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Research article

Parameter estimation of modeling schistosomiasis transmission for four provinces in China

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Abstract: According to monitoring data of Anhui, Jiangxi, Hubei, Jiangsu Provinces, in this paper the transmission of schistosomiasis is studied based on Barbour's mathematical model. The values of the basic reproduction number and key parameters are obtained with two methods. The first method is to calculate directly by using parameter values in references. The second one is to estimate parameter values by the methods of noise measurement and data smoothing and then to obtain new values of basic reproduction number. Comparing these two methods, we found the second method is good to fit the data. This parameter values can be used as reference values in other provinces. Finally, some numerical simulations are carried out to discuss the development trend of prevalence of humans and snails in each province. It is found that schistosomiasis in four provinces is expected to be eliminated with the improvement or maintenance of the standards of prevention and control. Furthermore, the time needed is different in the different four provinces.

Keywords: schistosomiasis; Barbour's model; basic reproduction number; parameter estimation.

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1. Introduction

Schistosomiasis is one of the major parasitic diseases in China, which has caused serious damage in our country. Although the founding of new China made great achievements for the investigation and prevention work of the schistosomiasis epidemiology, schistosomiasis is still a serious public health problem in parts of China at present. Anhui, Jiangxi, Hubei and Jiangsu, as the focus endemic provinces of schistosomiasis in China, have reached the criterion of basic elimination of schistosomiasis after long-term prevention. However, due to the society, natural environment and other factors, schistosomiasis in those provinces has some recovery and rebound.

Anhui province is located in the downstream of Yangtze and Huaihe River in North China, and schistosomiasis epidemic is more serious. The schistosomiasis endemic areas are mainly distributed on both sides of the Yangtze River, in the mountain areas of South Anhui province and beside the Lake Gaoyou ([22]).

In Jiangxi province, after years' effort of prevention and treatment, the epidemic situation is still serious, and schistosomiasis control task is still arduous. The reasons are that the screw area of Poyang Lake region is vast, the epidemic factors are complex, and the sources of infection have not been well controlled ([4]). Schistosomiasis in Hubei province has been prevalent for at least 2100 years, and has been effectively controlled after many years of large-scale prevention and control ([3]).

In Jiangsu province, the epidemic situation of schistosomiasis has been effectively controlled because of the large-scale prevention carried on since the fifties of the 20th century. However, Jiangsu province is located in the lower reaches of the Yangtze River, the flood and other natural factors have caused rebound of schistosomiasis endemic in the whole province ([20]).

At present, the prevention and control work in the four provinces are at different stages, and the measures of the implementation of prevention and control work in different provinces should be adapted to local conditions to achieve different objectives. The Epidemic situations of schistosomiasis in the four provinces are affected by varying natural environmental factors. For example, the influence of lake and marshland along the Yangtze River on prevention and control work is stronger than the influence of the surround area and the lower reaches. Hence, the reversal of schistosomiasis endemic should not be ignored. In summary, it requires a rather long period to completely reach the goal of eliminating schistosomiasis Yangtze River beach areas in China.

The prevalence rate of humans, the infection rate of snails, the changes of snail density of different monitoring sites in the four provinces from 2005 to 2010 are shown as follows (Figure 1-3).

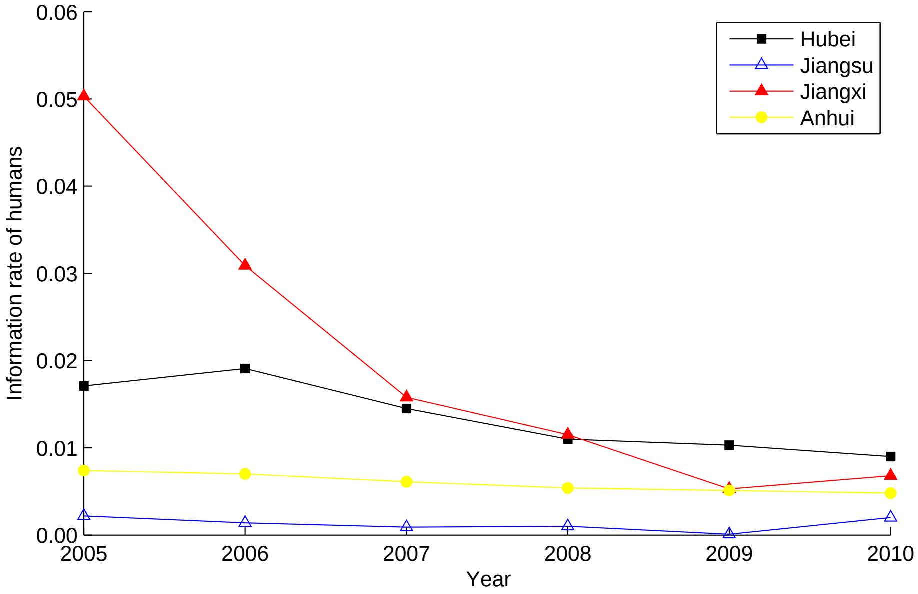

Figure 1. The prevalence rate of humans of four provinces from 2005 to 2010.

The green, red, black, and blue lines in Figure 1-3 represent the change trajectories of some relevant factors in Anhui, Jiangxi, Hubei, Jiangsu province, respectively. Figure 1-3 indicate the trajectories of

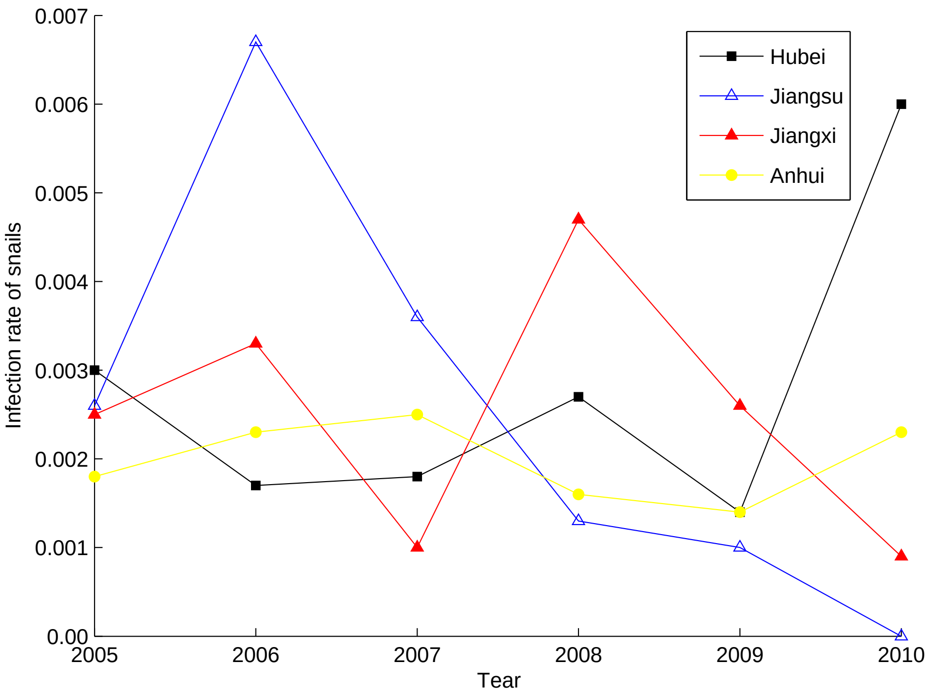

Figure 2. The infection rate of snails of four provinces from 2005 to 2010.

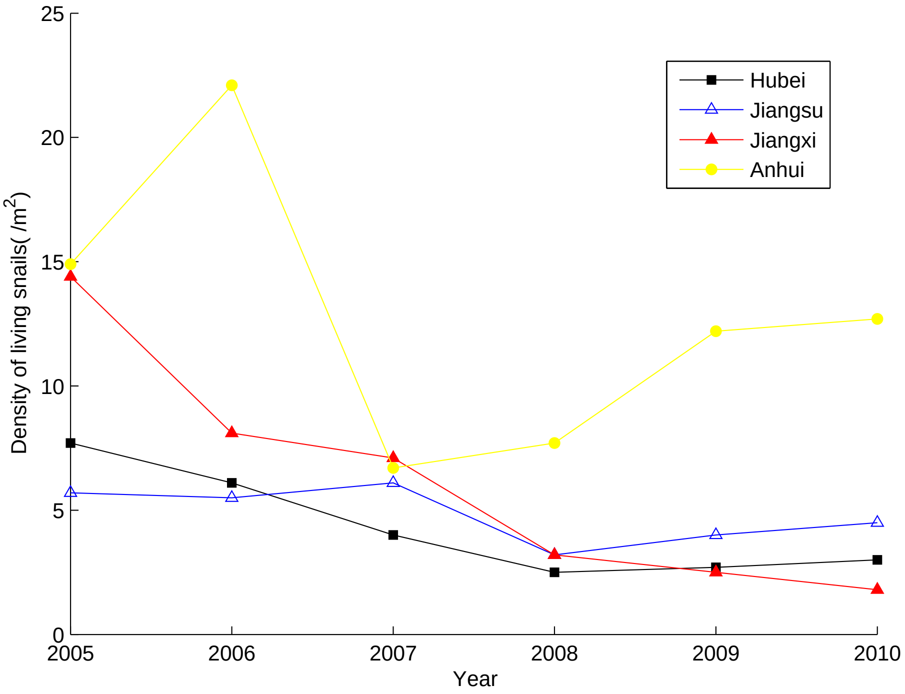

Figure 3. The changes of snail density of four provinces from 2005 to 2010.

the prevalence rate of humans, the infection rate of snails and the snail density of monitoring sites in four provinces in 2005-2010, respectively.

The main purpose of this paper is combining monitoring data with mathematical model to estimate some transmission rates and then to discuss these differences on the dynamic behavior of schistosomiasis in different four provinces.

2. Mathematical model

Mathematical model can describe the actual transmission process of schistosomiasis, and has been regarded as a powerful tool to explore the complex relationship in the process of the transmission of schistosomiasis for a long time. In spite that the values of the parameters in mathematical model change with place and times, their meaning in physiology, biology and society behalf are always the same. Macdonald had improved the famous Ross malaria model and proposed the first schistosomiasis deterministic differential equation model, namely Macdonald model in the 1950s ([11]). The model laid the foundation for the subsequent mathematical model of schistosomiasis transmission dynamics, and put forward the concept of ”basic reproduction number”, which is still widely used today for a wide variety of diseases. An advantage of Macdonald model is that it can make the direct reflection of the influence of the average worm burden on snail infection rate, and even on the whole transmission process. However, the average worm burden is not easy to investigate and estimate in practice. In 1966, based on Macdonald's model, Barbour replaced the change rate of worm burden with the change rate that reflects the prevalence rate of definitive host ([1]). The advantage of this model is that as long as the prevalence rate of local human host, the inflected snail prevalence, the density of human host and snails are known, we can estimate the related factors of schistosomiasis and the values of related parameters through the model, and therefore manage to do some further analysis and computation of prevalence rate ([9]).

Using Barbour's model and the concept of the basic reproduction number R_0, Wu revealed clearly the characteristics and the inherent spread rules of schistosomiasis ([19]), predicted and evaluated the effect of various prevention and control measures of schistosomiasis. The main parameters in this model, a and b are difficult to quantify, as it's also difficult to investigate and collect them and be directly used to calculate the basic reproduction number nowadays. The two parameters could only be estimated indirectly through the equilibrium prevalence rate or the equilibrium state of the disease spread. This shows that some design of parameters in this model still need to be further improved. Furthermore, the prediction and evaluation in theory must be combined with practice, tested and corrected by practice. Gao had studied the characteristics of schistosomiasis transmission in Xingzi County, Jiujiang City Liao Nan Xiang, Jiangxi Province using Barbour's model to calculate the basic reproduction number ([7]). This research is carried out in a closed village, but villages are always connected with each other in actual situation, and human host and snails will move between the neighboring villages.

Here, motivated by the Gao's paper we study the transmission of schistosomiasis by monitoring data and Barbour's model in four provinces. Because variables in Barbour's model can be monitored in practice, and the previous work has confirmed that it is consistent with the dynamic behavior of schistosomiasis transmission, we choose Barbour's model. In 1965, Barbour established two differential equations based on Ross malaria model, reflecting the change rates of prevalence rate of human host and the infection rate of snails, respectively, and designed the related parameters. The corresponding model is as following ([19]):

$$\begin{cases} \frac{dP}{dt} = a\Delta y(1-P) - gP, \\ \frac{dy}{dt} = b(\frac{\Sigma}{\Delta})P(1-y) - \mu y. \end{cases} \tag{2.1}$$

The parameters are described as follows:

a	-the incidence rate of people at unit density of infected snails
Δ	-the density of snails
y	-the proportion of infected snails
b	-the rate at which an infected people causes snail infections
P	-the prevalence rate of infection in people population
g	-the recovery rate for people infections
Σ	-the density of population
μ	-per capita death rate of infected snails

Both human host and snails are divided into infected (P and y) and uninfected ($1-P$ and $1-y$) in (2.1). The population and snail populations were assumed to be constant closed systems, in which the birth and death rates are equal. The mortality rate of human host is very small and is negligible in the system, and the dead are compensated by the same amount of newborn snails at any time so that the death of uninfected snails is also omitted in the equation. In addition, it is easy to see from the equations that, the difference of P, y, Δ and Σ will result in different values of a, b.

3. Basic reproduction number R_0

Based on its biological meanings the basic reproduction number can be defined by

$$R_0 = \frac{ab\Sigma}{g\mu}.$$

In the above formula, infectious definitive hosts with density Σ can cause $b\Sigma$ snail infections in their lifetimes $\frac{1}{g}$. These snails can infect $\frac{ab\Sigma}{g\mu}$ definitive hosts in their lifetimes $\frac{1}{\mu}$. This formula gives the total number of second offspring of infectious human infected by infectious snails during their lifetimes in susceptible human populations.

In our previous work, the stability analysis of the system (2.1) has been completed ([12]). The results show that schistosomiasis transmission will gradually disappear if $R_0 < 1$. When $R_0 > 1$, the spread of disease will continue until to a certain level of balance. That means the ultimate goal of disease control is to make the basic reproduction number less than 1 through the influence of the relevant parameters, and then to make the transmission disappear finally. In [12], numerical simulation did not performed because there was no data at that time. In the paper, based on monitoring data parameter estimation and simulation will be carried out.

From the formula, we can see parameters a and b are key to calculate the basic reproduction number R_0. However, to obtain the values of a and b is not easy. Ross had used R_0' instead of R_0.

$$R_0' = \frac{1}{(1-\overline{y})(1-\overline{P})}.$$

When the spread develops to a certain stage, the local epidemic can be seen as steady state. At this time, the prevalence of infection in humans and snails can be think as the equilibrium values in the

Table 1. Transmission indicators of schistosomiasis in Anhui province

Year	$\overline{P}$	$\overline{y}$	Δ	R_0'	a	b
2005	0.0074	0.0018	14.9	1.0093	0.00019	0.004591
2006	0.0070	0.0023	22.1	1.0094	0.00009	0.040026
2007	0.0061	0.0025	6.7	1.0087	0.00025	0.003481
2008	0.0054	0.0016	7.7	1.0070	0.00030	0.002890
2009	0.0051	0.0014	12.2	1.0065	0.00020	0.004240
2010	0.0048	0.0023	12.7	1.0071	0.00011	0.007712

system (2.1). Hence, the prevalence rate of humans ($\overline{P}$) and the infection rate of snails ($\overline{y}$) are as following

$$\overline{P} = \frac{(ab\Sigma - \mu g)\Delta}{b\Sigma(g + a\Delta)},$$
$$\overline{y} = \frac{ab\Sigma - \mu g}{a(b\Sigma + \mu\Delta)}.$$

The values of these two prevalence can obtained from the monitoring data. Then R_0' can be calculated by $\overline{P}$ and $\overline{y}$.

Remark: In fact, from the formula of R_0', it is obvious that R_0' is certainly greater than 1. It's impossible to make R_0' smaller than 1 because the prevalence rate of humans and snails $\overline{P}$ and $\overline{y}$ are both positive number. This result does not conform with the actual situation. The existence of patients does not necessarily mean that schistosomiasis will continue. Especially in the situation of no-mass transmission, the basic reproduction number R_0' may not explain the actual phenomenon quite well.

3.1. Method 1: Calculate directly

According to the calculation method in the reference ([19]), the basic reproduction number R_0' and the key parameters a and b can be obtained. From the national monitoring sites in Anhui, Jiangxi, Hubei, Jiangsu provinces ([2, 4, 20, 22]), the values of $\overline{P}$, $\overline{y}$ and Δ can be obtained. In order to obtain the values of the combined parameters a and b, we get the data of the population density (Σ) of in Anhui, Jiangxi, Hubei, Jiangsu provinces from related references, which are, respectively, 4.35 people $/m^2$, 0.1 people $/m^2$, 127 people $/m^2$, 1.09 people $/m^2$ ([3, 8, 10, 18, 20]). The average infection duration of humans is 4 years ($g = \frac{1}{1460} = 0.00068$) and that of snails is of 6 months ($\mu = 0.0055$) ([14, 19]). Then the basic reproduction number and values of a and b are listed in the following Table 1,2,3,4.

Through the calculation and analysis of the transmission dynamics, the epidemic characteristics of schistosomiasis and the epidemic characteristics of different endemic areas are revealed. The basic reproduction numbers of the monitoring sites in the four provinces are relatively low and are between 1 to 1.1. This means that one patient in the whole transmission process can spread and produce one or more new patients. In the four provinces schistosomiasis will continue to spread and may develop into local disease. In additional, from the four tables, we can see that the basic reproduction numbers of Jiangxi and Hubei are greater than that of Anhui and Jiangsu. In summary, the continuous monitoring results of six years show that schistosomiasis has been effectively controlled in those provinces

Table 2. Transmission indicators of schistosomiasis in Jiangxi province

Year	$\overline{P}$	$\bar{y}$	Δ	R_0'	a	b
2005	0.0503	0.0025	14.4	1.0556	0.00100	0.039472
2006	0.0309	0.0033	8.1	1.0353	0.00089	0.047748
2007	0.0158	0.0010	7.1	1.0171	0.00153	0.024869
2008	0.0115	0.0047	3.2	1.0164	0.00052	0.073124
2009	0.0053	0.0026	2.5	1.0079	0.00056	0.067487
2010	0.0068	0.0009	1.8	1.0078	0.00295	0.0127782

Table 3. Transmission indicators of schistosomiasis in Hubei province

Year	$\overline{P}$	$\bar{y}$	Δ	R_0'	a	b
2005	0.0171	0.0030	7.7	1.0204	0.000514	0.005754
2006	0.0191	0.0017	6.1	1.0212	0.001277	0.002356
2007	0.0145	0.0018	4.0	1.0165	0.001395	0.002147
2008	0.0110	0.0027	2.5	1.0134	0.001333	0.002238
2009	0.0103	0.0014	2.7	1.0118	0.001914	0.001556
2010	0.0090	0.0060	3.0	1.0097	0.003548	0.000838

Table 4. Transmission indicators of schistosomiasis in Jiangsu province

Year	$\overline{P}$	$\bar{y}$	Δ	R_0'	a	b
2005	0.0022	0.0026	5.7	1.0048	0.000101	0.034199
2006	0.0014	0.0067	5.5	1.0082	0.000026	0.134183
2007	0.0009	0.0036	6.1	1.0045	0.001038	0.123566
2008	0.0010	0.0013	3.2	1.0023	0.000017	0.020756
2009	0.0001	0.0010	4.0	1.0011	0.000017	0.200016
2010	0.0020	0.0000	4.5	1.0020	–	0.00000

Table 5. New values of a, b and R_0 by parameter estimation

Province	a	b	R_0
Anhui	0.000098	0.005524	0.6307
Jiangxi	0.000369	0.037184	0.3667
Hubei	0.0018036	0.000337	0.2046
Jiangsu	0.0000103	0.059264	0.1781

through the implementation of effective prevention strategies and measures. However, it still need to strengthen the monitoring of external infection sources and comprehensive management to further reduce schistosomiasis endemic level.

3.2. Method 2: Parameter estimation

Note that in the first method the basic reproduction number R_0' is calculated firstly, and then the value of a and b is calculated by R_0'. If we want to obtain the value of the basic reproduction number R_0, we need to get the values of parameters a and b firstly. Using the method of noise measurement and data smoothing in [15], the follows are to estimate new values of parameter a and b based on the mathematical model (2.1) and monitoring data in four provinces. Then the basic reproduction number R_0 are obtained from the new values of a and b. Summarize the results in Table 5.

In the following four figures (Figure 4, 5, 6, 7), the blue points represent the real data, the green trajectories represent the paths of P and y with the values of a and b obtained by the first method in 2005, and the red trajectories represent the paths of P and y by parameter estimation method.

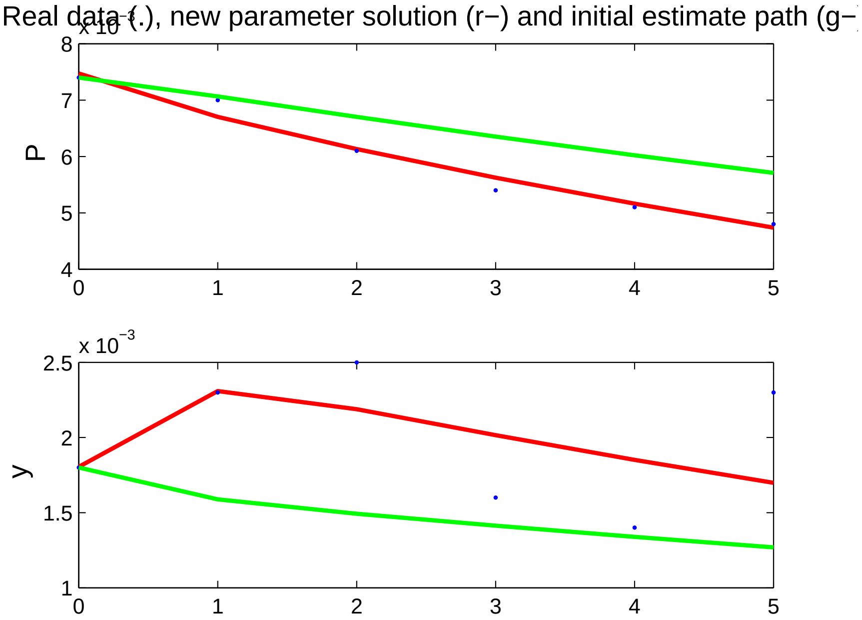

Figure 4. Parameter estimation for Anhui

It's clear to see that the curves by parameter estimation method fit the monitoring data in four

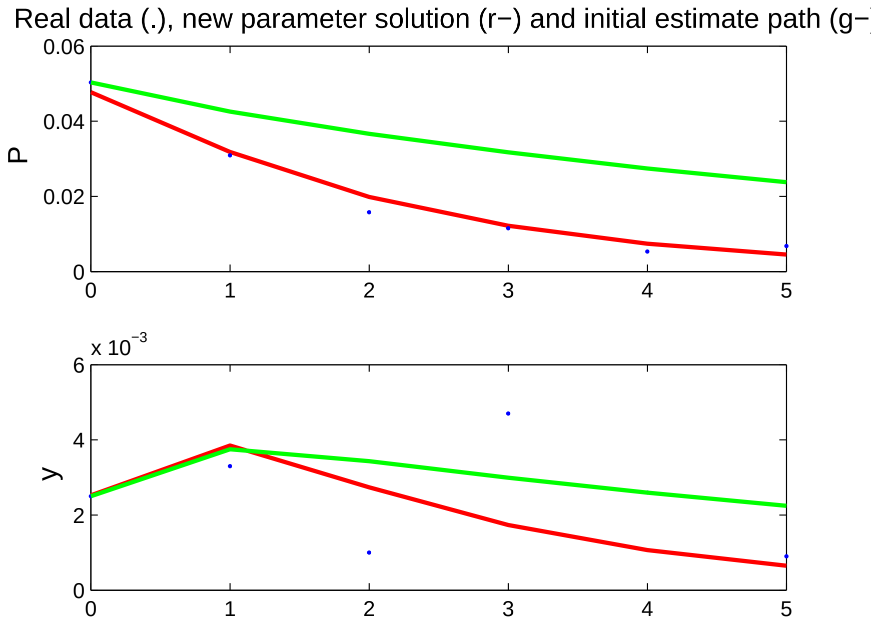

Figure 5. Parameter estimation for Jiangxi

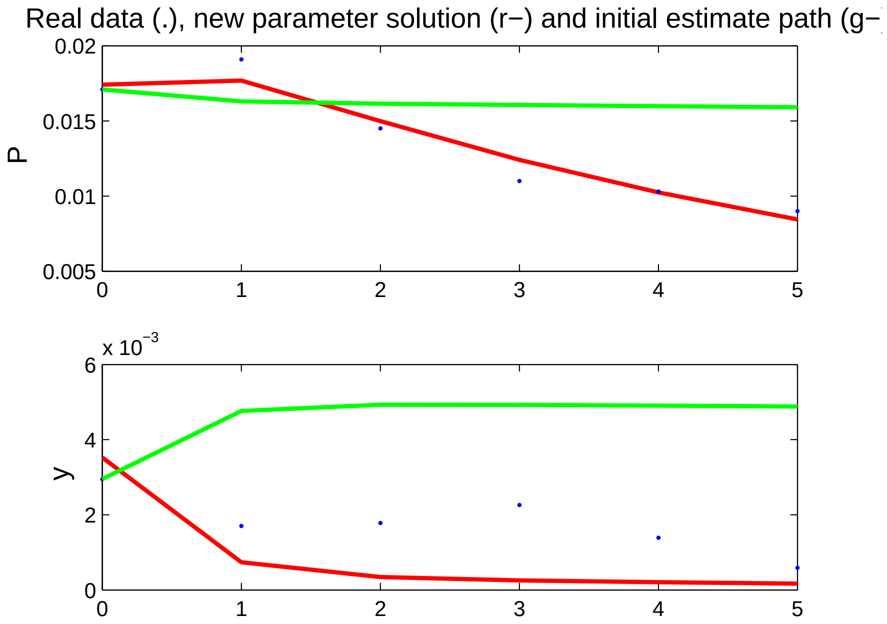

Figure 6. Parameter estimation for Hubei

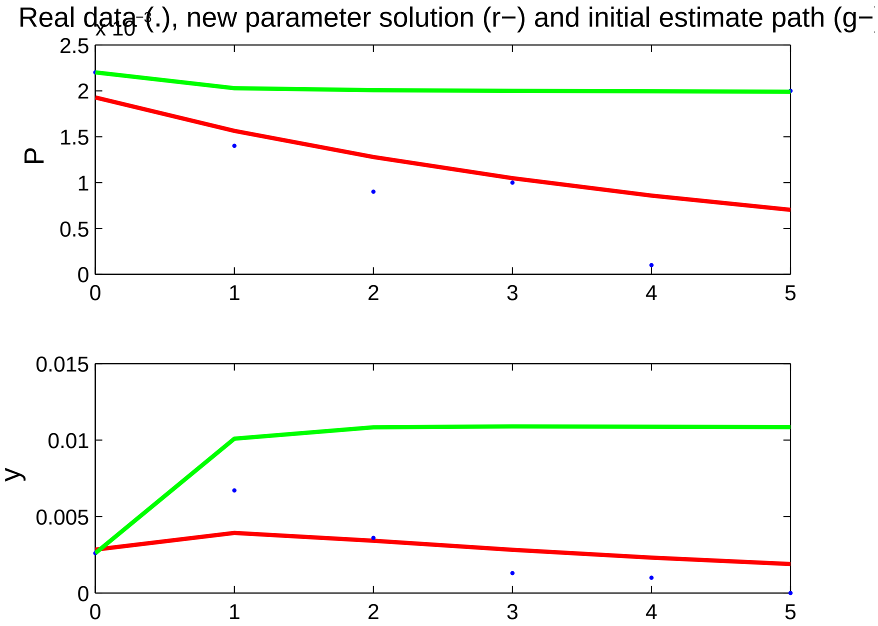

Figure 7. Parameter estimation for Jiangsu

provinces better than that by the first method. We also found an interesting phenomenon. That is all the values of the basic reproduction number R_0 in the four provinces are smaller than 1. This is in contradiction with the results by the first method, where the basic reproduction number R_0' is always greater than 1. This is because R_0' is calculated by the prevalence rate of humans ($\overline{P}$) and infection rate of snails ($\overline{y}$). Furthermore, the prevalence rate of humans and the infection rate of snails are between the 0.1%-10.0% in the actual situation. Thus the value of R_0' is in the range of $1.0 - 1.1$.

4. Numerical simulation and Discussion

In order to predict the future trend of schistosomiasis transmission in those four provinces after 2010, we carry out some numerical simulations about prevalence of humans and snails by using the new values of a and b in the above section.

From Figure 8, 9, 10, 11, we can see all the prevalence of human and snails in four provinces eventually tend to be 0. It may indicate that schistosomiasis in the four provinces will eventually be eliminated, but the premise is that the current standards of prevention and control must be maintained or improved. In addition, from these figures, we can see that the four provinces to eliminate schistosomiasis probably take a different time. For Anhui and Jiangxi province, it takes about 50 and 30 years to eradicate schistosomiasis patients and infectious snails, respectively. For Hubei province, no patients need to take about 25 years and no infectious snails need to take about 15 years. For Jiangsu province, it needs about 25 and 10 years to have no patients and infectious snails, respectively.

In fact, based on the new data from Anhui Provincial Institute of Schistosomiasis Control in 2011-2016 ([4, 5, 6]), we can find the control effect of schistosomiasis is better than expected due to the strengthening of local control policies (Figure 12).

Comparison of the two methods, the reasons for different results may have two aspects. Firstly, in

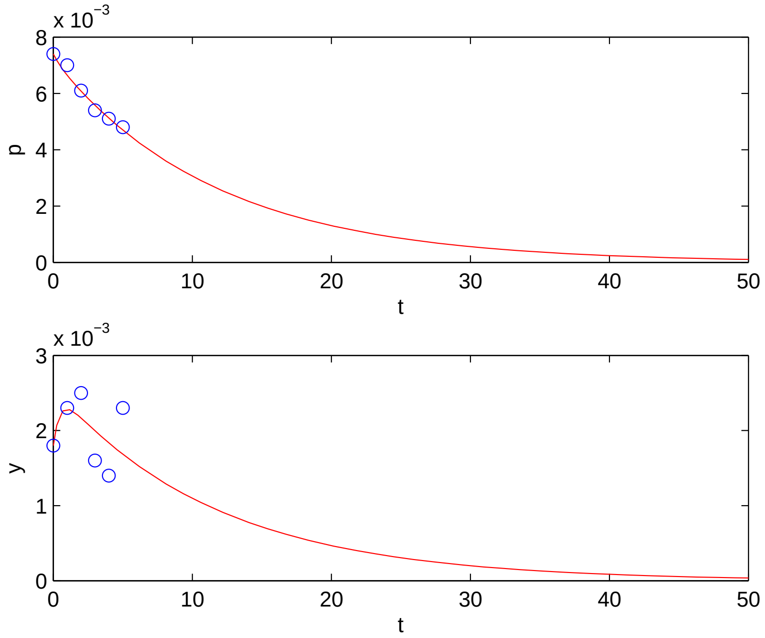

Figure 8. Prevalence of human and snails in Anhui

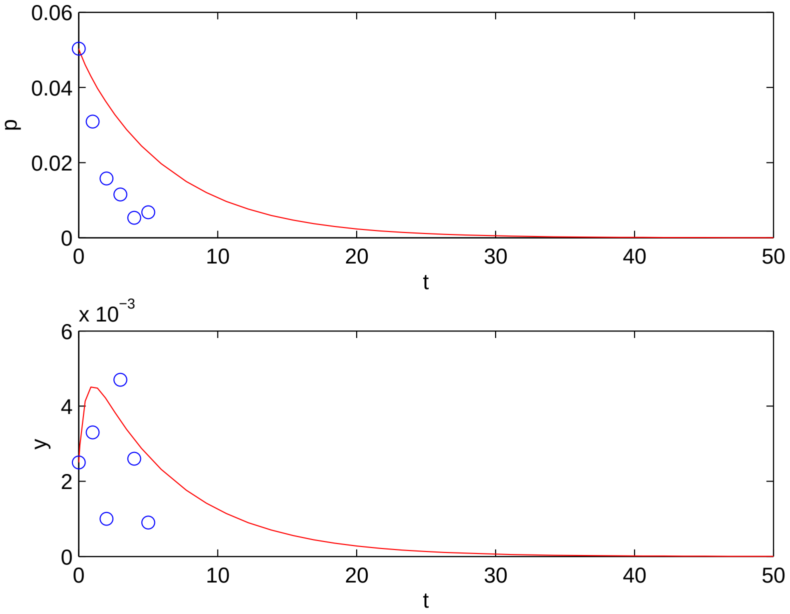

Figure 9. Prevalence of human and snails in Jiangxi

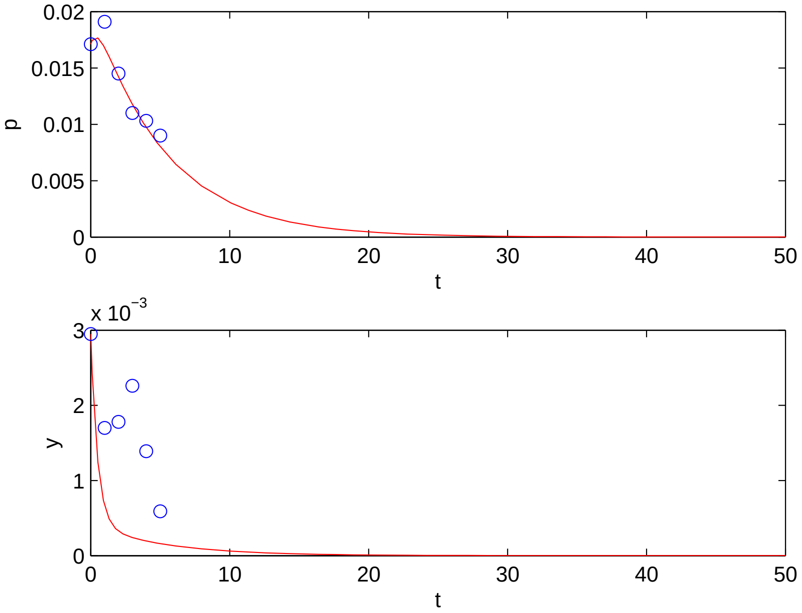

Figure 10. Prevalence of human and snails in Hubei

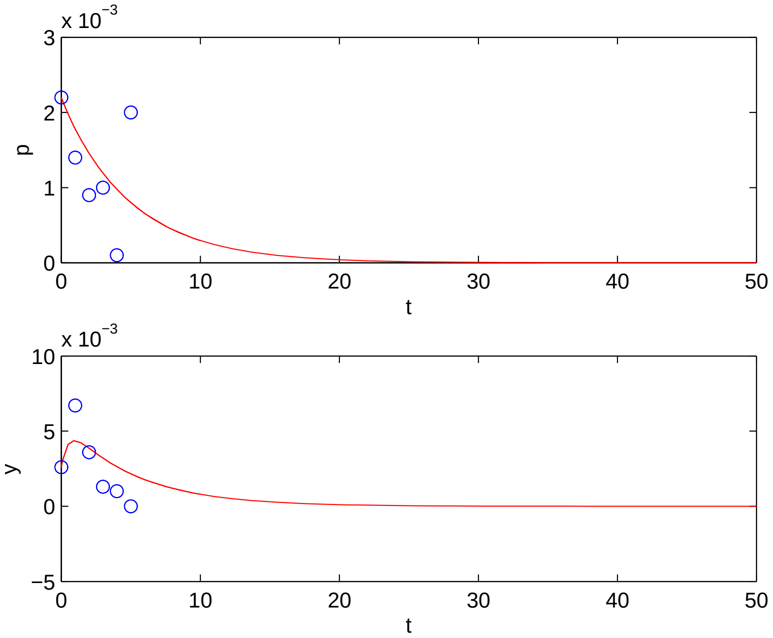

Figure 11. Prevalence of human and snails in Jiangsu

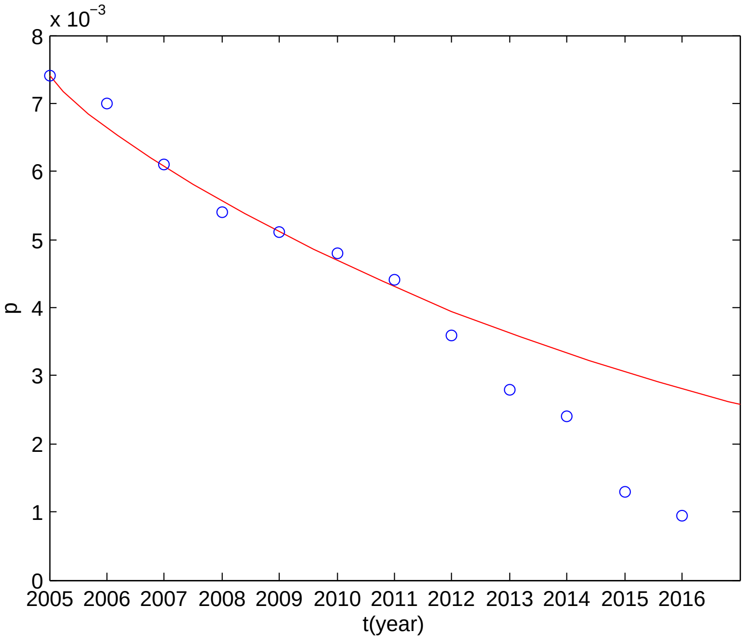

Figure 12. The prevalence of human in Anhui from 2005 to 2016

some areas the spread of schistosomiasis has been significantly inhibited due to the implementation of control measures. At present, there are some patients and disease snails. This does not mean that schistosomiasis will continue to go on. Hence, we cannot say the basic reproduction number must be greater than 1. Secondly, it is also possible that, there are other new thresholds for schistosomiasis transmission expect for the threshold condition $R_0 = 1$. For example, some backward bifurcations occur in many disease transmission. In one of our work, a backward bifurcation can happen in a schistosomiasis model with multiple infection ([13]). When $R_0 < 1$, the disease is still in the spread. In this case, to control the spread of schistosomiasis the value of R_0 must be less than a new threshold.

In addition, from the figures above, it can be seen that there is a little gap between the simulation of the infection rate of snails and the data, and the prevalence rate of humans is in good agreement. This is mainly because the infection rate of snails is affected by natural factors (such as floods and climate), biological factors (snails diffusion), human factors (the artificial transplanting of reed and poplar) and other factors. For example, in the flood year of Anhui Province, the annual average increase of the recovery areas of snails and the areas of snails are as much as 2.56 times and 2.16 times of that in a normal year ([21]). Hence, more careful consideration of these factors in the model is the direction of our work in the future.

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Conflict of interest

The authors declared that they have no conflicts of interest to this work.

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