Review of TB research in China

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Abstract. The original Paper suggests that the study should be based age-structure SEIR Model in order to analysis TB in mainland China. However, In this review, a SIR model based on no latent population and dynamic health index is introduced to refine the model. Advanced Internet self diagnosis and advanced health facility can detect patients when they show slight symptom, which can isolates the patients before they are sick and infectious.That is the assumption to remove the latent component of the model. The dynamic health index is that a dynamic index growing with time, which indicates the improvement of medical facility and society health environment. Another assumption is that health index grows with time. This paper test the different models to show the effect of each additional component of the model and refine it.

Keywords: vaccination coverage ,TB, dynamic health index

1 Introduction:

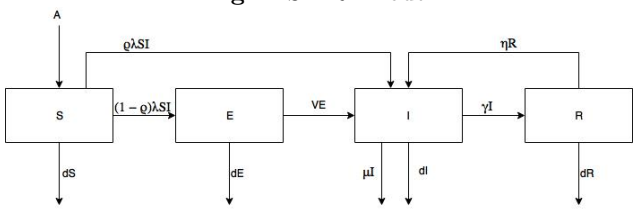
Smallpox is believed to have been acquired by humans originally as a zoonosis from a terrestrial African rodent between 16,000 and 68,000 years ago, well before the dawn of agriculture and civilization.After vaccination campaigns throughout the 19th and 20th centuries, the WHO certified the global eradication of smallpox in 1980.[1] The vaccine technically solves the problem existed 10 thousands years ago. There are thousand hundreds diseases inside the human world,which threat people's health.But immune system of body defends the diseases like a great fire wall. People who infected with HIV die of broken down of immune system rather than HIV itself. So the vaccine is the patch to the immune system. Vaccines avert between 2 and 3 million deaths each year.[2] It takes around 100 dollars and half day to get TB vaccine, but more than 20000 dollars and years to cure TB patients.The review starts with vaccine to study how it affect the model.
In the second section, to study the transmission dynamics of TB, original model are decomposed to several different models. Each model focuses on one additional function.SEIR1 is the simplest model eliminated the age structure.SEIR2 is the model with two age groups with changing immunity rate of the BCG vaccine $\varphi(t)$ to investigate the role of immunity rate on transmission process.By exploring the more background of vaccine, the report shows wide TB vaccine coverage in China is required for infant TB protection around 1985, which indicates the changing immunity rate is stable since then. So more complex model is necessary. SEIR3 is the original model with three age groups, which can detect the effect of different infectious and recovery rates of each age group. And the complete SEIR model is implemented numerically to simulate the annual TB data from WHO from 2005 to 2016. However, result of the paper is not reachable and indicate wrong trend of epidemic. In section 3, a population model is introduced to study the correctness of the global parameter about the population changing rate. By comparing the statistics of the model and investigate the TB treatment in China, the latent component of model is eliminated and the dynamic health index is introduced to fit the data, which is supported by data collection and data fitting.In the end, the review gives a prediction of when the epidemic dies down to WHO level.

2 Models and data fitting:

In this section,two deterministic TB models are introduced—simplest model SEIR1 and model with dynamic immunity rate SEIR2.Two models can neither fit the data good enough, which indicates the necessity of

a more complexed model. The first model is SEIR model in the figure 1 without age structure. Supposing the entire population is classified into four classes: susceptible (S), latency (E), infectious (I) and recovered (R).The susceptible class belongs to just one class(S).Birth rate is denoted by A,Moreover,the health index ξ and BCG vaccine is constant in this model. The assumptions for the model is the dynamic transmission of TB in China without age groupings. People infect with TB and recover from TB with the same rate. And people dies with the natural death rate. If the model is feasible, the age structure and vaccine rate will show trivial function in controlling the epidemic.

Fig. 1. SEIR1 Model



$$\frac{dS}{dt} = A - \lambda SI - dS \tag{1}$$

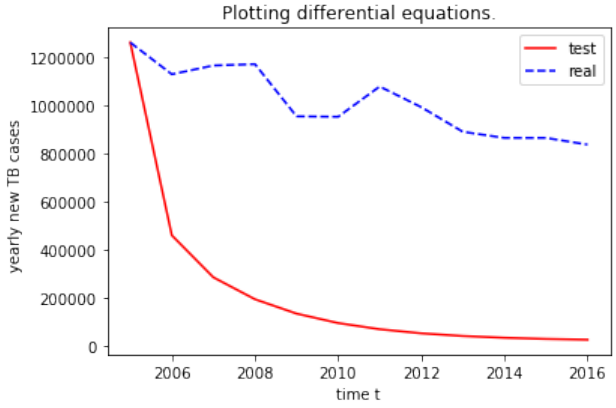
$$\frac{dE}{dt} = (1-\rho)(1-\varphi)\lambda SI - \nu E - dE \tag{2}$$

$$\frac{dI}{dt} = \rho\lambda(1-\varphi)SI + \nu E + \eta R - dI - \mu I - (1+\xi)\gamma I \tag{3}$$

$$\frac{dR}{dt} = (1+\xi)\gamma I - \eta R - dR \tag{4}$$

$$\tag{5}$$

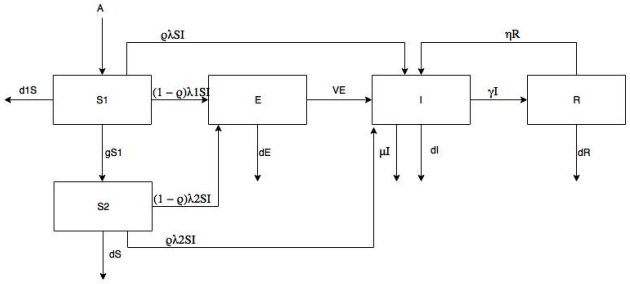
Fig. 2. SEIR1 test



The model can not fit into data well. By reading the reference of China vaccine report according to WHO, the vaccine can only protect child for 10 to 15 years after the first injection and protection of BCG for adult

is trivial.So BCG vaccine can not protect people of TB disease for the whole life span. Because of that,the morbidity among adult is relative higher. Moreover,the transmission method of TB depends on air-human and human to human. Adult have larger activity area and less immunity, which indicates adults are more vulnerable than children to TB. And that is why it is necessary to introduce a more complex model including the two susceptible class: child/adult according to different immunity to TB.

Fig. 3. SEIR2 Model



$$\frac{dS_1}{dt} = A - \lambda_1 S_1 I - dS_1 \tag{6}$$

$$\frac{dS_2}{dt} = \lambda_1 S_1 I - \lambda_2 S_2 I - dS_2 \tag{7}$$

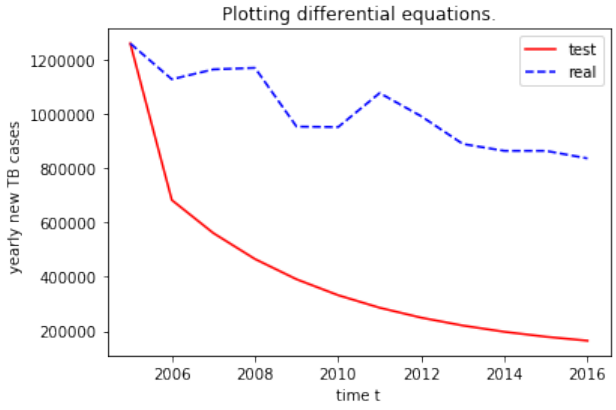
$$\frac{dE}{dt} = (1-\rho)(1-\varphi)\lambda_1 S_1 I + (1-\rho)\lambda_2 S_2 I - \nu E - dE \tag{8}$$

$$\frac{dI}{dt} = \rho(1-\varphi)\lambda_1 S_1 I + \rho\lambda_2 S_2 I + \nu E + \eta R - dI - \mu I - (1+\xi)\gamma I \tag{9}$$

$$\frac{dR}{dt} = (1+\xi)\gamma I - \eta R - dR \tag{10}$$

$$\tag{11}$$

Fig. 4. SEIR2 test

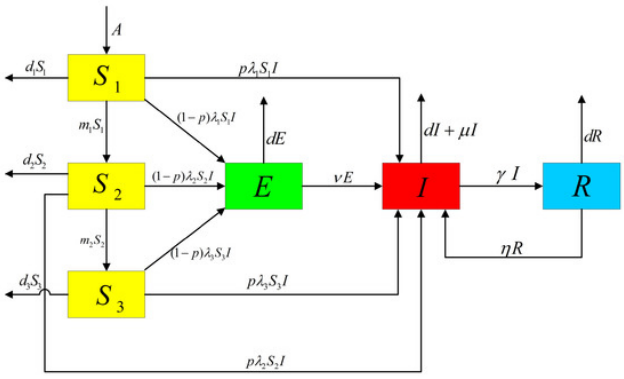


The model performs better but still can not fit into data.Epidemic dies far more rapid than the reality situation.The vaccine coverage φ is a very sensitive parameter which can change experiment entirely. If φ is low than 0.8, the government will lost control of epidemic and the TB cases number grows exponentially.By reading the reference of China vaccine report of WHO, the vaccine coverage rate has met 90% since 1985 and remain stable around 95% nowadays.Although BCG vaccine injection rate is among the most effective parameters, it stays constant in the model. Additionally, despite of implementing two age groups, the morbidity still drop far rapidly comparing to the reality data. This shows the infected groups could have higher infectious rate. While senior tends to be more infectious than the middle aged. So it is reasonable to introduce a more complex model including the three susceptible class according to different age group: childhood (S1), middle-aged (S2), and senior (S3).

3 Models and data fitting:

The SEIR3 model is introduced with three age groups, childhood(S1),adult(S2),senior(S3). It is the original model in the paper , assuming child ,adult, senior have different possibility to be infected and infect others.And senior have the most serious infectious rate. 95% people contacted TB are transfered into latent component while 5% are transfered to infectious component directly.Infectious rate of child is λ_1, while the death rate is d1.Infectious rate of adult is λ_2, while the death rate is d2. Infectious rate of senior is λ_3, while the death rate is d3. This model focuses on the different infectious/recovery rate of each age group. These are the most sensitive parameters in this model. However, the latent population and recovered population are arbitrary number guessed by writers in the original paper.

Fig. 5. SEIR3 Model



$$\frac{dS_1}{dt} = A - \lambda_1 S_1 I - d_1 S_1 \tag{12}$$

$$\frac{dS_2}{dt} = \lambda_1 S_1 I - \lambda_2 S_2 I - d_2 S_2 \tag{13}$$

$$\frac{dS_3}{dt} = \lambda_2 S_2 I - \lambda_3 S_3 I - d_3 S_3 \tag{14}$$

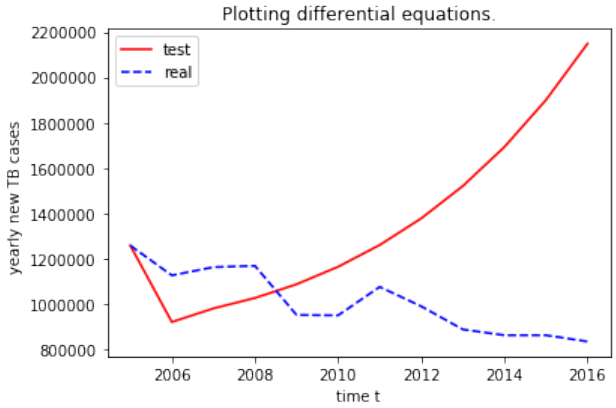
$$\frac{dE}{dt} = (1-\rho)(1-\varphi)\lambda_1 S_1 I + (1-\rho)\lambda_2 S_2 I + (1-\rho)\lambda_3 S_3 I - \nu E - dE \tag{15}$$

$$\frac{dI}{dt} = \rho(1-\varphi)\lambda_1 S_1 I + \rho\lambda_2 S_2 I + \rho\lambda_3 S_3 I + \nu E + \eta R - dI - \mu I - (1+\xi)\gamma I \tag{16}$$

$$\frac{dR}{dt} = (1+\xi)\gamma I - \eta R - dR \tag{17}$$

$$\tag{18}$$

Fig. 6. SEIR3 test



The result of the paper is unreachable despite of all parameter are checked. First fact, the Infectious component drops dramatically comparing to reality.Second fact, the model goes to infinity after some point. Third fact, the trend of the model is wrong. In order to answer these problems, it is necessary to testify the parameters first and rethink the assumption of the model. The model has very sensitive parameters, such as the infectious rate and the recovery rate, the trend of epidemic will change dramatically even the environment parameter changes slightly. So several parameter tests are introduced to testify the global parameters such as growth rate, birth/death rate. After experiment of the parameters, the assumption of the SEIR3 model are modified according to real data to refine it.

The figure 7 shows the population growth rate from 2005 to 2016. The growth model uses growth/death rate in the paper to fit the data from the National Bureau of Statistics of China. Then compare the population computed in the SEIR3 model.The figure shows the global parameter is correct as the enough overlap of the curves. The figure 8 shows the death/birth rate, which is visually constant. This supports the global parameter is correct in another view. To modify the original assumption,latent component is removed and a dynamic health index function is introduced to refined the curve in the SIR4 model after hundreds times experiments. New assumption is there is no latent cases and the health index ξ is changing.

Fig. 7. Population test

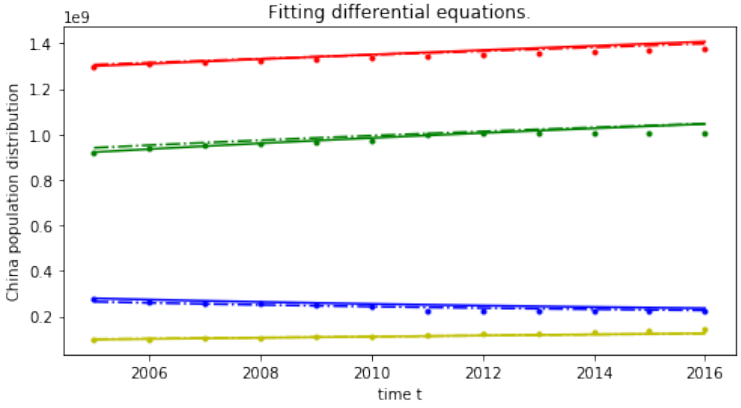
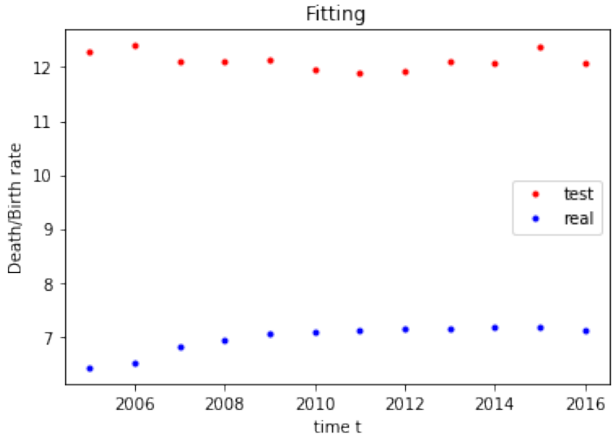
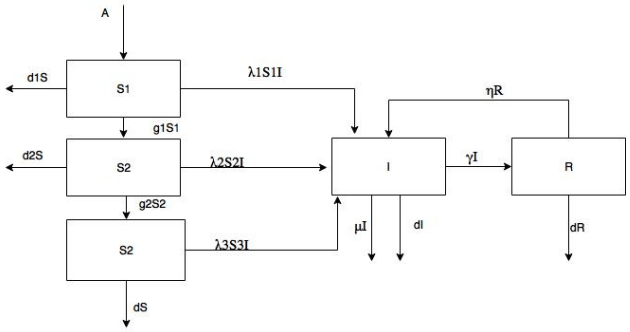


Fig. 8. Birth/Death rate



The SIR4 model catches much more variation comparing with the model in the paper. First, the Infectious component stop dropping dramatically after removing the latent component.This evidence can be explained by new treatment method and short course chemotherapy. For the slightly infected patients, they are detected early and isolated at home with single room. For the vitally infected patients, they are not infectious anymore after two weeks chemotherapy. Probability of infection is low and the instant treatment and isolation after discovery can support the assumption. Second, the model stops going to infinity after introducing the health index which indicates the enforcement of treatment and development of public health. No matter the increase of the recovery rate and decrease of infectious rate, these can all be concluded into growth of health index. Improvement of hospital facility, less people spitting to the ground but swallowing it,increasing family income are all evidences counted as health index to support the assumption. Third, the trend of the model fits and the new report case will drop more and more slowly when less infectious case are left untreated.The next step is to use LSE to fit the data better and evaluate the confidence interval of the curve.But let's see when the model will reach the WHO TB level.

Fig. 9. SIR4 model



$$\frac{dS_1}{dt} = A - \lambda_1 S_1 I - d_1 S_1 \tag{19}$$

$$\frac{dS_2}{dt} = \lambda_1 S_1 I - \lambda_2 S_2 I - d_2 S_2 \tag{20}$$

$$\frac{dS_3}{dt} = \lambda_2 S_2 I - \lambda_3 S_3 I - d_3 S_3 \tag{21}$$

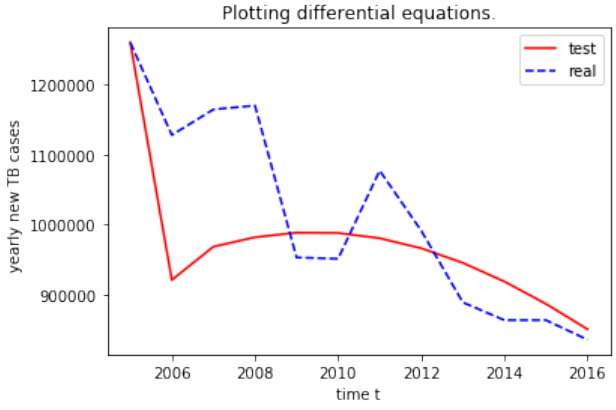
$$\frac{dI}{dt} = (1-\varphi)\lambda_1 S_1 I + \lambda_2 S_2 I + \lambda_3 S_3 I + \nu E + \eta R - dI - \mu I - (1+\xi)\gamma I \tag{22}$$

$$\frac{dR}{dt} = (1+\xi)\gamma I - \eta R - dR \tag{23}$$

$$\frac{d\xi}{dt} = c_1 f(t) \tag{24}$$

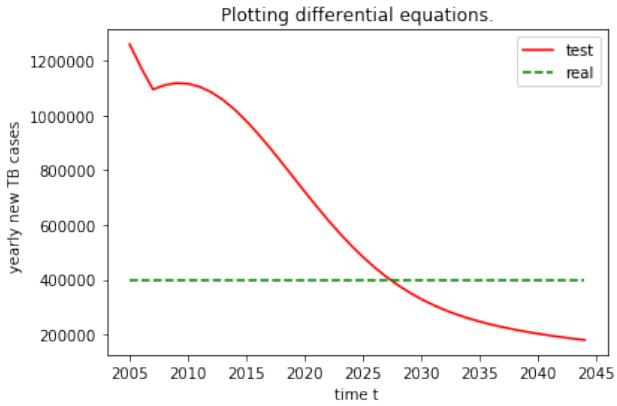
$$\tag{25}$$

Fig. 10. SIR4 test



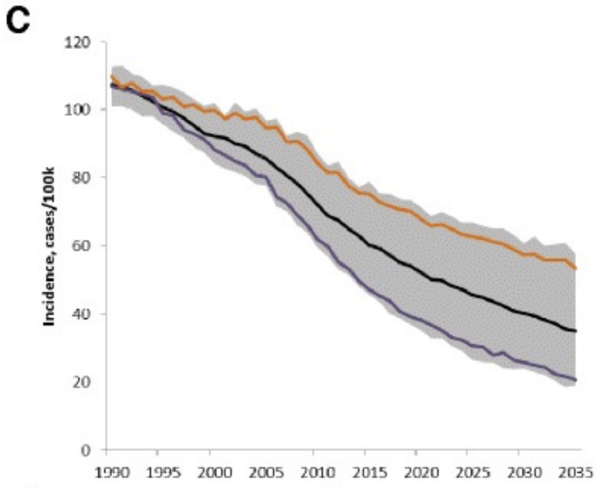
The model shows the epidemic will be controlled into WHO level around 2027 year with SIR3. If the government put more effort in recovery rate and controlling the infectious rate of TB, the epidemic could be controlled before 2025. The SIR4 model gives the similar prediction in the original paper and paper "Tuber-

Fig. 11. SIR4 test



culosis control strategies to reach the 2035 global targets in China: the role of changing demographics and reactivation disease".The figure 12 is the prediction per 100K population.

Fig. 12. TB prediction



To sum up, this review presents several simplified SEIR models and one refined SIR model to fit into reality data. The age-structure is reasonable to classify different infectious/recovery rate group. The latent population is testified to trivial according to this model.That is the assumption to remove the latent component of the model. And dynamic health index is another assumption that help fit the data,which assumes health index grows with time. In the prediction part,the SIR model gets the similar result that epidemic can be control around 2025 to 2030. The similar prediction is also advised by another paper named "Tuberculosis control strategies to reach the 2035 global targets in China: the role of changing demographics and reactivation disease".

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