine, a conservative scenario, where the vaccine has the properties of $VE_P = 60\%$, $VE_I = 0\%$, $VE_{P_{VLS}} = 0\%$, $f_{Vac} = 1$ and $D_{vp} = 33$ years. We also model a pre-exposure vaccine with additional effects, an optimistic scenario where we assume that the vaccine has the properties of $VE_P = 60\%$, $VE_I = 50\%$, $VE_{P_{VLS}} = 50\%$, $f_{Vac} = 1$ and $D_{vp} = 33$ years.

Additionally, we used explored the effectiveness of a short mass vaccination campaign instituted at 2015 that lasts two to three years, wherein susceptible persons of all ages receive the vaccine, and only new susceptible infants receive the vaccine in subsequent years.

Post exposure vaccine is parameterized such that latent fast infected persons receiving post exposure vaccine move to vaccinated latent fast, while those latent slow infected persons receiving post exposure vaccine move to vaccinated latent slow with no cross-over between categories ($a_{L_F \to VL_F} = 1; a_{L_S \to VL_S} = 1$).

To explore the synergy between vaccination strategies, we employ the following equation:

$Synergy = \frac{I_1 * I_2}{I_{1+2} * I_{none}}$, where $I_1$ = annual incidence of active TB disease with only Intervention 1; $I_2$ = annual incidence of active TB disease with only Intervention 2; $I_{1+2}$ = annual incidence of active TB disease with both Interventions 1 and 2; and $I_{none}$ = annual incidence of active TB disease with neither intervention. When this equation is computed, a synergy of value greater than 1 indicates at least some synergy between vaccination strategies. The synergy equation can be solved by assuming that when vaccine strategies are independent, $\frac{I_1}{I_{none}} * \frac{I_2}{I_{none}} = \frac{I_{1+2}}{I_{none}}$.

The synergy was computed between mass vaccination at all ages (including infants) and mass vaccination at all ages with a post-exposure vaccine. Because our model does not include a separate natural history for those receiving post-exposure vaccine, we are unable to separate out the effects of $VE_P$ for post-exposure versus vaccination of susceptibles. Therefore a conservative estimate of synergy between the two strategies is computed using $VE_P = 60\%$, $VE_I = 0\%$ and $VE_{P_{VLS}} = 0\%$ ($I_1$); $VE_P = 0\%$, $VE_I = 0\%$ and $VE_{P_{VLS}} = 50\%$ ($I_2$); and $VE_P = 60\%$, $VE_I = 0\%$ and $VE_{P_{VLS}} = 50\%$ ($I_{1+2}$).

DIAGNOSTICS:

The effect of novel diagnostic technologies (60) is incorporated in the model through improvement in the case detection rate (CDR) and reduction of the average duration of infectiousness (ADI), which are assumed to be nearly independent variables.

To dissociate the ADI from the CDR, disease is modeled as occurring in four stages (each of which is represented in the model by a compartment) of different time lengths (Figure 2).

The rate of transition $rate_S^{j \to j+1}$ from one stage (*j*) to the next (*j+1*) is a function of the total duration of infectiousness and of the proportion of the total time of infectiousness that, on average, individuals spend in that stage. The expected shortening of the duration of infectiousness of the novel diagnostics was modeled by adjusting the duration of two middle compartments.

Diagnosis, recovery and death occur, at rates $\tilde{\chi}_S$, $\tilde{\nu}_S$ and $\tilde{\theta}_S$, when individuals reach the fourth stage (compartment) of disease. Individuals spend, on average, 4% of the total time of infectiousness ($1/rate_S^{4\to} = 0.04 ADI_S$), in the fourth and final compartment. Thus, the average duration of infectiousness is nearly independent of the case detection rate.

Following the introduction of new diagnostics, the reduction of the duration of infectiousness is obtained by bypassing stage 2 and 3 (i.e. "disconnecting" the first from the second compartment and the third from the fourth compartment and "connecting" the first to the fourth compartment), while individuals in stage 2 and 3 are progressively diagnosed and treated (i.e. moved to the "treated" compartment). To avoid residual modeling effects from this transformation, such as a sudden temporary increase in mortality and recovery, all individuals in stage 2 and 3 are treated; none of them immediately dies or recovers.

[Figure 2 extracted for submission]

Four main approaches to improved diagnostics are being developed. The first would likely not improve diagnosis in much of the developing world, thus we do not model its effect. We model the effects of diagnostic approaches 2 through 4.

1) Mycobacteria Growth Indicator Tube (MGIT) culture. This diagnostic technology is administered at the level of a referral hospital or laboratory. Currently, the use of culture for case detection is very limited in the developing world, particularly all 22 high burden countries (see Section V). For example, out of nearly 2 million reported cases in the South East Asia Region in 2005, we estimate that <1000 cases were diagnosed using culture. Globally, the total number of diagnoses by culture is perhaps just over 100,000, many of which may have received treatment before culture confirmation. These estimates were obtained by calculating the difference between smear-positive diagnoses and all bacteria-positive cases found in public reporting systems and reported to the World Health Organization (WHO) (excluding private sector) (61). Most of the current culture use is for laboratory confirmation of infection or drug susceptibility testing (DST), and is concentrated regionally in Europe including Eastern Europe. Therefore, it is reasonable to assume that the introduction of MGIT culture without accompanying changes in infrastructure is not likely to lead to improvement in case detection in the developing world.

2) LED-fluorescence microscopy. This diagnostic technology is administered at the level of microscopy laboratory. It is expected that this technology will lead to a 10% (8-12%) improvement in the case detection rate of smear-positive cases relative to Ziehl Neelsen microscopy (62). Relative to an average duration between onset of illness and diagnosis of 24 months, achieve a one-month reduction (4%) in average duration of smear-positive cases relative to Ziehl Neelsen microscopy. However, due to absence of definitive evidence and mechanism of action, we assume that this tool has no sensitivity to both smear-negative and non-pulmonary forms of TB disease.

3) Nucleic Acid Amplification Test (NAAT) technologies including loop-mediated isothermal amplification (LAMP) (also known as Eiken NAAT), and Cepheid, which incorporates an integrated platform for specimen processing, real time PCR, and probing for rifampin resistance. These diagnostic technologies are administered at the level of a microscopy laboratory and are expected to yield sensitivities of 95% for smear-positive (compared to 85% for existing microscopy), 60% for smear-negative, and 50% for non-pulmonary (62). It is not clear whether these technologies will be administered as replacements or additions to existent technologies. NAAT is expected to reduce a 24-month duration from onset of disease to detection by three months (12.5%) to 21 months for all three types of active TB cases.

4) Dipstick for Antigen (Ag) or Antibody (Ab). These diagnostic technologies are administered at the level of the health post and are expected to yield sensitivities of 85% for smear-positive, 60% for smear-negative, and 60% for non-pulmonary (62). It is not clear whether these technologies will be administered as replacements or additions to existent technologies. The Dipstick is expected to reduce a 24-month duration to detection by four months (16.5%) to 20 months for all three types of TB cases.

A similar relative shortening is expected for other baseline durations between onset of illness and detection. In the South-East Asia region, the relative shortenings for the novel diagnostics were computed based on 15.4 months average duration from onset of disease to detection in smear-positive cases and 23.0

months in smear-negative cases (63). We varied the proportion of reduction in average duration of infectiousness from 0 to 1.0 in a sensitivity analysis.

TREATMENT:

When applied, treatment is provided at a rate that depends on TB disease type and is derived from the case detection rates[1] in each region using the WHO data and estimates (61). The treatment success proportion ($z$) is also derived from the WHO data for each region. Persons who are successfully treated no longer experience TB-related mortality, and are not infectious; this is true for both vaccinated and unvaccinated persons. Persons move from treatment to the recovered state at an annual rate of 2.0 per year, reflecting the typical 6 month course of treatment under the directly observed treatment short-course (DOTS). The treatment-related rates and proportions in the model are assumed equivalent for vaccinated and unvaccinated persons.

Novel drug regimens improve on current regimens by first reducing the duration of treatment and second being efficacious against drug-resistant TB disease. We provide two estimates for the potential impact of each novel regimen; the first is an optimistic estimate for the impact while the second is a conservative estimate. These two estimates bracket the likely impact of the novel regimens.

For the optimistic estimate, we assume that the novel regimens would reduce treatment failure due to the WHO categories of "default", "transferred" from the site of treatment, "death" during treatment, and loss to follow-up of those listed as "not evaluated". The increase in treatment success proportion ($z$) reflects the shorter duration of treatment according to

$$\delta_z = \left( \frac{L_{Cur} - L_{Nov}}{L_{Cur}} \right) (\text{Default + Transferred + Death during treatment + Not evaluated}),$$

where $L_{Cur}$ is the duration of treatment of the current typical regimen and $L_{Nov}$ is the duration of treatment of the novel regimen.

For the conservative estimate, we assume that the novel regimens would reduce treatment failure due only to WHO categories of "default" and "transferred" from the site of treatment. Therefore, the increase in treatment success proportion is given by

$$\delta_z = \left( \frac{L_{Cur} - L_{Nov}}{L_{Cur}} \right) (\text{Default + Transferred}).$$

Moreover, a novel regimen with an efficacy against drug-resistant TB disease would further increase the treatment success proportion by reducing the WHO categories of "treatment failure" and "death" during treatment (the proportion of death not reduced by the shorter duration of the regimen) by the efficacy of the novel regimen against drug-resistant TB ($RE_{Nov}$) according to

$$\delta_z = RE_{Nov} (\text{Treatment Failure + Death on treatment}).$$

[1] $$\textit{Treatment rate} = \frac{\textit{case detection rate}\,(\textit{tuberculosis related mortality rate} + \textit{spontaneous recovery rate})}{1 - \textit{case detection rate}}$$

This assumption for the impact of the effect of efficacy against drug-resistant TB should be considered to be on the optimistic side. An alternative assumption for the effect of this efficacy is to assume that the treatment success proportion would simply increase by 4.3%, which is the estimate for the fraction of multi-drug resistant TB (MDR) and extensively drug-resistant TB (XDR) among all TB incident cases (64).

We model the impact of three novel drug regimens:

1) Moxifloxacin with a 4-month drug regimen but no efficacy against MDR or XDR TB ($RE_{Nov} = 0\%$).
2) Novel Regimen 2 consists of a 2-month regimen and efficacy against MDR and XDR TB of $RE_{Nov} = 90\%$. This regimen consists of three drugs, two of which will be developed by the TB Alliance.
3) Novel Regimen 3 consists of a 10-day regimen and $RE_{Nov} = 90\%$. It also consists of three drugs with at least one developed by the TB Alliance.

## FITTING THE MODEL

The respiratory contact rate was one of two parameters obtained by fitting the model. is value is chosen by fitting the incidence of smear-positive disease in each region respectively. Using the Downhill Simplex method(65), both the contact rate and the case detection rate were permitted to vary while fitting the model to the regional annual incidence rates of pulmonary smear-positive disease and tuberculosis-related mortality reported by the WHO for 2006 (2). The case detection rate was permitted to vary because of suspected under-reporting of treatment among cases. The fitted incidence was assumed to capture the current BCG vaccination, treatment, and diagnostics. The novel intervention effects were included as improvements on the current status.

# III. MODEL EQUATIONS:

$$\mu_{TBTotal} = \sum_{i'=1,..,n}\left(\vartheta_{D_{EDF}} D_{EDF}[i'] + \vartheta_{D_{EDS}} D_{EDS}[i'] + \vartheta_{D_{SP}} D_{SP}[i'] + \vartheta_{D_{SN}} D_{SN}[i'] + \vartheta_{D_{NP}} D_{NP}[i']\right)$$
$$+ \sum_{i'=1,..,n}\left(\vartheta_{T_{EDF}} T_{EDF}[i'] + \vartheta_{T_{EDS}} T_{EDS}[i'] + \vartheta_{T_{SP}} T_{SP}[i'] + \vartheta_{T_{SN}} T_{SN}[i'] + \vartheta_{T_{NP}} T_{NP}[i']\right)$$
$$+ \sum_{i'=1,..,n}\left(\vartheta_{VD_{EDF}} VD_{EDF}[i'] + \vartheta_{VD_{EDS}} VD_{EDS}[i'] + \vartheta_{VD_{SP}} VD_{SP}[i'] + \vartheta_{VD_{SN}} VD_{SN}[i'] + \vartheta_{VD_{NP}} VD_{NP}[i']\right)$$
$$+ \sum_{i'=1,..,n}\left(\vartheta_{VT_{EDF}} VT_{EDF}[i'] + \vartheta_{VT_{EDS}} VT_{EDS}[i'] + \vartheta_{VT_{SP}} VT_{SP}[i'] + \vartheta_{VT_{SN}} VT_{SN}[i'] + \vartheta_{VT_{NP}} VT_{NP}[i']\right)$$

## A: UNVACCINATED BRANCH OF THE MODEL

### A.1: UNINFECTED AND SUSCEPTIBLE

$$\frac{d}{dt}S[i=1] = (1-f_{Vac})\zeta N[n] + (1-f_{Vac})\mu_{TBTotal} - \alpha S[1] - \rho_S S[1] - \lambda S[1]$$

$$\frac{d}{dt}S[i=2,...,k-1] = \alpha S[i-1] - \alpha S[i] - \lambda S[i] - \rho_S S[i]$$

$$\frac{d}{dt}S[i=k,...,n] = \alpha S[i-1] - \alpha S[i] - \lambda S[i] - \rho_S S[i]$$

### A.2: LATENT WITH FAST PROGRESSION TO TB DISEASE

$$\frac{d}{dt}L_F[1] = -\alpha L_F[1] + p_F^{Ch}\lambda(S[1] + WS[1]) + p_F^{Ch}(1-q)\lambda L_S[1] + p_F^{Ch}(1-q)\lambda T_{EDF}[1] + p_F^{Ch}(1-q)\lambda T_{EDS}[1]$$
$$+ p_F^{Ch}(1-q)\lambda T_{SP}[1] + p_F^{Ch}(1-q)\lambda T_{SN}[1] + p_F^{Ch}(1-q)\lambda T_{NP}[1] + p_F^{Ch}(1-q)\lambda R[1]$$
$$- \omega_{L_F} L_F[1] - \tau_F \Xi L_F[1] - \rho_{PExp} L_F[1]$$

$$\frac{d}{dt}L_F[i=2,...,k-1] = \alpha L_F[i-1] - \alpha L_F[i] + p_F^{Ch}\lambda(S[i] + WS[i]) + p_F^{Ch}(1-q)\lambda T_{EDF}[i] + p_F^{Ch}(1-q)\lambda T_{EDS}[i]$$
$$+ p_F^{Ch}(1-q)\lambda T_{SP}[i] + p_F^{Ch}(1-q)\lambda T_{SN}[i] + p_F^{Ch}(1-q)\lambda T_{NP}[i] + p_F^{Ch}(1-q)\lambda R[i]$$
$$+ p_F^{Ch}(1-q)\lambda L_S[i] - \omega_{L_F} L_F[i] - \tau_F \Xi L_F[i] - \rho_{PExp} L_F[i]$$

$$\frac{d}{dt}L_F[i=k,...,n] = \alpha L_F[i-1] - \alpha L_F[i] + p_F^{Ad}\lambda(S[i] + WS[i]) + p_F^{Ad}(1-q)\lambda T_{EDF}[i] + p_F^{Ad}(1-q)\lambda T_{EDS}[i]$$
$$+ p_F^{Ad}(1-q)\lambda T_{SP}[i] + p_F^{Ad}(1-q)\lambda T_{SN}[i] + p_F^{Ad}(1-q)\lambda T_{NP}[i] + p_F^{Ad}(1-q)\lambda R[i]$$
$$+ p_F^{Ad}(1-q)\lambda L_S[i] - \omega_{L_F} L_F[i] - \tau_F \Xi L_F[i] - \rho_{PExp} L_F[i]$$

### A.3: LATENT WITH SLOW PROGRESSION TO TB DISEASE

$$\frac{d}{dt}L_S[1] = -\alpha L_S[1] + \left(1-p_F^{Ch}\right)\lambda(S[1]+WS[1]) + \left(1-p_F^{Ch}\right)(1-q)\lambda T_{EDF}[1] + \left(1-p_F^{Ch}\right)(1-q)\lambda T_{EDS}[1]$$
$$+\left(1-p_F^{Ch}\right)(1-q)\lambda T_{SP}[1] + \left(1-p_F^{Ch}\right)(1-q)\lambda T_{SN}[1] + \left(1-p_F^{Ch}\right)(1-q)\lambda T_{NP}[1]$$
$$+\left(1-p_F^{Ch}\right)(1-q)\lambda R[1] - p_F^{Ch}(1-q)\lambda L_S[1] - \omega_{L_S} L_S[1] - \tau_S \Xi L_S[1] - \rho_{PExp} L_S[1]$$

$$\frac{d}{dt}L_S[i=2,...,k-1] = \alpha L_S[i-1] - \alpha L_S[i] + \left(1-p_F^{Ch}\right)\lambda(S[i]+WS[i]) + \left(1-p_F^{Ch}\right)(1-q)\lambda T_{EDF}[i]$$
$$+\left(1-p_F^{Ch}\right)(1-q)\lambda T_{EDS}[i] + \left(1-p_F^{Ch}\right)(1-q)\lambda T_{SP}[i] + \left(1-p_F^{Ch}\right)(1-q)\lambda T_{SN}[i]$$
$$+\left(1-p_F^{Ch}\right)(1-q)\lambda T_{NP}[i] + \left(1-p_F^{Ch}\right)(1-q)\lambda R[i] - p_F^{Ch}(1-q)\lambda L_S[i] - \omega_{L_S} L_S[i]$$
$$-\tau_S \Xi L_S[i] - \rho_{PExp} L_S[i]$$

$$\frac{d}{dt}L_S[i=k,...,n] = \alpha L_S[i-1] - \alpha L_S[i] + \left(1-p_F^{Ad}\right)\lambda(S[i]+WS[i]) + \left(1-p_F^{Ad}\right)(1-q)\lambda T_{EDF}[i]$$
$$+\left(1-p_F^{Ad}\right)(1-q)\lambda T_{EDS}[i] + \left(1-p_F^{Ad}\right)(1-q)\lambda T_{SP}[i] + \left(1-p_F^{Ad}\right)(1-q)\lambda T_{SN}[i]$$
$$+\left(1-p_F^{Ad}\right)(1-q)\lambda T_{NP}[i] + \left(1-p_F^{Ad}\right)(1-q)\lambda R[i] - p_F^{Ad}(1-q)\lambda L_S[i] - \omega_{L_S} L_S[i]$$
$$-\tau_S \Xi L_S[i] - \rho_{PExp} L_S[i]$$

### A.4: EARLY TB DISEASE STAGE ARISING FROM FAST PROGRESSORS

$$\frac{d}{dt}D_{EDF}[1] = -\alpha D_{EDF}[1] + \omega_{L_F} L_F[1] - \vartheta_{D_{EDF}} D_{EDF}[1] - z_{ED}\chi_{D_{EDF}} D_{EDF}[1]$$
$$-\nu_{D_{EDF}} D_{EDF}[1] - \pi_{D_{EDF}} D_{EDF}[1]$$

$$\frac{d}{dt}D_{EDF}[i=2,...,k-1] = \alpha D_{EDF}[i-1] - \alpha D_{EDF}[i] + \omega_{L_F} L_F[i] - \vartheta_{D_{EDF}} D_{EDF}[i]$$
$$-z_{ED}\chi_{D_{EDF}} D_{EDF}[i] - \nu_{D_{EDF}} D_{EDF}[i] - \pi_{D_{EDF}} D_{EDF}[i]$$

$$\frac{d}{dt}D_{EDF}[i=k,...,n] = \alpha D_{EDF}[i-1] - \alpha D_{EDF}[i] + \omega_{L_F} L_F[i] - \vartheta_{D_{EDF}} D_{EDF}[i]$$
$$-z_{ED}\chi_{D_{EDF}} D_{EDF}[i] - \nu_{D_{EDF}} D_{EDF}[i] - \pi_{D_{EDF}} D_{EDF}[i]$$

### A.5: Treated Early TB Disease Stage Arising From Fast Progressors

$$\frac{d}{dt}T_{EDF}[1] = -\alpha T_{EDF}[1] + z_{ED}\chi_{D_{EDF}}D_{EDF}[1] - \vartheta_{T_{EDF}}T_{EDF}[1] - \nu_{T_{EDF}}T_{EDF}[1] - \psi_{T_{EDF}}T_{EDF}[1] \quad -(1-q)\lambda T_{EDF}[1]$$

$$\frac{d}{dt}T_{EDF}[i=2,...,k-1] = \alpha T_{EDF}[i-1] - \alpha T_{EDF}[i] + z_{ED}\chi_{D_{EDF}}D_{EDF}[i] - \vartheta_{T_{EDF}}T_{EDF}[i] - \nu_{T_{EDF}}T_{EDF}[i] - \psi_{T_{EDF}}T_{EDF}[i] - (1-q)\lambda T_{EDF}[i]$$

$$\frac{d}{dt}T_{EDF}[i=k,...,n] = \alpha T_{EDF}[i-1] - \alpha T_{EDF}[i] + z_{ED}\chi_{D_{EDF}}D_{EDF}[i] - \vartheta_{T_{EDF}}T_{EDF}[i] - \nu_{T_{EDF}}T_{EDF}[i] - \psi_{T_{EDF}}T_{EDF}[i] - (1-q)\lambda T_{EDF}[i]$$

### A.6: Early TB Disease Stage Arising From Slow Progressors

$$\frac{d}{dt}D_{EDS}[1] = -\alpha D_{EDS}[1] + \omega_{L_S}L_S[1] - \vartheta_{D_{EDS}}D_{EDS}[1] - z_{ED}\chi_{D_{EDS}}D_{EDS}[1] - \nu_{D_{EDS}}D_{EDS}[1] - \pi_{D_{EDS}}D_{EDS}[1]$$

$$\frac{d}{dt}D_{EDS}[i=2,...,k-1] = \alpha D_{EDS}[i-1] - \alpha D_{EDS}[i] + \omega_{L_S}L_S[i] - \vartheta_{D_{EDS}}D_{EDS}[i] - z_{ED}\chi_{D_{EDS}}D_{EDS}[i] - \nu_{D_{EDS}}D_{EDS}[i] - \pi_{D_{EDS}}D_{EDS}[i]$$

$$\frac{d}{dt}D_{EDS}[i=k,...,n] = \alpha D_{EDS}[i-1] - \alpha D_{EDS}[i] + \omega_{L_S}L_S[i] - \vartheta_{D_{EDS}}D_{EDS}[i] - z_{ED}\chi_{D_{EDS}}D_{EDS}[i] - \nu_{D_{EDS}}D_{EDS}[i] - \pi_{D_{EDS}}D_{EDS}[i]$$

### A.7: Treated Early TB Disease Stage Arising From Slow Progressors

$$\frac{d}{dt}T_{EDS}[1] = -\alpha T_{EDS}[1] + z_{ED}\chi_{D_{EDS}}D_{EDS}[1] - \vartheta_{T_{EDS}}T_{EDS}[1] - \nu_{T_{EDS}}T_{EDS}[1] - \psi_{T_{EDS}}T_{EDS}[1] \quad -(1-q)\lambda T_{EDS}[1]$$

$$\frac{d}{dt}T_{EDS}[i=2,...,k-1] = \alpha T_{EDS}[i-1] - \alpha T_{EDS}[i] + z_{ED}\chi_{D_{EDS}}D_{EDS}[i] - \vartheta_{T_{EDS}}T_{EDS}[i] - \nu_{T_{EDS}}T_{EDS}[i] - \psi_{T_{EDS}}T_{EDS}[i] - (1-q)\lambda T_{EDS}[i]$$

$$\frac{d}{dt}T_{EDS}[i=k,...,n] = \alpha T_{EDS}[i-1] - \alpha T_{EDS}[i] + z_{ED}\chi_{D_{EDS}}D_{EDS}[i] - \vartheta_{T_{EDS}}T_{EDS}[i] - \nu_{T_{EDS}}T_{EDS}[i] - \psi_{T_{EDS}}T_{EDS}[i] - (1-q)\lambda T_{EDS}[i]$$

## A.8: ACTIVE SMEAR-POSITIVE PULMONARY TB DISEASE

### A.8-1: FIRST COMPARTMENT

$$\frac{d}{dt}D_{SP_1}[1] = -\alpha D_{SP_1}[1] + a_{D_{EDF}[1]\to D_{SP}[1]}\pi_{D_{EDF}} D_{EDF}[1] + a_{D_{EDS}[1]\to D_{SP}[1]}\pi_{D_{EDS}} D_{EDS}[1] - \mho_{SP} D_{SP_1}[1]$$

$$\frac{d}{dt}D_{SP_1}[i=2,...,k-1] = \alpha D_{SP_1}[i-1] - \alpha D_{SP_1}[i] + a_{D_{EDF}[i]\to D_{SP}[i]}\pi_{D_{EDF}} D_{EDF}[i] + a_{D_{EDS}[i]\to D_{SP}[i]}\pi_{D_{EDS}} D_{EDS}[i] - \mho_{SP} D_{SP_1}[i]$$

$$\frac{d}{dt}D_{SP_1}[i=k,...,n] = \alpha D_{SP_1}[i-1] - \alpha D_{SP_1}[i] + a_{D_{EDF}[i]\to D_{SP}[i]}\pi_{D_{EDF}} D_{EDF}[i] + a_{D_{EDS}[i]\to D_{SP}[i]}\pi_{D_{EDS}} D_{EDS}[i] - \mho_{SP} D_{SP_1}[i]$$

### A.8-2: SECOND COMPARTMENT

$$\frac{d}{dt}D_{SP_2}[1] = (1-\Upsilon)\mho_{SP} D_{SP_1}[1] - \alpha D_{SP_2}[1] - \mho_{M_{SP}} D_{SP_2}[1]$$

$$\frac{d}{dt}D_{SP_2}[i=2,...,k-1] = (1-\Upsilon)\mho_{SP} D_{SP_1}[i] + \alpha D_{SP_2}[i-1] - \alpha D_{SP_2}[i] - \mho_{M_{SP}} D_{SP_2}[i]$$

$$\frac{d}{dt}D_{SP_2}[i=k,...,n] = (1-\Upsilon)\mho_{SP} D_{SP_1}[i] + \alpha D_{SP_2}[i-1] - \alpha D_{SP_2}[i] - \mho_{M_{SP}} D_{SP_2}[i]$$

### A.8-3: THIRD COMPARTMENT

$$\frac{d}{dt}D_{SP_3}[1] = \mho_{M_{SP}} D_{SP_2}[1] - \alpha D_{SP_3}[1] - \mho_{M_{SP}} D_{SP_3}[1]$$

$$\frac{d}{dt}D_{SP_3}[i=2,...,k-1] = \mho_{M_{SP}} D_{SP_2}[i] + \alpha D_{SP_3}[i-1] - \alpha D_{SP_3}[i] - \mho_{M_{SP}} D_{SP_3}[i]$$

$$\frac{d}{dt}D_{SP_3}[i=k,...,n] = \mho_{M_{SP}} D_{SP_2}[i] + \alpha D_{SP_3}[i-1] - \alpha D_{SP_3}[i] - \mho_{M_{SP}} D_{SP_3}[i]$$

### A.8-4: FOURTH COMPARTMENT

$$\frac{d}{dt}D_{SP}[1] = (1-\Upsilon)\mho_{M_{SP}} D_{SP_3}[1] - \alpha D_{SP}[1] - \mho_{F_{SP}} D_{SP}[1] + \Upsilon\mho_{SP} D_{SP}[1]$$

$$\frac{d}{dt}D_{SP}[i=2,...,k-1] = (1-\Upsilon)\mho_{M_{SP}} D_{SP_3}[i] + \alpha D_{SP}[i-1] - \alpha D_{SP}[i] - \mho_{F_{SP}} D_{SP}[i] + \Upsilon\mho_{SP} D_{SP}[i]$$

$$\frac{d}{dt}D_{SP}[i=k,...,n] = (1-\Upsilon)\mho_{M_{SP}} D_{SP_3}[i] + \alpha D_{SP}[i-1] - \alpha D_{SP}[i] - \mho_{F_{SP}} D_{SP}[i] + \Upsilon\mho_{SP} D_{SP}[i]$$

## A.9 TREATED ACTIVE SMEAR-POSITIVE PULMONARY TB DISEASE

$$\frac{d}{dt}T_{SP}[1] = -\alpha T_{SP}[1] + \aleph_{SP_0} z_D \chi_{D_{SP}} D_{SP}[1] + \mho_{M_{SP}} \Upsilon D_{SP_3}[i] - \vartheta_{T_{SP}} T_{SP}[1] - \nu_{T_{SP}} T_{SP}[1]$$
$$-\psi_{T_{SP}} T_{SP}[1] - (1-q)\lambda T_{SP}[1]$$

$$\frac{d}{dt}T_{SP}[i=2,...,k-1] = \alpha T_{SP}[i-1] - \alpha T_{SP}[i] + \aleph_{SP_0} z_D \chi_{D_{SP}} D_{SP}[i] + \mho_{M_{SP}} \Upsilon D_{SP_3}[i] - \vartheta_{T_{SP}} T_{SP}[i]$$
$$-\nu_{T_{SP}} T_{SP}[i] - \psi_{T_{SP}} T_{SP}[i] - (1-q)\lambda T_{SP}[i]$$

$$\frac{d}{dt}T_{SP}[i=k,...,n] = \alpha T_{SP}[i-1] - \alpha T_{SP}[i] + \aleph_{SP_0} z_D \chi_{D_{SP}} D_{SP}[i] + \mho_{M_{SP}} \Upsilon D_{SP_3}[i] - \vartheta_{T_{SP}} T_{SP}[i]$$
$$-\nu_{T_{SP}} T_{SP}[i] - \psi_{T_{SP}} T_{SP}[i] - (1-q)\lambda T_{SP}[i]$$

## A.10: ACTIVE SMEAR-NEGATIVE PULMONARY TB DISEASE

### A.10-1: FIRST COMPARTMENT

$$\frac{d}{dt}D_{SN_1}[1] = -\alpha D_{SN_1}[1] + a_{D_{EDF}[1]\to D_{SN}[1]} \pi_{D_{EDF}} D_{EDF}[1] + a_{D_{EDS}[1]\to D_{SN}[1]} \pi_{D_{EDS}} D_{EDS}[1] - \mho_{SN} D_{SN_1}[1]$$

$$\frac{d}{dt}D_{SN_1}[i=2,...,k-1] = \alpha D_{SN_1}[i-1] - \alpha D_{SN_1}[i] + a_{D_{EDF}[i]\to D_{SN}[i]} \pi_{D_{EDF}} D_{EDF}[i]$$
$$+a_{D_{EDS}[i]\to D_{SN}[i]} \pi_{D_{EDS}} D_{EDS}[i] - \mho_{SN} D_{SN_1}[i]$$

$$\frac{d}{dt}D_{SN_1}[i=k,...,n] = \alpha D_{SN_1}[i-1] - \alpha D_{SN_1}[i] + a_{D_{EDF}[i]\to D_{SN}[i]} \pi_{D_{EDF}} D_{EDF}[i]$$
$$+a_{D_{EDS}[i]\to D_{SN}[i]} \pi_{D_{EDS}} D_{EDS}[i] - \mho_{SN} D_{SN_1}[i]$$

### A.10-2: SECOND COMPARTMENT

$$\frac{d}{dt}D_{SN_2}[1] = (1-\Upsilon_2)\mho_{SN} D_{SN_1}[1] - \alpha D_{SN_2}[1] - \mho_{M_{SN}} D_{SN_2}[1]$$

$$\frac{d}{dt}D_{SN_2}[i=2,...,k-1] = (1-\Upsilon_2)\mho_{SN} D_{SN_1}[i] + \alpha D_{SN_2}[i-1] - \alpha D_{SN_2}[i] - \mho_{M_{SN}} D_{SN_2}[i]$$

$$\frac{d}{dt}D_{SN_2}[i=k,...,n] = (1-\Upsilon_2)\mho_{SN} D_{SN_1}[i] + \alpha D_{SN_2}[i-1] - \alpha D_{SN_2}[i] - \mho_{M_{SN}} D_{SN_2}[i]$$

### A.10-3: THIRD COMPARTMENT

$$\frac{d}{dt}D_{SN_3}[1] = \mho_{M_{SN}} D_{SN_2}[1] - \alpha D_{SN_3}[1] - \mho_{M_{SN}} D_{SN_3}[1]$$

$$\frac{d}{dt}D_{SN_3}[i=2,...,k-1] = \mho_{M_{SN}} D_{SN_2}[i] + \alpha D_{SN_3}[i-1] - \alpha D_{SN_3}[i] - \mho_{M_{SN}} D_{SN_3}[i]$$

$$\frac{d}{dt}D_{SN_3}[i=k,...,n] = \mho_{M_{SN}} D_{SN_2}[i] + \alpha D_{SN_3}[i-1] - \alpha D_{SN_3}[i] - \mho_{M_{SN}} D_{SN_3}[i]$$

### A.10-4: FOURTH COMPARTMENT

$$\frac{d}{dt}D_{SN}[1] = (1-\Upsilon_2)\mho_{M_{SN}}D_{SN_3}[1] - \alpha D_{SN}[1] - \mho_{F_{SN}}D_{SN}[1] + \Upsilon_2\mho_{SN}D_{SN}[1]$$

$$\frac{d}{dt}D_{SN}[i=2,...,k-1] = (1-\Upsilon_2)\mho_{M_{SN}}D_{SN_3}[i] + \alpha D_{SN}[i-1] - \alpha D_{SN}[i] - \mho_{F_{SN}}D_{SN}[i] + \Upsilon_2\mho_{SN}D_{SN}[i]$$

$$\frac{d}{dt}D_{SN}[i=k,...,n] = (1-\Upsilon_2)\mho_{M_{SN}}D_{SN_3}[i] + \alpha D_{SN}[i-1] - \alpha D_{SN}[i] - \mho_{F_{SN}}D_{SN}[i] + \Upsilon_2\mho_{SN}D_{SN}[i]$$

### A.11: TREATED ACTIVE SMEAR-NEGATIVE PULMONARY TB DISEASE

$$\frac{d}{dt}T_{SN}[1] = -\alpha T_{SN}[1] + \aleph_{SN_0}z_D\chi_{D_{SN}}D_{SN}[1] + \mho_{M_{SN}}\Upsilon_2 D_{SN_3}[1] - \vartheta_{T_{SN}}T_{SN}[1] - \nu_{T_{SN}}T_{SN}[1] - \psi_{T_{SN}}T_{SN}[1] - (1-q)\lambda T_{SN}[1]$$

$$\frac{d}{dt}T_{SN}[i=2,...,k-1] = \alpha T_{SN}[i-1] - \alpha T_{SN}[i] + \aleph_{SN_0}z_D\chi_{D_{SN}}D_{SN}[i] + \mho_{M_{SN}}\Upsilon_2 D_{SN_3}[i] - \vartheta_{T_{SN}}T_{SN}[i] - \nu_{T_{SN}}T_{SN}[i] - \psi_{T_{SN}}T_{SN}[i] - (1-q)\lambda T_{SN}[i]$$

$$\frac{d}{dt}T_{SN}[i=k,...,n] = \alpha T_{SN}[i-1] - \alpha T_{SN}[i] + \aleph_{SN_0}z_D\chi_{D_{SN}}D_{SN}[i] + \mho_{M_{SN}}\Upsilon_2 D_{SN_3}[i] - \vartheta_{T_{SN}}T_{SN}[i] - \nu_{T_{SN}}T_{SN}[i] - \psi_{T_{SN}}T_{SN}[i] - (1-q)\lambda T_{SN}[i]$$

### A.12: ACTIVE NON-PULMONARY TB DISEASE

#### A.12-1: FIRST COMPARTMENT

$$\frac{d}{dt}D_{NP_1}[1] = -\alpha D_{NP_1}[1] + a_{D_{EDF}[1]\to D_{NP}[1]}\pi_{D_{EDF}}D_{EDF}[1] + a_{D_{EDS}[1]\to D_{NP}[1]}\pi_{D_{EDS}}D_{EDS}[1] - \mho_{NP}D_{NP_1}[1]$$

$$\frac{d}{dt}D_{NP_1}[i=2,...,k-1] = \alpha D_{NP_1}[i-1] - \alpha D_{NP_1}[i] + a_{D_{EDF}[i]\to D_{NP}[i]}\pi_{D_{EDF}}D_{EDF}[i] + a_{D_{EDS}[i]\to D_{NP}[i]}\pi_{D_{EDS}}D_{EDS}[i] - \mho_{NP}D_{NP_1}[i]$$

$$\frac{d}{dt}D_{NP_1}[i=k,...,n] = \alpha D_{NP_1}[i-1] - \alpha D_{NP_1}[i] + a_{D_{EDF}[i]\to D_{NP}[i]}\pi_{D_{EDF}}D_{EDF}[i] + a_{D_{EDS}[i]\to D_{NP}[i]}\pi_{D_{EDS}}D_{EDS}[i] - \mho_{NP}D_{NP_1}[i]$$

#### A.12-2: SECOND COMPARTMENT

$$\frac{d}{dt}D_{NP_2}[1] = (1-\Upsilon_2)\mho_{NP}D_{NP_1}[1] - \alpha D_{NP_2}[1] - \mho_{M_{NP}}D_{NP_2}[1]$$

$$\frac{d}{dt}D_{NP_2}[i=2,...,k-1] = (1-\Upsilon_2)\mho_{NP}D_{NP_1}[i] + \alpha D_{NP_2}[i-1] - \alpha D_{NP_2}[i] - \mho_{M_{NP}}D_{NP_2}[i]$$

$$\frac{d}{dt}D_{NP_2}[i=k,...,n] = (1-\Upsilon_2)\mho_{NP}D_{NP_1}[i] + \alpha D_{NP_2}[i-1] - \alpha D_{NP_2}[i] - \mho_{M_{NP}}D_{NP_2}[i]$$

#### A.12-3: THIRD COMPARTMENT

$$\frac{d}{dt}D_{NP_3}[1] = \mho_{M_{NP}} D_{NP_2}[1] - \alpha D_{NP_3}[1] - \mho_{M_{NP}} D_{NP_3}[1]$$

$$\frac{d}{dt}D_{NP_3}[i = 2,...,k-1] = \mho_{M_{NP}} D_{NP_2}[i] + \alpha D_{NP_3}[i-1] - \alpha D_{NP_3}[i] - \mho_{M_{NP}} D_{NP_3}[i]$$

$$\frac{d}{dt}D_{NP_3}[i = k,...,n] = \mho_{M_{NP}} D_{NP_2}[i] + \alpha D_{NP_3}[i-1] - \alpha D_{NP_3}[i] - \mho_{M_{NP}} D_{NP_3}[i]$$

A.12-4: FOURTH COMPARTMENT

$$\frac{d}{dt}D_{NP}[1] = (1-\Upsilon_2)\mho_{M_{NP}} D_{NP_3}[1] - \alpha D_{NP}[1] - \mho_{F_{NP}} D_{NP}[1] + \Upsilon\mho_{NP} D_{NP}[1]$$

$$\frac{d}{dt}D_{NP}[i = 2,...,k-1] = (1-\Upsilon_2)\mho_{M_{NP}} D_{NP_3}[i] + \alpha D_{NP}[i-1] - \alpha D_{NP}[i] - \mho_{F_{NP}} D_{NP}[i] + \Upsilon\mho_{NP} D_{NP}[i]$$

$$\frac{d}{dt}D_{NP}[i = k,...,n] = (1-\Upsilon_2)\mho_{M_{NP}} D_{NP_3}[i] + \alpha D_{NP}[i-1] - \alpha D_{NP}[i] - \mho_{F_{NP}} D_{NP}[i] + \Upsilon\mho_{NP} D_{NP}[i]$$

## A.13: TREATED ACTIVE NON-PULMONARY TB DISEASE

$$\frac{d}{dt}T_{NP}[1] = -\alpha T_{NP}[1] + \aleph_{NP_0} z_D \chi_{D_{NP}} D_{NP}[1] + \Upsilon_2 \mho_{M_{NP}} D_{NP_3}[1] - \vartheta_{T_{NP}} T_{NP}[1] - \nu_{T_{NP}} T_{NP}[1]$$
$$-\psi_{T_{NP}} T_{NP}[1] - (1-q)\lambda T_{NP}[1]$$

$$\frac{d}{dt}T_{NP}[i = 2,...,k-1] = \alpha T_{NP}[i-1] - \alpha T_{NP}[i] + \aleph_{NP_0} z_D \chi_{D_{NP}} D_{NP}[i] + \Upsilon_2 \mho_{M_{NP}} D_{NP_3}[i] - \vartheta_{T_{NP}} T_{NP}[i]$$
$$-\nu_{T_{NP}} T_{NP}[i] - \psi_{T_{NP}} T_{NP}[i] - (1-q)\lambda T_{NP}[i]$$

$$\frac{d}{dt}T_{NP}[i = k,...,n] = \alpha T_{NP}[i-1] - \alpha T_{NP}[i] + \aleph_{NP_0} z_D \chi_{D_{NP}} D_{NP}[i] + \Upsilon_2 \mho_{M_{NP}} D_{NP_3}[i] - \vartheta_{T_{NP}} T_{NP}[i]$$
$$-\nu_{T_{NP}} T_{NP}[i] - \psi_{T_{NP}} T_{NP}[i] - (1-q)\lambda T_{NP}[i]$$

### A.14: CURED

$$\frac{d}{dt}R[1] = -\alpha R[1] + \psi_{T_{EDF}} T_{EDF}[1] + \psi_{T_{EDS}} T_{EDS}[1] + \psi_{T_{SP}} T_{SP}[1] + \psi_{T_{SN}} T_{SN}[1] + \psi_{T_{NP}} T_{NP}[1]$$
$$+\nu_{D_{EDF}} D_{EDF}[1] + \nu_{D_{EDS}} D_{EDS}[1] + \aleph_{SP_0}\nu_{D_{SP}} D_{SP}[1] + \aleph_{SN_0}\nu_{D_{SN}} D_{SN}[1] + \aleph_{NP_0}\nu_{D_{NP}} D_{NP}[1]$$
$$+\nu_{T_{SP}} T_{SP}[1] + \nu_{T_{SN}} T_{SN}[1] + \nu_{T_{NP}} T_{NP}[1] + \nu_{T_{EDF}} T_{EDF}[1] + \nu_{T_{EDS}} T_{EDS}[1] - (1-q)\lambda R[1] + \tau_F \Xi L_F[1] + \tau_S \Xi L_S[1]$$

$$\frac{d}{dt}R[i = 2,...,k-1] = \alpha R[i-1] - \alpha R[i] + \psi_{T_{EDF}} T_{EDF}[i] + \psi_{T_{EDS}} T_{EDS}[i] + \psi_{T_{SP}} T_{SP}[i]$$
$$+\psi_{T_{SN}} T_{SN}[i] + \psi_{T_{NP}} T_{NP}[i] + \nu_{D_{EDF}} D_{EDF}[i] + \nu_{D_{EDS}} D_{EDS}[i] + \aleph_{SP_0}\nu_{D_{SP}} D_{SP}[i]$$
$$+\aleph_{SN_0}\nu_{D_{SN}} D_{SN}[i] + \aleph_{NP_0}\nu_{D_{NP}} D_{NP}[i] + \nu_{T_{SP}} T_{SP}[i] + \nu_{T_{SN}} T_{SN}[i] + \nu_{T_{NP}} T_{NP}[i]$$
$$+\nu_{T_{EDF}} T_{EDF}[i] + \nu_{T_{EDS}} T_{EDS}[i] - (1-q)\lambda R[i] + \tau_F \Xi L_F[1] + \tau_S \Xi L_S[1]$$

$$\frac{d}{dt}R[i = k,...,n] = \alpha R[i-1] - \alpha R[i] + \psi_{T_{EDF}} T_{EDF}[i] + \psi_{T_{EDS}} T_{EDS}[i] + \psi_{T_{SP}} T_{SP}[i]$$
$$+\psi_{T_{SN}} T_{SN}[i] + \psi_{T_{NP}} T_{NP}[i] + \nu_{D_{EDF}} D_{EDF}[i] + \nu_{D_{EDS}} D_{EDS}[i] + \aleph_{SP_0}\nu_{D_{SP}} D_{SP}[i]$$
$$+\aleph_{SN_0}\nu_{D_{SN}} D_{SN}[i] + \aleph_{NP_0}\nu_{D_{NP}} D_{NP}[i] + \nu_{T_{SP}} T_{SP}[i] + \nu_{T_{SN}} T_{SN}[i] + \nu_{T_{NP}} T_{NP}[i]$$
$$+\nu_{T_{EDF}} T_{EDF}[i] + \nu_{T_{EDS}} T_{EDS}[i] - (1-q)\lambda R[i] + \tau_F \Xi L_F[1] + \tau_S \Xi L_S[1]$$

## B: VACCINATED BRANCH OF THE MODEL

### B.1: VACCINATED, UNINFECTED AND SUSCEPTIBLE

$$\frac{d}{dt}VS[i=1] = (f_{Vac})\zeta N[n] + f_{Vac}\mu_{TBTotal} - \alpha VS[1] - \lambda(1 - VE_S^{Ch})VS[1] - \gamma VS[1] + \rho S[1] + \rho_{WS} WS[1]$$

$$\frac{d}{dt}VS[i = 2,...,k-1] = \alpha VS[i-1] - \alpha VS[i] - \lambda(1 - VE_S^{Ch})VS[i] - \gamma VS[i] + \rho S[1] + \rho_{WS} WS[i]$$

$$\frac{d}{dt}VS[i = k,...,n] = \alpha VS[i-1] - \alpha VS[i] - \lambda(1 - VE_S^{Ad})VS[i] - \gamma VS[i] + \rho S[1] + \rho_{WS} WS[i]$$

### B.2: VACCINATED, UNINFECTED, WANING SUSCEPTIBLE

$$\frac{d}{dt}WS[i=1] = -\alpha WS[1] + \gamma VS[1] - \rho_{WS} WS[1] - \lambda WS[1]$$

$$\frac{d}{dt}S[i=2,...,k-1] = \alpha WS[i-1] - \alpha WS[i] + \gamma VS[i] - \lambda WS[i] - \rho_{WS} WS[i]$$

$$\frac{d}{dt}S[i=k,...,n] = \alpha WS[i-1] - \alpha WS[i] + \gamma VS[i] - \lambda WS[i] - \rho_{WS} WS[i]$$

### B.3: VACCINATED AND LATENT WITH FAST PROGRESSION TO TB DISEASE

$$\frac{d}{dt}VL_F[1] = -\alpha VL_F[1] + (1-VE_P^{Ch})\,p_F^{Ch}\lambda(1-VE_S^{Ch})VS[1] + p_F^{Ch}(1-q)\lambda VL_S[1]$$
$$+(1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VT_{EDF}[1] + (1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VT_{EDS}[1]$$
$$+(1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VT_{SP}[1] + (1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VT_{SN}[1]$$
$$+(1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VT_{NP}[1] + (1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VR[1]$$
$$-\omega_{VL_F}VL_F[1] - \tau_{VF}\Xi VL_F[1] + a_{L_F\to VL_F}\rho_{PExp}L_F[1] + a_{L_S\to VL_F}\rho_{PExp}L_S[1]$$

$$\frac{d}{dt}VL_F[i=2,\ldots,k-1] = \alpha VL_F[i-1] - \alpha VL_F[i] + (1-VE_P^{Ch})\,p_F^{Ch}\lambda(1-VE_S^{Ch})VS[i] + p_F^{Ch}(1-q)\lambda VL_S[i]$$
$$+(1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VT_{EDF}[i] + (1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VT_{EDS}[i]$$
$$+(1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VT_{SP}[i] + (1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VT_{SN}[i]$$
$$+(1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VT_{NP}[i] + (1-VE_P^{Ch})\,p_F^{Ch}(1-q)\lambda VR[i]$$
$$-\omega_{VL_F}VL_F[i] - \tau_{VF}\Xi VL_F[i] + a_{L_F\to VL_F}\rho_{PExp}L_F[i] + a_{L_S\to VL_F}\rho_{PExp}L_S[i]$$

$$\frac{d}{dt}VL_F[i=k,\ldots,n] = \alpha VL_F[i-1] - \alpha VL_F[i] + (1-VE_P^{Ad})\,p_F^{Ad}\lambda(1-VE_S^{Ad})VS[i] + p_F^{Ad}(1-q)\lambda VL_S[i]$$
$$+(1-VE_P^{Ad})\,p_F^{Ad}(1-q)\lambda VT_{EDF}[i] + (1-VE_P^{Ad})\,p_F^{Ad}(1-q)\lambda VT_{EDS}[i]$$
$$+(1-VE_P^{Ad})\,p_F^{Ad}(1-q)\lambda VT_{SP}[i] + (1-VE_P^{Ad})\,p_F^{Ad}(1-q)\lambda VT_{SN}[i]$$
$$+(1-VE_P^{Ad})\,p_F^{Ad}(1-q)\lambda VT_{NP}[i] + (1-VE_P^{Ad})\,p_F^{Ad}(1-q)\lambda VR[i]$$
$$-\omega_{VL_F}VL_F[i] - \tau_{VF}\Xi VL_F[i] + a_{L_F\to VL_F}\rho_{PExp}L_F[i] + a_{L_S\to VL_F}\rho_{PExp}L_S[i]$$

### B.4: VACCINATED AND LATENT WITH SLOW PROGRESSION TO TB DISEASE

$$\frac{d}{dt}VL_S[1] = -\alpha VL_S[1] + (1-(1-VE_P^{Ch})p_F^{Ch})\lambda(1-VE_S^{Ch})VS[1] + (1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VT_{EDF}[1]$$
$$+(1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VT_{EDS}[1] + (1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VT_{SP}[1]$$
$$+(1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VT_{SN}[1] + (1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VT_{NP}[1]$$
$$+(1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VR[1] - p_F^{Ch}(1-q)\lambda VL_S[1] - \omega_{VL_S}VL_S[1]$$
$$-\tau_{VS}\Xi VL_S[i] + a_{L_F\to VL_S}\rho_{PExp}L_F[1] + a_{L_S\to VL_S}\rho_{PExp}L_S[1]$$

$$\frac{d}{dt}VL_S[i=2,...,k-1] = \alpha L_S[i-1] - \alpha VL_S[i] + (1-(1-VE_P^{Ch})p_F^{Ch})\lambda(1-VE_S^{Ch})VS[i]$$
$$+(1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VT_{EDF}[i] + (1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VT_{EDS}[i]$$
$$+(1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VT_{SP}[i] + (1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VT_{SN}[i]$$
$$+(1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VT_{NP}[i] + (1-(1-VE_P^{Ch})p_F^{Ch})(1-q)\lambda VR[i]$$
$$-p_F^{Ch}(1-q)\lambda VL_S[i] - \omega_{VL_S}VL_S[i] - \tau_{VS}\Xi VL_S[i] + a_{L_F\to VL_S}\rho_{PExp}L_F[1]$$
$$+a_{L_S\to VL_S}\rho_{PExp}L_S[1]$$

$$\frac{d}{dt}VL_S[i=k,...,n] = \alpha L_S[i-1] - \alpha VL_S[i] + (1-(1-VE_P^{Ad})p_F^{Ad})\lambda(1-VE_S^{Ad})VS[i]$$
$$+(1-(1-VE_P^{Ad})p_F^{Ad})(1-q)\lambda VT_{EDF}[i] + (1-(1-VE_P^{Ad})p_F^{Ad})(1-q)\lambda VT_{EDS}[i]$$
$$+(1-(1-VE_P^{Ad})p_F^{Ad})(1-q)\lambda VT_{SP}[i] + (1-(1-VE_P^{Ad})p_F^{Ad})(1-q)\lambda VT_{SN}[i]$$
$$+(1-(1-VE_P^{Ad})p_F^{Ad})(1-q)\lambda VT_{NP}[i] + (1-(1-VE_P^{Ad})p_F^{Ad})(1-q)\lambda VR[i]$$
$$-p_F^{Ad}(1-q)\lambda VL_S[i] - \omega_{VL_S}VL_S[i] - \tau_{VS}\Xi VL_S[i] + a_{L_F\to VL_S}\rho_{PExp}L_F[1]$$
$$+a_{L_S\to VL_S}\rho_{PExp}L_S[1]$$

### B.5: VACCINATED AND EARLY TB DISEASE STAGE ARISING FROM FAST PROGRESSORS

$$\frac{d}{dt}VD_{EDF}[1] = -\alpha VD_{EDF}[1] + \omega_{VL_F}VL_F[1] - \vartheta_{VD_{EDF}}VD_{EDF}[1] - z_{VED}\chi_{VD_{EDF}}VD_{EDF}[1] - \nu_{VD_{EDF}}VD_{EDF}[1]$$
$$-\pi_{VD_{EDF}}VD_{EDF}[1]$$

$$\frac{d}{dt}VD_{EDF}[i=2,...,k-1] = \alpha VD_{EDF}[i-1] - \alpha VD_{EDF}[i] + \omega_{VL_F}VL_F[i] - \vartheta_{VD_{EDF}}VD_{EDF}[i] - z_{VED}\chi_{VD_{EDF}}VD_{EDF}[i]$$
$$-\nu_{VD_{EDF}}VD_{EDF}[i] - \pi_{VD_{EDF}}VD_{EDF}[i]$$

$$\frac{d}{dt}VD_{EDF}[i=k,...,n] = \alpha VD_{EDF}[i-1] - \alpha VD_{EDF}[i] + \omega_{VL_F}VL_F[i] - \vartheta_{VD_{EDF}}VD_{EDF}[i] - z_{VED}\chi_{VD_{EDF}}VD_{EDF}[i]$$
$$-\nu_{VD_{EDF}}VD_{EDF}[i] - \pi_{VD_{EDF}}VD_{EDF}[i]$$

### B.6: Vaccinated And Treated Early TB Disease Stage Arising From Fast Progressors

$$\frac{d}{dt}VT_{EDF}[1] = -\alpha VT_{EDF}[1] + z_{VED}\chi_{VD_{EDF}}VD_{EDF}[1] - \vartheta_{VT_{EDF}}VT_{EDF}[1] - \nu_{VT_{EDF}}VT_{EDF}[1] - \psi_{VT_{EDF}}VT_{EDF}[1] - (1-q)\lambda VT_{EDF}[1]$$

$$\frac{d}{dt}VT_{EDF}[i=2,...,k-1] = \alpha VT_{EDF}[i-1] - \alpha VT_{EDF}[i] + z_{VED}\chi_{VD_{EDF}}VD_{EDF}[i] - \vartheta_{VT_{EDF}}VT_{EDF}[i] - \nu_{VT_{EDF}}VT_{EDF}[i] - \psi_{VT_{EDF}}VT_{EDF}[i] - (1-q)\lambda VT_{EDF}[i]$$

$$\frac{d}{dt}VT_{EDF}[i=k,...,n] = \alpha VT_{EDF}[i-1] - \alpha VT_{EDF}[i] + z_{VED}\chi_{VD_{EDF}}VD_{EDF}[i] - \vartheta_{VT_{EDF}}VT_{EDF}[i] - \nu_{VT_{EDF}}VT_{EDF}[i] - \psi_{VT_{EDF}}VT_{EDF}[i] - (1-q)\lambda VT_{EDF}[i]$$

### B.7: Vaccinated And Early TB Disease Stage Arising From Slow Progressors

$$\frac{d}{dt}VD_{EDS}[1] = -\alpha VD_{EDS}[1] + \omega_{VL_S}VL_S[1] - \vartheta_{VD_{EDS}}VD_{EDS}[1] - z_{VED}\chi_{VD_{EDS}}VD_{EDS}[1] - \nu_{VD_{EDS}}VD_{EDS}[1] - \pi_{VD_{EDS}}VD_{EDS}[1]$$

$$\frac{d}{dt}VD_{EDS}[i=2,...,k-1] = \alpha VD_{EDS}[i-1] - \alpha VD_{EDS}[i] + \omega_{VL_S}VL_S[i] - \vartheta_{VD_{EDS}}VD_{EDS}[i] - z_{VED}\chi_{VD_{EDS}}VD_{EDS}[i] - \nu_{VD_{EDS}}VD_{EDS}[i] - \pi_{VD_{EDS}}VD_{EDS}[i]$$

$$\frac{d}{dt}VD_{EDS}[i=k,...,n] = \alpha VD_{EDS}[i-1] - \alpha VD_{EDS}[i] + \omega_{VL_S}VL_S[i] - \vartheta_{VD_{EDS}}VD_{EDS}[i] - z_{VED}\chi_{VD_{EDS}}VD_{EDS}[i] - \nu_{VD_{EDS}}VD_{EDS}[i] - \pi_{VD_{EDS}}VD_{EDS}[i]$$

### B.8: Vaccinated And Treated Early TB Disease Stage Arising From Slow Progressors

$$\frac{d}{dt}VT_{EDS}[1] = -\alpha VT_{EDS}[1] + z_{VED}\chi_{VD_{EDS}}VD_{EDS}[1] - \vartheta_{VT_{EDS}}VT_{EDS}[1] - \nu_{VT_{EDS}}VT_{EDS}[1] - \psi_{VT_{EDS}}VT_{EDS}[1] - (1-q)\lambda VT_{EDS}[1]$$

$$\frac{d}{dt}VT_{EDS}[i=2,...,k-1] = \alpha VT_{EDS}[i-1] - \alpha VT_{EDS}[i] + z_{VED}\chi_{VD_{EDS}}VD_{EDS}[i] - \vartheta_{VT_{EDS}}VT_{EDS}[i] - \nu_{VT_{EDS}}VT_{EDS}[i] - \psi_{VT_{EDS}}VT_{EDS}[i] - (1-q)\lambda VT_{EDS}[i]$$

$$\frac{d}{dt}VT_{EDS}[i=k,...,n] = \alpha VT_{EDS}[i-1] - \alpha VT_{EDS}[i] + z_{VED}\chi_{VD_{EDS}}VD_{EDS}[i] - \vartheta_{VT_{EDS}}VT_{EDS}[i] - \nu_{VT_{EDS}}VT_{EDS}[i] - \psi_{VT_{EDS}}VT_{EDS}[i] - (1-q)\lambda VT_{EDS}[i]$$

## B.9: VACCINATED AND ACTIVE SMEAR-POSITIVE PULMONARY TB DISEASE

### B.9-1: FIRST COMPARTMENT

$$\frac{d}{dt}VD_{SP_1}[1] = -\alpha VD_{SP_1}[1] + a_{VD_{EDF}[1]\to VD_{SP}[1]}\pi_{VD_{EDF}}VD_{EDF}[1] + a_{VD_{EDS}[1]\to VD_{SP}[1]}\pi_{VD_{EDS}}VD_{EDS}[1] - \mho_{VSP}VD_{SP_1}[1]$$

$$\frac{d}{dt}VD_{SP_1}[i=2,...,k-1] = \alpha VD_{SP_1}[i-1] - \alpha VD_{SP_1}[i] + a_{VD_{EDF}[i]\to VD_{SP}[i]}\pi_{VD_{EDF}}VD_{EDF}[i]$$
$$+ a_{VD_{EDS}[i]\to VD_{SP}[i]}\pi_{VD_{EDS}}VD_{EDS}[i] - \mho_{VSP}VD_{SP_1}[i]$$

$$\frac{d}{dt}VD_{SP_1}[i=k,...,n] = \alpha VD_{SP_1}[i-1] - \alpha VD_{SP_1}[i] + a_{VD_{EDF}[i]\to VD_{SP}[i]}\pi_{VD_{EDF}}VD_{EDF}[i]$$
$$+ a_{VD_{EDS}[i]\to VD_{SP}[i]}\pi_{VD_{EDS}}VD_{EDS}[i] - \mho_{VSP}VD_{SP_1}[i]$$

### B.9-2: SECOND COMPARTMENT

$$\frac{d}{dt}VD_{SP_2}[1] = (1-\Upsilon)\mho_{VSP}VD_{SP_1}[1] - \alpha VD_{SP_2}[1] - \mho^M_{VSP}VD_{SP_2}[1]$$

$$\frac{d}{dt}VD_{SP_2}[i=2,...,k-1] = (1-\Upsilon)\mho_{VSP}VD_{SP_1}[i] + \alpha VD_{SP_2}[i-1] - \alpha VD_{SP_2}[i] - \mho^M_{VSP}VD_{SP_2}[i]$$

$$\frac{d}{dt}VD_{SP_2}[i=k,...,n] = (1-\Upsilon)\mho_{VSP}VD_{SP_1}[i] + \alpha VD_{SP_2}[i-1] - \alpha VD_{SP_2}[i] - \mho^M_{VSP}VD_{SP_2}[i]$$

### B.9-3: THIRD COMPARTMENT

$$\frac{d}{dt}VD_{SP_3}[1] = \mho^M_{VSP}VD_{SP_2}[1] - \alpha VD_{SP_3}[1] - \mho^M_{VSP}VD_{SP_3}[1]$$

$$\frac{d}{dt}VD_{SP_3}[i=2,...,k-1] = \mho^M_{VSP}VD_{SP_2}[i] + \alpha VD_{SP_3}[i-1] - \alpha VD_{SP_3}[i] - \mho^M_{VSP}VD_{SP_3}[i]$$

$$\frac{d}{dt}VD_{SP_3}[i=k,...,n] = \mho^M_{VSP}VD_{SP_2}[i] + \alpha VD_{SP_3}[i-1] - \alpha VD_{SP_3}[i] - \mho^M_{VSP}VD_{SP_3}[i]$$

### B.9-4: FOURTH COMPARTMENT

$$\frac{d}{dt}VD_{SP}[1] = (1-\Upsilon)\mho^M_{VSP}VD_{SP_3}[1] - \alpha VD_{SP}[1] - \mho^F_{VSP}VD_{SP}[1] + \Upsilon\mho_{VSP}VD_{SP}[1]$$

$$\frac{d}{dt}VD_{SP}[i=2,...,k-1] = (1-\Upsilon)\mho^M_{VSP}VD_{SP_3}[i] + \alpha VD_{SP}[i-1] - \alpha VD_{SP}[i] - \mho^F_{VSP}VD_{SP}[i] + \Upsilon\mho_{VSP}VD_{SP}[i]$$

$$\frac{d}{dt}VD_{SP}[i=k,...,n] = (1-\Upsilon)\mho^M_{VSP}VD_{SP_3}[i] + \alpha VD_{SP}[i-1] - \alpha VD_{SP}[i] - \mho^F_{VSP}VD_{SP}[i] + \Upsilon\mho_{VSP}VD_{SP}[i]$$

## B.10: VACCINATED AND TREATED ACTIVE SMEAR-POSITIVE PULMONARY TB DISEASE

$$\frac{d}{dt}VT_{SP}[1] = -\alpha VT_{SP}[1] + \aleph_{VSP_0} z_{VD} \chi_{VD_{SP}} VD_{SP}[1] + \mho^{M}_{VSP} \Upsilon VD_{SP_3}[1] - \vartheta_{VT_{SP}} VT_{SP}[1] - \nu_{VT_{SP}} VT_{SP}[1]$$
$$-\psi_{VT_{SP}} VT_{SP}[1] - (1-q)\lambda VT_{SP}[1]$$

$$\frac{d}{dt}VT_{SP}[i=2,...,k-1] = \alpha VT_{SP}[i-1] - \alpha VT_{SP}[i] + \aleph_{VSP_0} z_{VD} \chi_{VD_{SP}} VD_{SP}[i] + \mho^{M}_{VSP} \Upsilon VD_{SP_3}[i] - \vartheta_{VT_{SP}} VT_{SP}[i]$$
$$-\nu_{VT_{SP}} VT_{SP}[i] - \psi_{VT_{SP}} VT_{SP}[i] - (1-q)\lambda VT_{SP}[i]$$

$$\frac{d}{dt}VT_{SP}[i=k,...,n] = \alpha VT_{SP}[i-1] - \alpha VT_{SP}[i] + \aleph_{VSP_0} z_{VD} \chi_{VD_{SP}} VD_{SP}[i] + \mho^{M}_{VSP} \Upsilon VD_{SP_3}[i] - \vartheta_{VT_{SP}} VT_{SP}[i]$$
$$-\nu_{VT_{SP}} VT_{SP}[i] - \psi_{VT_{SP}} VT_{SP}[i] - (1-q)\lambda VT_{SP}[i]$$

### B.11: VACCINATED AND ACTIVE SMEAR-NEGATIVE PULMONARY TB DISEASE

#### B.11-1: FIRST COMPARTMENT

$$\frac{d}{dt}VD_{SN_1}[1] = -\alpha VD_{SN_1}[1] + a_{VD_{EDF}[1]\to VD_{SN}[1]} \pi_{VD_{EDF}} VD_{EDF}[1] + a_{VD_{EDS}[1]\to VD_{SN}[1]} \pi_{VD_{EDS}} VD_{EDS}[1] - \mho_{VSN} VD_{SN_1}[1]$$

$$\frac{d}{dt}VD_{SN_1}[i=2,...,k-1] = \alpha VD_{SN_1}[i-1] - \alpha VD_{SN_1}[i] + a_{VD_{EDF}[i]\to VD_{SN}[i]} \pi_{VD_{EDF}} VD_{EDF}[i]$$
$$+a_{D_{EDS}[i]\to D_{SN}[i]} \pi_{D_{EDS}} D_{EDS}[i] - \mho_{VSN} D_{SN_1}[i]$$

$$\frac{d}{dt}VD_{SN_1}[i=k,...,n] = \alpha VD_{SN_1}[i-1] - \alpha VD_{SN_1}[i] + a_{VD_{EDF}[i]\to VD_{SN}[i]} \pi_{VD_{EDF}} VD_{EDF}[i]$$
$$+a_{VD_{EDS}[i]\to VD_{SN}[i]} \pi_{VD_{EDS}} VD_{EDS}[i] - \mho_{VSN} VD_{SN_1}[i]$$

#### B.11-2: SECOND COMPARTMENT

$$\frac{d}{dt}VD_{SN_2}[1] = (1-\Upsilon_2)\mho_{VSN} VD_{SN_1}[1] - \alpha VD_{SN_2}[1] - \mho^{M}_{VSN} VD_{SN_2}[1]$$

$$\frac{d}{dt}VD_{SN_2}[i=2,...,k-1] = (1-\Upsilon_2)\mho_{VSN} VD_{SN_1}[i] + \alpha VD_{SN_2}[i-1] - \alpha VD_{SN_2}[i] - \mho^{M}_{VSN} D_{SN_2}[i]$$

$$\frac{d}{dt}VD_{SN_2}[i=k,...,n] = (1-\Upsilon_2)\mho_{VSN} VD_{SN_1}[i] + \alpha VD_{SN_2}[i-1] - \alpha VD_{SN_2}[i] - \mho^{M}_{VSN} D_{SN_2}[i]$$

#### B.11-3: THIRD COMPARTMENT

$$\frac{d}{dt}VD_{SN_3}[1] = \mho_{VSN} VD_{SN_2}[1] - \alpha VD_{SN_3}[1] - \mho_{VSN} VD_{SN_3}[1]$$

$$\frac{d}{dt}VD_{SN_3}[i=2,...,k-1] = \mho_{VSN} VD_{SN_2}[i] + \alpha VD_{SN_3}[i-1] - \alpha VD_{SN_3}[i] - \mho_{VSN} VD_{SN_3}[i]$$

$$\frac{d}{dt}VD_{SN_3}[i=k,...,n] = \mho_{VSN} VD_{SN_2}[i] + \alpha VD_{SN_3}[i-1] - \alpha VD_{SN_3}[i] - \mho_{VSN} VD_{SN_3}[i]$$

#### B.11-4: FOURTH COMPARTMENT

$$\frac{d}{dt}VD_{SN}[1] = (1-\Upsilon_2)\mho^{M}_{VSN}VD_{SN_3}[1] - \alpha VD_{SN}[1] - \mho^{F}_{VSN}VD_{SN}[1] + \Upsilon_2\mho_{VSN}VD_{SN}[1]$$

$$\frac{d}{dt}VD_{SN}[i=2,...,k-1] = (1-\Upsilon_2)\mho^{M}_{VSN}VD_{SN_3}[i] + \alpha VD_{SN}[i-1] - \alpha VD_{SN}[i] - \mho^{F}_{VSN}VD_{SN}[i] + \Upsilon_2\mho_{VSN}VD_{SN}[i]$$

$$\frac{d}{dt}VD_{SN}[i=k,...,n] = (1-\Upsilon_2)\mho^{M}_{VSN}VD_{SN_3}[i] + \alpha VD_{SN}[i-1] - \alpha VD_{SN}[i] - \mho^{F}_{VSN}VD_{SN}[i] + \Upsilon_2\mho_{VSN}VD_{SN}[i]$$

### B.12: Vaccinated And Treated Active Smear-Negative Pulmonary TB Disease

$$\frac{d}{dt}VT_{SN}[1] = -\alpha VT_{SN}[1] + \aleph_{VSN_0}z_{VD}\chi_{VD_{SN}}VD_{SN}[1] + \Upsilon_2\mho^{M}_{VSN}VD_{SN_3}[1] - \vartheta_{VT_{SN}}VT_{SN}[1] - \nu_{VT_{SN}}VT_{SN}[1] - \psi_{VT_{SN}}VT_{SN}[1] - (1-q)\lambda VT_{SN}[1]$$

$$\frac{d}{dt}VT_{SN}[i=2,...,k-1] = \alpha VT_{SN}[i-1] - \alpha VT_{SN}[i] + \aleph_{VSN_0}z_{VD}\chi_{VD_{SN}}VD_{SN}[i] + \Upsilon_2\mho^{M}_{VSN}VD_{SN_3}[i] - \vartheta_{VT_{SN}}VT_{SN}[i] - \nu_{VT_{SN}}VT_{SN}[i] - \psi_{VT_{SN}}VT_{SN}[i] - (1-q)\lambda VT_{SN}[i]$$

$$\frac{d}{dt}VT_{SN}[i=k,...,n] = \alpha VT_{SN}[i-1] - \alpha VT_{SN}[i] + \aleph_{VSN_0}z_{VD}\chi_{VD_{SN}}VD_{SN}[i] + \Upsilon_2\mho^{M}_{VSN}VD_{SN_3}[i] - \vartheta_{VT_{SN}}VT_{SN}[i] - \nu_{VT_{SN}}VT_{SN}[i] - \psi_{VT_{SN}}VT_{SN}[i] - (1-q)\lambda VT_{SN}[i]$$

### B.13: Vaccinated And Active Non-Pulmonary TB Disease

#### B.13-1: First Compartment

$$\frac{d}{dt}VD_{NP_1}[1] = -\alpha VD_{NP_1}[1] + a_{VD_{EDF}[1]\to VD_{NP}[1]}\pi_{VD_{EDF}}VD_{EDF}[1] + a_{VD_{EDS}[1]\to VD_{NP}[1]}\pi_{VD_{EDS}}VD_{EDS}[1] - \mho_{VNP}VD_{NP_1}[1]$$

$$\frac{d}{dt}VD_{NP_1}[i=2,...,k-1] = \alpha VD_{NP_1}[i-1] - \alpha VD_{NP_1}[i] + a_{VD_{EDF}[i]\to VD_{NP}[i]}\pi_{VD_{EDF}}VD_{EDF}[i] + a_{VD_{EDS}[i]\to VD_{NP}[i]}\pi_{VD_{EDS}}VD_{EDS}[i] - \mho_{VNP}VD_{NP_1}[i]$$

$$\frac{d}{dt}VD_{NP_1}[i=k,...,n] = \alpha VD_{NP_1}[i-1] - \alpha VD_{NP_1}[i] + a_{VD_{EDF}[i]\to VD_{NP}[i]}\pi_{VD_{EDF}}VD_{EDF}[i] + a_{VD_{EDS}[i]\to VD_{NP}[i]}\pi_{VD_{EDS}}VD_{EDS}[i] - \mho_{VNP}VD_{NP_1}[i]$$

#### B.13-2: Second Compartment

$$\frac{d}{dt}VD_{NP_2}[1] = (1-\Upsilon_2)\mho_{VNP}VD_{NP_1}[1] - \alpha VD_{NP_2}[1] - \mho^{M}_{VNP}VD_{NP_2}[1]$$

$$\frac{d}{dt}VD_{NP_2}[i=2,...,k-1] = (1-\Upsilon_2)\mho_{VNP}VD_{NP_1}[i] + \alpha VD_{NP_2}[i-1] - \alpha VD_{NP_2}[i] - \mho^{M}_{VNP}VD_{NP_2}[i]$$

$$\frac{d}{dt}VD_{NP_2}[i=k,...,n] = (1-\Upsilon_2)\mho_{VNP}VD_{NP_1}[i] + \alpha VD_{NP_2}[i-1] - \alpha VD_{NP_2}[i] - \mho^{M}_{VNP}VD_{NP_2}[i]$$

B.13-3: THIRD COMPARTMENT

$$\frac{d}{dt}VD_{NP_3}[1] = \mho^{M}_{VNP}VD_{NP_2}[1] - \alpha VD_{NP_3}[1] - \mho^{M}_{VNP}VD_{NP_3}[1]$$

$$\frac{d}{dt}VD_{NP_3}[i=2,...,k-1] = \mho^{M}_{VNP}VD_{NP_2}[i] + \alpha VD_{NP_3}[i-1] - \alpha VD_{NP_3}[i] - \mho^{M}_{VNP}VD_{NP_3}[i]$$

$$\frac{d}{dt}VD_{NP_3}[i=k,...,n] = \mho^{M}_{VNP}VD_{NP_2}[i] + \alpha VD_{NP_3}[i-1] - \alpha VD_{NP_3}[i] - \mho^{M}_{VNP}VD_{NP_3}[i]$$

B.13-4: FOURTH COMPARTMENT

$$\frac{d}{dt}VD_{NP}[1] = (1-\Upsilon_2)\mho^{M}_{VNP}VD_{NP_3}[1] - \alpha VD_{NP}[1] - \mho^{F}_{VNP}VD_{NP}[1] + \Upsilon\mho_{VNP}VD_{NP}[1]$$

$$\frac{d}{dt}VD_{NP}[i=2,...,k-1] = (1-\Upsilon_2)\mho^{M}_{VNP}VD_{NP_3}[i] + \alpha VD_{NP}[i-1] - \alpha VD_{NP}[i] - \mho^{F}_{VNP}VD_{NP}[i] + \Upsilon\mho_{VNP}VD_{NP}[i]$$

$$\frac{d}{dt}VD_{NP}[i=k,...,n] = (1-\Upsilon_2)\mho^{M}_{VNP}VD_{NP_3}[i] + \alpha VD_{NP}[i-1] - \alpha VD_{NP}[i] - \mho^{F}_{VNP}VD_{NP}[i] + \Upsilon\mho_{VNP}VD_{NP}[i]$$

## B.14: VACCINATED AND TREATED ACTIVE NON-PULMONARY TB DISEASE

$$\frac{d}{dt}VT_{NP}[1] = -\alpha VT_{NP}[1] + \aleph_{VNP_0}z_{VD}\chi_{VD_{NP}}VD_{NP}[1] + \mho^{M}_{VNP}\Upsilon_2 VD_{VNP_3}[1] - \vartheta_{VT_{NP}}VT_{NP}[1] - \nu_{VT_{NP}}VT_{NP}[1]$$
$$-\psi_{VT_{NP}}VT_{NP}[1] - (1-q)\lambda VT_{NP}[1]$$

$$\frac{d}{dt}VT_{NP}[i=2,...,k-1] = \alpha VT_{NP}[i-1] - \alpha VT_{NP}[i] + \aleph_{VNP_0}z_{VD}\chi_{VD_{NP}}VD_{NP}[i] + \mho^{M}_{VNP}\Upsilon_2 VD_{VNP_3}[i] - \vartheta_{VT_{NP}}VT_{NP}[i]$$
$$-\nu_{VT_{NP}}VT_{NP}[i] - \psi_{VT_{NP}}VT_{NP}[i] - (1-q)\lambda VT_{NP}[i]$$

$$\frac{d}{dt}VT_{NP}[i=k,...,n] = \alpha VT_{NP}[i-1] - \alpha VT_{NP}[i] + \aleph_{VNP_0}z_{VD}\chi_{VD_{NP}}VD_{NP}[i] + \mho^{M}_{VNP}\Upsilon_2 VD_{VNP_3}[i] - \vartheta_{VT_{NP}}VT_{NP}[i]$$
$$-\nu_{VT_{NP}}VT_{NP}[i] - \psi_{VT_{NP}}VT_{NP}[i] - (1-q)\lambda VT_{NP}[i]$$

## B.15: VACCINATED AND CURED

$$\frac{d}{dt}VR[1] = -\alpha VR[1] + \psi_{VT_{EDF}} VT_{EDF}[1] + \psi_{VT_{EDS}} VT_{EDS}[1] + \psi_{VT_{SP}} VT_{SP}[1] + \psi_{VT_{SN}} VT_{SN}[1]$$
$$+\psi_{VT_{NP}} VT_{NP}[1] + \nu_{VD_{EDF}} VD_{EDF}[1] + \nu_{VD_{EDS}} VD_{EDS}[1] + \aleph_{VSP_0} \nu_{VD_{SP}} VD_{SP}[1]$$
$$+\aleph_{VSN_0} \nu_{VD_{SN}} VD_{SN}[1] + \aleph_{VNP_0} \nu_{VD_{NP}} VD_{NP}[1] + \nu_{VT_{SP}} VT_{SP}[1] + \nu_{VT_{SN}} VT_{SN}[1]$$
$$+\nu_{VT_{NP}} VT_{NP}[1] + \nu_{VT_{EDF}} VT_{EDF}[1] + \nu_{VT_{EDS}} VT_{EDS}[1] - (1-q)\lambda VR[1]$$
$$+\tau_{VS} \Xi VL_S[1] + \tau_{VF} \Xi VL_F[1]$$

$$\frac{d}{dt}VR[i = 2,...,k-1] = \alpha VR[i-1] - \alpha VR[i] + \psi_{VT_{EDF}} VT_{EDF}[i] + \psi_{VT_{EDS}} VT_{EDS}[i] + \psi_{VT_{SP}} VT_{SP}[i]$$
$$+\psi_{VT_{SN}} VT_{SN}[i] + \psi_{VT_{NP}} VT_{NP}[i] + \nu_{VD_{EDF}} VD_{EDF}[i] + \nu_{VD_{EDS}} VD_{EDS}[i]$$
$$+\aleph_{VSP_0} \nu_{VD_{SP}} VD_{SP}[i] + \aleph_{VSN_0} \nu_{VD_{SN}} VD_{SN}[i] + \aleph_{VNP_0} \nu_{VD_{NP}} VD_{NP}[i]$$
$$+\nu_{VT_{SP}} VT_{SP}[i] + \nu_{VT_{SN}} VT_{SN}[i] + \nu_{VT_{NP}} VT_{NP}[i] + \nu_{VT_{EDF}} VT_{EDF}[i]$$
$$+\nu_{VT_{EDS}} VT_{EDS}[i] - (1-q)\lambda VR[i] + \tau_{VS} \Xi VL_S[i] + \tau_{VF} \Xi VL_F[i]$$

$$\frac{d}{dt}VR[i = k,...,n] = \alpha VR[i-1] - \alpha VR[i] + \psi_{VT_{EDF}} VT_{EDF}[i] + \psi_{VT_{EDS}} VT_{EDS}[i] + \psi_{VT_{SP}} VT_{SP}[i]$$
$$+\psi_{VT_{SN}} VT_{SN}[i] + \psi_{VT_{NP}} VT_{NP}[i] + \nu_{VD_{EDF}} VD_{EDF}[i] + \nu_{VD_{EDS}} VD_{EDS}[i]$$
$$+\aleph_{VSP_0} \nu_{VD_{SP}} VD_{SP}[i] + \aleph_{VSN_0} \nu_{VD_{SN}} VD_{SN}[i] + \aleph_{VNP_0} \nu_{VD_{NP}} VD_{NP}[i]$$
$$+\nu_{VT_{SP}} VT_{SP}[i] + \nu_{VT_{SN}} VT_{SN}[i] + \nu_{VT_{NP}} VT_{NP}[i] + \nu_{VT_{EDF}} VT_{EDF}[i]$$
$$+\nu_{VT_{EDS}} VT_{EDS}[i] - (1-q)\lambda VR[i] + \tau_{VS} \Xi VL_S[i] + \tau_{VF} \Xi VL_F[i]$$

## C: FORCE OF INFECTION

$$\lambda = u\eta \frac{\sum_{i'=1,\ldots,n} \left( h_{D_{EDF}} D_{EDF}[i'] + h_{D_{EDS}} D_{EDS}[i'] + h_{D_{SP}} (D_{SP}[i'] + D_{SP_1}[i'] + D_{SP_2}[i'] + D_{SP_3}[i']) \right)}{\sum_{i'=1,\ldots,n} N[i']}$$

$$+ u\eta \frac{\sum_{i'=1,\ldots,n} \left( h_{D_{SN}} (D_{SN}[i'] + D_{SN_1}[i'] + D_{SN_2}[i'] + D_{SN_3}[i']) + h_{D_{NP}} (D_{NP}[i'] + D_{NP_1}[i'] + D_{NP_2}[i'] + D_{NP_3}[i']) \right)}{\sum_{i'=1,\ldots,n} N[i']}$$

$$+ u\eta \frac{\sum_{i'=1,\ldots,n} \left( h_{T_{EDF}} T_{EDF}[i'] + h_{T_{EDS}} T_{EDS}[i'] + h_{T_{SP}} T_{SP}[i'] + h_{T_{SN}} T_{SN}[i'] + h_{T_{NP}} T_{NP}[i'] \right)}{\sum_{i'=1,\ldots,n} N[i']}$$

$$+(1-VE_I)u\eta \frac{\sum_{i'=1,\ldots,n} \left( h_{D_{EDF}} VD_{EDF}[i'] + h_{D_{EDS}} VD_{EDS}[i'] + h_{D_{SP}} (VD_{SP}[i'] + VD_{SP_1}[i'] + VD_{SP_2}[i'] + VD_{SP_3}[i']) + \right)}{\sum_{i'=1,\ldots,n} N[i']}$$

$$+(1-VE_I)u\eta \frac{\sum_{i'=1,\ldots,n} \left( h_{D_{SN}} (VD_{SN}[i'] + VD_{SN_1}[i'] + VD_{SN_2}[i'] + VD_{SN_3}[i']) \right)}{\sum_{i'=1,\ldots,n} N[i']}$$

$$+(1-VE_I)u\eta \frac{\sum_{i'=1,\ldots,n} \left( h_{D_{NP}} (VD_{NP}[i'] + VD_{NP_1}[i'] + VD_{NP_2}[i'] + VD_{NP_3}[i']) \right)}{\sum_{i'=1,\ldots,n} N[i']}$$

$$+(1-VE_I)u\eta \frac{\sum_{i'=1,\ldots,n} \left( h_{T_{EDF}} VT_{EDF}[i'] + h_{T_{EDS}} VT_{EDS}[i'] + h_{T_{SP}} VT_{SP}[i'] + h_{T_{SN}} VT_{SN}[i'] + h_{T_{NP}} VT_{NP}[i'] \right)}{\sum_{i'=1,\ldots,n} N[i']}$$

## D: Population Of Each Age Group

$$N[i] = S[i] + WS[i] + L_F[i] + L_S[i] + D_{EDF}[i] + D_{EDS}[i] + D_{SP}[i] + D_{SP_1}[i] + D_{SP_2}[i] + D_{SP_3}[i] + D_{SN}[i]$$
$$+ D_{SN_1}[i] + D_{SN_2}[i] + D_{SN_3}[i] + D_{NP}[i] + D_{NP_1}[i] + D_{NP_2}[i] + D_{NP_3}[i] + T_{EDF}[i] + T_{EDS}[i] + T_{SP}[i]$$
$$+ T_{SN}[i] + T_{NP}[i] + R[i] + VS[i] + VL_F[i] + VL_S[i] + VD_{EDF}[i] + VD_{EDS}[i] + VD_{SP}[i] + VD_{SP_1}[i]$$
$$+ VD_{SP_2}[i] + VD_{SP_3}[i] + VD_{SN}[i] + VD_{SN_1}[i] + VD_{SN_2}[i] + VD_{SN_3}[i] + VD_{NP}[i] + VT_{EDF}[i]$$
$$+ VT_{EDS}[i] + VD_{NP_1}[i] + VD_{NP_2}[i] + VD_{NP_3}[i] + VT_{SP}[i] + VT_{SN}[i] + VT_{NP}[i] + VR[i]$$

## IV. MODEL SPECIFICATIONS:

The following table summarizes the parameters of this model and their values per the above discussion of these parameters. The values of the parameters representing proportions are presented as percentages.

[Table 1 extracted for submission]

## V. WORLD HEALTH ORGANIZATION REGIONS:

Countries classified by the WHO as having a high burden of tuberculosis are listed in bold type.

SUB-SAHARAN AFRICA, HIGH[2] HIV PREVALENCE (AFRH): N = 22

Botswana, Burundi, Cameroon, Central African Republic, Congo, Côte d'Ivoire, **Democratic Republic of Congo**, **Ethiopia**, Gabon, **Kenya**, Lesotho, Malawi, **Mozambique**, Namibia, **Nigeria**, Rwanda, **South Africa**, Swaziland, **Uganda**, **United Republic of Tanzania**, Zambia, **Zimbabwe**

SUB-SAHARAN AFRICA, LOW HIV PREVALENCE (AFRL): N = 24

Algeria, Angola, Benin, Burkina Faso, Cape Verde, Chad, Comoros, Equatorial Guinea, Eritrea, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Madagascar, Mali, Mauritania, Mauritius, Niger, Sao Tome & Principe, Senegal, Seychelles, Sierra Leone, Togo

LATIN AMERICAN REGION (AMR): N = 42

Anguilla, Antigua & Barbuda, Argentina, Bahamas, Barbados, Belize, Bermuda, Bolivia, **Brazil**, British Virgin Islands, Cayman Islands, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Montserrat, Netherlands Antilles, Nicaragua, Panama, Paraguay, Peru, Puerto Rico, Saint Kitts a

[2] Annual HIV infection rate $\geq$ 4% among those 15-49 years of age in 2004 61. WHO (2007) Global Tuberculosis Control: Surveillance, Planning, Financing. in *WHO Report 2007* (World Health Organization (WHO), Geneva), p 270.

nd Nevis, Saint Lucia, St Vincent and the Grenadines, Suriname, Trinidad and Tobago, Turks & Caicos Islands, Uruguay, US Virgin Islands, Venezuela

EASTERN EUROPEAN REGION (EEUR): N = 18

Armenia, Azerbaijan, Belarus, Bulgaria, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Romania, **Russian Federation**, Tajikistan, Turkey, Turkmenistan, Ukraine, Uzbekistan

ESTABLISHED MARKET ECONOMIES AND CENTRAL EUROPEAN REGION (EME-CEUR): N = 41

Albania, Andorra, Australia, Austria, Belgium, Bosnia and Herzegovina, Canada, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Malta, Monaco, Montenegro, Netherlands, New Zealand, Norway, Poland, Portugal, San Marino, Serbia, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland, The Former Yugoslav Republic of Macedonia, United Kingdom, USA

EASTERN MEDITERRANEAN REGION (EMR): N = 22

**Afghanistan**, Bahrain, Djibouti, Egypt, Iraq, Islamic Republic of Iran, Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Morocco, Oman, **Pakistan**, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates, West Bank & Gaza Strip, Yemen

SOUTH AND SOUTHEAST ASIAN REGION (SEAR): N = 11

**Bangladesh**, Bhutan, Democratic People's Republic of Korea, **India**, **Indonesia**, Maldives, **Myanmar**, Nepal, Sri Lanka, **Thailand**, Timor-Leste

WESTERN PACIFIC REGION (WPR): N = 30

American Samoa, Brunei Darussalam, **Cambodia**, **China**, Cook Islands, Fiji, French Polynesia, Guam, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia, Mongolia, Nauru, New Caledonia, Niue, Northern Mariana Islands, Palau, Papua New Guinea, **Philippines**, Republic of Korea, Samoa, Solomon Islands, Tokelau, Tonga, Tuvalu, Vanuatu, **Viet Nam**, Wallis & Futuna Islands

# VII. ESTABLISHING REGIONAL PARAMETERS:

Regional parameters are established by summing country-specific estimates for each quantity at a regional level. The number of countries within each region ($N_{Country}$) are as follows: AFRH, 22; AFRL, 24; AMR, 42; EEUR, 18; EME/CEUR, 41; EMR, 22; SEAR, 11; and WPR, 29. Sources for data are in the WHO Global Tuberculosis Control Report for 2007 (61). In the WHO Report, data for countries in the Established Market Economies and Central European Region (EME/CEUR) were incorporated into several of the other 7 regions, based upon geographic location. For the purposes of this model, data associated with these countries have been reassigned to the EME/CEUR region.

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## FIGURE CAPTIONS

**Figure 1.** Complete model schematic including tuberculosis dynamics and novel interventions

**Figure 2.** Graphical representation of diagnostic model. The left panel demonstrates the four compartments of disease; with the inclusion of novel diagnostics, the second and third compartments are short circuited, as shown in the right panel.

## TABLE CAPTIONS

**Table 1.** Demographic and TB Transmission Parameter Descriptions