Analysis of the effectiveness of control measures against *Schistosoma mekongi* using an intra- and inter-village model in Champasak Province, Lao PDR

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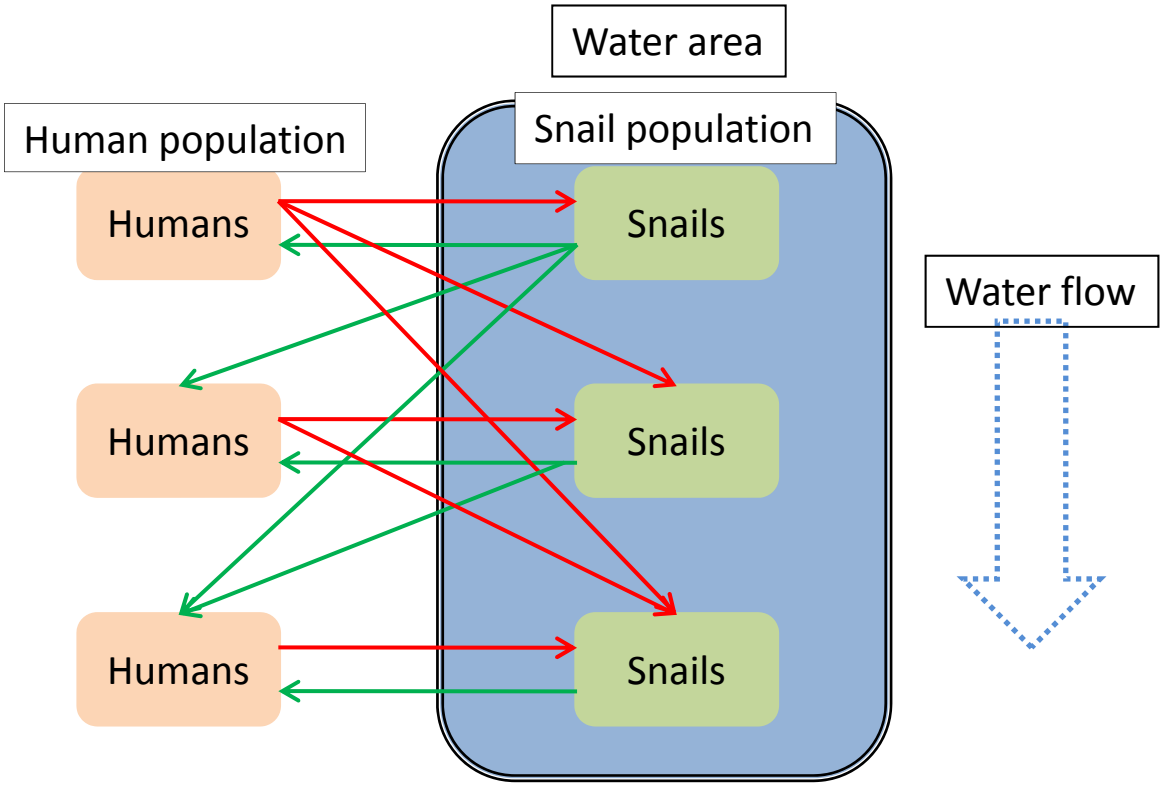
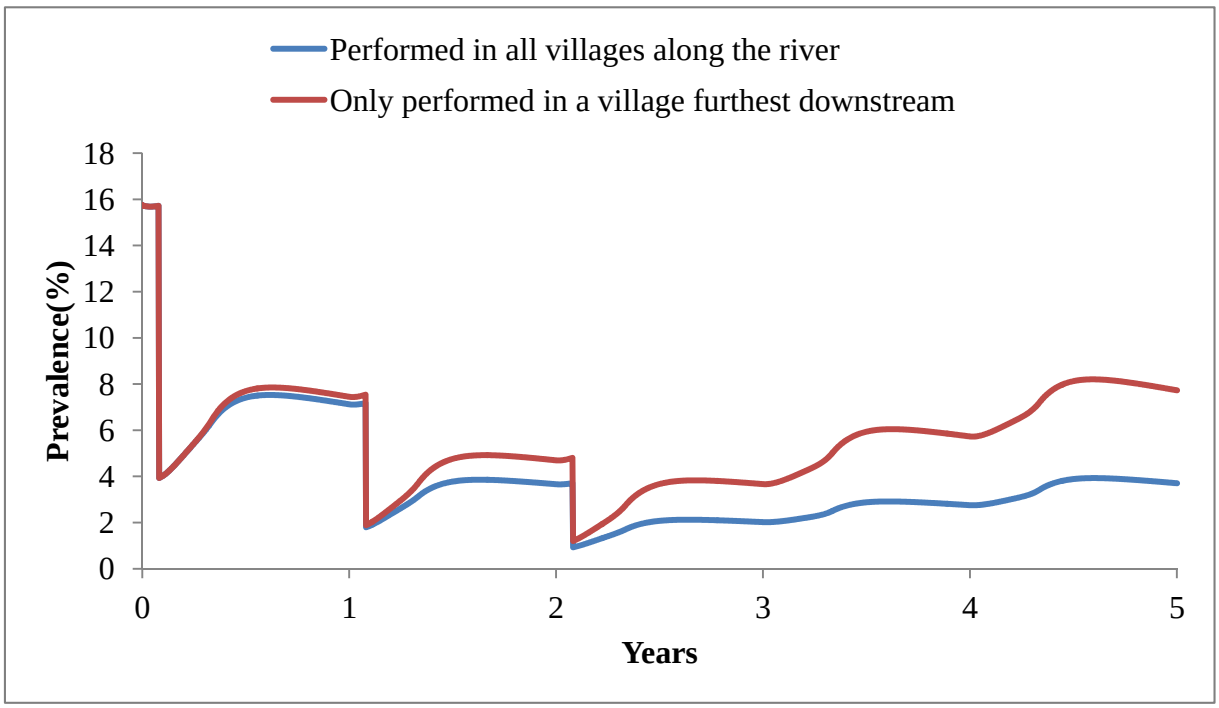
ABSTRACT

Schistosomiasis mekongi is prevalent in the Khong district of Lao PDR, made up of one big island, Khong, and numerous small islands in the Mekong River. *Schistosoma mekongi* is spread by *Neotricula aperta* as the intermediate host along the Mekong River. Therefore, even if an epidemic of *S. mekongi* were stamped out in a certain village, infection may recur if the source of infection is a village located in the upper reaches of the Mekong River. The purpose of this study was to construct a mathematical model for the transmission of *S. mekongi* among villages from the upper to lower Mekong River to estimate the effect of control measures against it. The chief characteristic of the present model is competence in dealing with the spread of infection among villages through the Mekong River in consideration of the reduction in longevity of cercariae and miracidia and their diffusion in the river. The model also takes into account seasonal fluctuation in the water level of the Mekong River, which affects human behavior in terms of water contact. The results of simulations indicated that the prevalence of schistosomiasis mekongi would be suppressed to a low level for a long time in a village further downstream when universal mass treatment is performed in villages further upstream simultaneously.


Water area
Human population
Snail population
Humans
Humans
Humans
Snails
Snails
Snails
Water flow


Performed in all villages along the river
Only performed in a village furthest downstream
Prevalence(%)
18
16
14
12
10
8
6
4
2
0
0
1
2
3
4
5
Years

Research Highlights:

Simulations evaluated the effect of control measures against *Schistosoma mekongi.*

The model treated intra- and inter- village transmission of *S. mekongi.*

The prevalence increases when mass treatment is only performed in a village upstream.

1. Introduction

Schistosomiasis mekongi is prevalent in the Mekong River basin from Southern Laos to Northern Cambodia. The total population at risk of exposure to schistosomiasis mekongi is estimated at approximately 60,000 in Lao PDR and 80,000 in Cambodia [1]. *Schistosoma mekongi* was first isolated in Laos in 1969 [2]. It was confirmed to be different from all known strains of *Schistosoma japonicum*, and then *S. mekongi* was subsequently recognized as a new *Schistosoma* species [3]. *S. mekongi* can be parasitic in various mammalian hosts such as humans, dogs and pigs [1]. *Neotricula aperta*, an aquatic snail, is known to be the intermediate host of *S. mekongi* [4]. The water level of the Mekong River fluctuates seasonally. The period of low water lasts from February to May, while that of high water lasts from June to January. The transmission of *S. mekongi* from snails to humans occurs during the low-water period because of water contact of humans during this period [1, 5, 6].

The purpose of this study is to construct a mathematical model for the transmission of *S. mekongi* among villages that are located from the upper- to lower reaches of the Mekong River to estimate the effect of control measures against it. In Lao PDR, a total of six programs of universal mass treatment (UT) were carried out from 1989 to 1999,

and consequently the prevalence in villages decreased to below 10%. Therefore, UT was discontinued in 1999 [7]. However, the surveillance in 2003 by WHO confirmed the increased prevalence of schistosomiasis mekongi; thereafter, the average prevalence rose to more than 30% according to surveillance in the next year [8, 9]. In view of this increased prevalence of schistosomiasis mekongi, it is useful to examine the effectiveness of control measures in order to restrain its revival in future.

A mathematical model is one of the most important tools to evaluate control measures against various infectious diseases [10]. A mathematical model for schistosome transmission was first developed in 1965 [11], and many models have been suggested since then [12-16]. Chan and Bundy proposed a mathematical model of schistosomiasis mansoni transmission with age structure to observe the effect of control measures on the morbidity of inhabitants in the long-term [17]. Williams et al. built a model for *S. japonicum* in China to estimate the effect of vaccination for the definitive hosts and bovines [15]. For the prevalence of schistosomiasis japonica in Bohol, Philippines, Ishikawa et al. evaluated the effects of UT for humans and molluscicide application for snails using a mathematical model [18]. For *S. mekongi*, Hisakane et al. first built a transmission model considering the age structure of humans and the seasonality of snails in Kratie province, Cambodia [19, 20].

In this study, we built a deterministic model for the intra- and inter-village transmission of *S. mekongi* in the Khong district of Lao PDR to evaluate the effectiveness of control measures. We chose two study areas in the Khong district from villages with a high prevalence of infection. The parameters that were used in the model were estimated in reference to field data or experimental data. The chief characteristic of the present model is competence in dealing with the spread of infection among villages along the Mekong River, in consideration of cercariae and also parasite eggs hatching miracidia that flow from villages upstream to those downstream on the Mekong River. Even if an epidemic of *S. mekongi* were stamped out in a certain village, infection may recur in the cause of the source of infection from a village upstream. The revival of *S. mekongi* infections in 2003 occurred in Lao PDR after the interruption of UT in 1999 [7-9, 21]. It was difficult to apply molluscicides against the intermediate hosts, *N. aperta*, of *S. mekongi* because of an abundance of water in the Mekong River [7, 22]. Therefore, it is useful to simulate UT or targeted treatment (TT) in villages of the Mekong River basin to suppress the prevalence of schistosomiasis mekongi.

2. Materials and Methods

2.1 Study area

In the Khong district of Lao PDR, where the Mekong River flows from north to south, there are many small islands in the Mekong River (Fig. 1). The Khong district, the largest towhead, which is 20 km from north and south and 10 km from east to west with the shape of an oval, is the capital of the Khong district. The Khong district with an area of approximately 2,400 km^2 had 13 commune, 131 villages and a population of 65,000 in 1990. In Lao PDR, a control program against schistosomiasis mekongi by WHO was started in 1988, in which UT with medication of praziquantel and health education programs were implemented, mainly for Khong Island [9].

After the termination of the program by the WHO, the Lao government continued the control program against schistosomiasis mekongi as well as *Opisthorchis viverrini* that spread widely during 1996-1999 under the technical support of WHO. The final surveillance in 1999 reported that 10 villages confirmed a prevalence of more than 1%, that only Hatosaikon located on the east riverbanks of the Mekong had a high prevalence of 26.7% and that the other villages had a prevalence of 1.3-7.7% [7]. The surveillance in the Khong district by WHO in May 2003 found that there were many villagers infected with *S. mekongi* in 10 villages and that the prevalence in these villages ranged from 1% to 47% with 11% on average [8, 9].

In this study, we chose as the study areas two sets of three villages in the Khong district that are located close together at 14° 00′ 29.99″ - 03′ 07.29″ N , 105° 54′ 03.87″ - 53′ 02.27″ E and 13° 57′ 34.08″ - 58′ 57.88″ N , 105° 55′ 00.52″ - 55′ 22.83″E, that is, Thamaakheb, Thakhaam, Somveuntok (A, B, C) and Det Ok, Khorn Neua, Khorn Tai (D, E, F), respectively, where villages A, B, C and D, E, F are lined up along the riverbanks of the Mekong (Fig. 1). Each village has a population of about 300-650 in 2003 (Table 1).

2.2 Water level of the Mekong River

In Laos, the rainy season lasts from May to October, and the heavy rainfall begins in August and then decreases in November. The dry season lasts from December to April. The high-water period begins in August owing to the heavy rainfall; the water level of the Mekong River reaches a peak of 10 m during September-October. Meanwhile, the water level decreases gradually after the arrival of the dry season in January. Observation of the water level in Pakse (2004-2005) (The Mekong River Commission) showed that the low-water period lasted from early January to late April (Fig. 2). The high-risk period of *S. mekongi* infection corresponds with the low-water period of the

Mekong River, when contact between the definitive and the intermediate hosts is possible [20, 23].

2.3 Intermediate hosts: *N. aperta*

N. aperta has been identified as having three strains (α, β and γ) that have been recognized as the intermediate hosts of *S. mekongi* [4]. *N. aperta* begins to release cercariae 45-53 days after the invasion of miracidia [24]; therefore, six weeks was adopted as the latent period (τ_s) in this model [20]. In the laboratory, the mortality of snails was estimated at approximately 1.8% per week [25] or 2.1% per week [26]. In general, for the intermediate host snails of other *schistosoma* species, the mortality of infected snails is higher than that of non-infected snails [27]. However, there was no significant difference in mortality among infected and non-infected *N. aperta* [28]. In this study, therefore, the mortalities of both infected and non-infected *N. aperta* (d_s) were set as 2% per week [20], but the severe water conditions cause considerable mortality in snails during high-water period [29]. Because the infection rate of *N. aperta*, which was reported as 0.22% [25] and 0.14% [26], is quite low, the infection rate was maintained below 1% throughout the year in the model [20].

The ecology of *N. aperta* is still unknown because of the difficulty in observation throughout the year, especially during the high-water period. Because the seasonal change in *N. aperta* density is one of the most important factors affecting the transmission of *S. mekongi*, the population dynamics model of *N. aperta* based on the "Post-spate survival" hypothesis that *N. aperta* survive and copulate during the high water period of the Mekong River, but that laying eggs are delayed until next January, and that thereafter eggs hatch from February [25], one of the dominant assumptions about the ecology of *N. aperta,* was incorporated into this transmission model [20].

In the model, the snail population was divided into two age categories: newborn and old snails. Newborn snails emerge in March and maintain a high density during April-May. In this period that matches the low water period, humans can make frequent water contact. The seasonal variations of *N. aperta* based on the population dynamics model are shown in Fig. 3.

2.4 Longevity of cercariae and miracidia

It is difficult to accurately observe the longevity of cercariae and miracidia that will maintain the ability of schistosome infection of humans and snails in the flow of the

Mekong River. A study on the experimental infection in mice reported that, with 100 m flow from the point of cercariae shedding, cercariae maintained almost the same infection ability as that at the shedding point, but that the ability gradually decreased with increased flow along a ditch, and that tests at a distance of about 400 m confirmed the preservation of ability of infection in cercariae [30]. We assume that the longevity of cercariae would remain unchanged 100 m from the shedding point, but that the longevity would decrease exponentially from 100 m to 1500 m with the decay rate (δ) and that the longevity would disappear beyond 1500 m (see Appendix). The maximum distances between adjacent villages in the study areas, A-C and D-F, are 720 m and 330 m, respectively, so such distances should affect the transmission of *S. mekongi*. In this model, it is assumed that the decrease in longevity of miracidia is equal to that of cercariae and also that the longevity of both would not be influenced by the seasons or the locations of villages.

2.5 Intra- and inter-village transmission model

In the study area, there are many villages along the riverbanks of the Mekong. We constructed a mathematical model for the transmission of *S. mekongi* within villages

and also among villages located close together along the Mekong River. The model includes the variables of epidemiological classes in human and snail populations for each village. The transmission of *S. mekongi* can occur within a village and to villages further downstream.

From the viewpoint of differences in the water contact rate by age, the human population is classified into 5 age categories: infants (age of less than 1), children under school-age (age of 1-4), elementary school students (age of 5-9), junior high school students (age of 10-14), and youths and adults (age of 15 or more). For each age category (a), we assign the risk of transmission from snails to humans ($\beta_h^{(a)}$) and the intensity of infection ($e_h^{(a)}$). The snail population consists of two age categories: new-born and old snails. For snails, we assign the risk of transmission from humans to snails (β_s). The intensity of infection for each age category in humans was estimated on the basis of epidemiological data of Char Thnaol and Samraong [31], while the risks of transmission were chosen to realize the initial age-specific prevalence (Table 2).

For each village (Q), humans (H_Q) and snails (S_Q) are divided into three epidemiological classes: negative class ($H_{Q,1}$, $S_{Q,1}$), incubation class ($H_{Q,2}$, $S_{Q,2}$), and infectious class ($H_{Q,3}$, $S_{Q,3}$) [20]. The suffixes Q and 1-3 stand for a village and an epidemiological class, while the superscript letters (a=1-5) and (b=1-2) stand for the age

category of $H_{Q,i}$ and $S_{Q,\mathrm{i}}$, respectively, if necessary. The model tracks the prevalence of schistosomiasis mekongi in each age category of the human population and the number of infected snails for each village with due consideration of the difference in the intensity of infection among age categories on transmission from humans to snails.

In the model, the densities of cercariae ($C_{c,(Q',Q)}$) and miracidia ($C_{m,(Q',Q)}$) on the riverbank of Q that are drifting from a village upstream, Q', were determined in consideration of cercariae- and miracidia-diffusion using the advection diffusion equation for Thamaakheb, Thakhaam and Somveuntok villages (A-C) which front a wide river, while these densities ($C_{c,(Q',Q)}$, $C_{m,(Q',Q)}$) were determined with no consideration of cercariae- and miracidia-diffusion for Det Ok, Khorn Neua and Khorn Tai villages (D-F), which front a narrow river. Since the transmission of *S. mekongi* can occur only in the low-water period, water contact ($w_{\mathrm{h,s}}$) and water contamination ($w_{\mathrm{h},n}$) were assumed to be 1 or 0 for January-April or May-December, respectively [20]. The other parameters in the model were estimated with reference to the field and laboratory data (Table 3). The model schemes are shown in Fig. 4, and their mathematical formulation is given in Appendix.

2.6 Control measures and simulations

The principal control measures against schistosomiasis mekongi in Lao PDR are medication and health education. In endemic areas of schistosomiasis japonica, snail control measures such as scattering molluscicides, environmental change together with medication contributed to the suppression of epidemics [18]. On the other hand, using molluscicides has little effect on inhibiting *S. mekongi* transmission because of the abundance of water in the Mekong River [7, 22].

Therefore, medication and education are the principal control measures against schistosomiasis mekongi. We investigated how the prevalence in a certain village downstream would be influenced by the sources of infection in villages further upstream through simulations. We arranged several simulations related to the situation of the execution of UT, TT and a combination of UT and TT, for school-aged children (5-14 years old) who showed higher prevalence and also higher likelihood of water contact.

3. Results

Firstly, we conducted a series of simulations of yearly UT for three years with three levels of coverage of UT, 35%, 55% and 75%, on A village furthest upstream, which is thus assumed not to be influenced by any villages located in the upper reaches of the river in order to investigate the influence of change in coverage of UT on the prevalence (Fig. 5). Yearly UT with 75% coverage for three years would keep the prevalence at 1% or below after the interruption of UT for several years, while the prevalence would slightly increase in the situation of yearly UT with 35% and 55% coverage after UT interruption.

Secondly, when yearly UT with coverage of 75% for three years would be executed in village B, C or F located furthest downstream, we compared the influence on the prevalence in B, C or F in terms of whether yearly UT with coverage of 75% would be executed simultaneously on all villages upstream A, A and B or D and E above B, C or F, respectively (Fig. 6). The execution of yearly UT with coverage of 75% on B, C or F together with all villages, A, A and B or D and E, simultaneously would suppress the increase of prevalence in B, C or F after the interruption of UT, while the execution of yearly UT on B, C or F without A, A and B or D and E would allow restoration of the prevalence.

Finally, we observed the effects of yearly or biyearly TT with coverage of 85% after

yearly UT for three years on village furthest downstream B, C or F with or without yearly UT with coverage of 75% for three years on all villages upstream, A, A and B or D and E, (Fig. 7). Yearly and biyearly TT after yearly UT for three years together with UT on all villages upstream would maintain low prevalence of below 2%, 1% and 2%, respectively, while yearly TT without UT on the villages upstream would restore the prevalence to 6%.

4. Discussion

This study aimed to quantitatively evaluate the prevalence of schistosomiasis mekongi in villages of the Khong district, Champasak Province in Lao PDR, in situations of various control methods using a mathematical model.

Young children showed a higher prevalence of schistosomiasis mekongi [9], which seems to be caused by a higher level of water contact in children and inadequate immunity due to episodes of past infections of schistosomiasis mekongi as well as other schistosome species [38,39]. Therefore, we included the risk of transmission in humans and the intensity of infection by fecal output for each age category in the model (Table 2). There is a concern about the small size of some age-category populations for some

small villages. However, the application of a deterministic model is adequate as a transmission model of *S. mekongi* because the transmission of *S. mekongi* from humans to snails is only dependent on the total amount of fecal output of the infected villagers over all age-categories in the model. Development into an individual based model connoting stochastic processes is one of the future challenges. In order to avoid undue complications of the model's structure, the probability of mating of *S. mekongi* in a human host was not considered.

One of the features of our model is the consideration of transmission from villages upstream to those downstream as well as within villages (Fig. 4). We investigated the influence on the prevalence of schistosomiasis mekongi in a village downstream according to the absence of UT in villages upstream. The change in prevalence in a village downstream was affected by the distance between the villages and by their populations. In Thamaakheb, Thakhaam, and Somveuntok (A-C), village A had a larger population (656) than village B (326). Then, the simulation indicated that, when yearly UT in only B for three years is executed, the prevalence in B would be restored soon after the interruption of UT (Fig. 6 (a)). The rates in A and B in 2004 were 10.8 and 38.8%, respectively [9], which indicated that a larger pool of infected villages upstream had an impact on infection in a village downstream. Regarding Det Ok, Khorn Neua,

and Khorn Tai (D-F), these villages are located close together and alongside a narrow stream, which limits the diffusion of cercariae and miracidia. The simulation indicated that the prevalence of schistosomiasis mekongi in a village downstream would be markedly influenced by the infection status of villages upstream (Fig. 6 (c)). E and F villages in 2004 showed high rates of 50 and 46.2%, respectively [9].

Dogs and pigs are naturally infected with *S. mekongi* in Laos aside from humans [40,41]. However, the intra- and inter-village model is limited to one definitive host, humans, to avoid a complicated model structure. A previous study which considered the contribution of an animal reservoir, dogs, for an *S. mekongi* transmission model targeting for a high endemic situation in Cambodia suggested that the prevalence in dogs gradually decreased from 11 to 6% on the execution of three courses of yearly UT with 70% coverage in villagers, and that yearly TT with an 85% coverage after three courses of yearly UT kept the prevalence in humans low and also reduced the prevalence in dogs throughout the 8-year simulation [20]. In addition, the model did not consider the movement of villagers among villages. There is a possibility that the daily movement of villagers, such as coming from and going to regions where schistosomiasis mekongi still prevails, would increase the risk of the revival of schistosomiasis mekongi prevalence in a village where the epidemic has declined due to

the execution of continual UT. A further advanced model that also considers the movement of villagers based on behavioral observations is desirable.

We considered the longevity and diffusion of cercariae with respect to the transmission of *S. mekongi* among villages. There is still little known about the relationship between distance and the longevity of cercariae. It is important to estimate the longevity of cercariae and miracidia in the Mekong River. We referred to the results of experimental infection by shedded cercariae of *S. japonica* in China along a ditch [30]. We assumed that the reduction in the longevity of cercariae in the Mekong River by flow was less than that in a ditch because of the broad width of the Mekong River (2.4). A change of the reduction in the longevity will affect the revival of the prevalence of schistosomiasis mekongi in a village downstream where the epidemic has declined due to continual UT. However, the prevalence in the village downstream will be automatically restored after some infected villagers accumulate there. It is desirable to conduct a study with experimental infection to investigate the longevity of cercariae in the Mekong River in the future. In addition, we assumed that the longevity and diffusion of miracidia were similar to those of cercariae. Further study on the longevity of miracidia is needed. For the situation of the villages (A-C) that front a wide river, the model took into consideration the diffusion of miracidia and cercariae besides the decrease in longevity.

The advection equation was numerically solved in a more simply rectangular domain instead of a real topology, and, furthermore, the model did not consider the edge effect of the riverside, which may be an important factor affecting the influence of diffusion. We look forward to developing studies on the process of diffusion of cercariae under consideration of the edge effect based on the configuration of riverbanks.

The active transmission of *S. mekongi* between humans and snails occurs in the low-water period of the Mekong River when *N. aperta* propagates abundantly and also villagers contact water in the Mekong River frequently. The density of *N. aperta* reaches a peak in April (Fig. 3) and the incidence in May is higher than that in any other month (data not shown) because it is assumed in the model that the water contact would only occur in the low-water period. The reduction in the probability of water contact or the amount of fecal output impacts on suppression of transmission of *S. mekongi* [20]. Further observational studies on water contact activities, such as frequency by sex or age, may contribute to improving the accuracy of the model.

Although UT decreased the prevalence of schistosomiasis mekongi in 1999, the surveillance by WHO confirmed the revival of the infection in 2003, and moreover, the prevalence rose to 30% in 2004 [9]. Since UT used to be carried out in villages that showed a high prevalence of *S. mekongi* on the basis of stool examination [7], it was

speculated that there still remained villages that had villagers infected with schistosomiasis mekongi but that were not targeted for UT. The result of the simulation indicated that, if UT was only executed in a certain village, the prevalence would be restored to that before (Fig. 6). According to the simulation, it is more desirable for the execution of UT to target villages that are located close together along the Mekong simultaneously.

In Cambodia, the prolongation of the interval between UT is considered from the viewpoint of cost-effectiveness [42]. The result of simulations indicated that yearly or biyearly TT could maintain a low prevalence after yearly UT for three years. With regard to the re-emergence of schistosomiasis mekongi in Laos, it is necessary to maintain a control program based on surveillance. The simulation result suggested that, instead of yearly UT, yearly or biyearly TT is efficacious in suppression of *S. mekongi* after sufficient reduction of the prevalence if the coverage is kept at more than 85%.

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The authors declare that we have no competing interests.

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Appendix

The model is governed by the following differential equations. The *Q* runs over the villages A, B and C, or D, E and F; $Q' \leq Q$ means that *Q'* is a village upstream above *Q* or *Q'*=*Q*.

Humans

The *a* runs over the age categories 1-5; the symbol $f^{(a)}$ stands for the transfer rate from $H_Q^{(a)}$ to $H_Q^{(a+1)}$ for *a*=1-4 but formally $f^{(0)} = f^{(5)} = 0$, $H_{Q,1}^{(0)} = H_{Q,2}^{(0)} = H_{Q,3}^{(0)} = 0$. $\delta_{a,1}$ is 1 for *a*=1 or 0 for otherwise.

$$\frac{dH_{Q,1}^{(a)}}{dt} = \delta_{a,1} d_h H_Q + f^{(a-1)} H_{Q,1}^{(a-1)} - \left(f^{(a)} + \lambda_{h,Q}^{(a)} + d_h\right) H_{Q,1}^{(a)} + \left(1 - f^{(a)}\right) \gamma_h H_{Q,3}^{(a)} + f^{(a-1)} \gamma_h H_{Q,3}^{(a-1)}$$

$$\frac{dH_{Q,2}^{(a)}}{dt} = f^{(a-1)} H_{Q,2}^{(a-1)} - \left(f^{(a)} + \sigma_h + d_h\right) H_{Q,2}^{(a)} + \left(1 - f^{(a)}\right) \lambda_{h,Q}^{(a)} H_{Q,1}^{(a)} + f^{(a-1)} \lambda_{h,Q}^{(a-1)} H_{Q,1}^{(a-1)}$$

$$\frac{dH_{Q,3}^{(a)}}{dt} = f^{(a-1)} H_{Q,3}^{(a-1)} - \left(f^{(a)} + \gamma_h + d_h\right) H_{Q,3}^{(a)} + \left(1 - f^{(a)}\right) \sigma_h H_{Q,2}^{(a)} + f^{(a-1)} \sigma_h H_{Q,2}^{(a-1)}$$

$$H_Q = \sum_{a=1}^{5} \left(H_{Q,1}^{(a)} + H_{Q,2}^{(a)} + H_{Q,3}^{(a)}\right)$$

The force of infection from infected snails to humans of age category (*a*)

$\lambda_{h,Q}^{(a)} = \beta_h^{(a)} w_{h,s} \sum_{Q' \leq Q} v_{(Q',Q)} C_{c,(Q',Q)}$ for *a*=1-5, but formally $\lambda_{h,Q}^{(0)} = 0$.

Here, *Q'* runs *Q* and all the villages upstream above *Q*.

Snails

The *b* runs over the age categories 1-2: new-born and old snails. We transfer the age-categories of snails from new-born snails ($S_{Q,i}^{(1)}$) to old snails ($S_{Q,i}^{(2)}$) on January 1st (*i*=1-3). $\delta_{b,1}$ is 1 for *b*=1 or 0 for *b*=2. b_s, $\phi_s^{(1)}$ and $\phi_s^{(2)}$ fluctuate seasonally (Table 3).

$$\frac{dS_{Q,1}^{(b)}}{dt} = \delta_{b,1} p_{ht} \xi_s b_s S_Q^{(2)} \left(t - \left(\tau_{s,ht} + \tau_{s,mt}\right)\right) e^{-\phi_s^{(1)} \tau_{s,mt}} - \left(\lambda_{s,Q} + \phi_s^{(b)}\right) S_{Q,1}^{(b)}$$

$$\frac{dS_{Q,2}^{(b)}}{dt} = \lambda_{s,Q} S_{Q,1}^{(b)} - \left(\sigma_s + \phi_s^{(b)}\right) S_{Q,2}^{(b)}$$

$$\frac{dS_{Q,3}^{(b)}}{dt} = \sigma_s S_{Q,2}^{(b)} - \phi_s^{(b)} S_{Q,3}^{(b)}$$

$$S_Q^{(2)} = S_{Q,1}^{(2)} + S_{Q,2}^{(2)} + S_{Q,3}^{(2)}$$

The force of infection from infected humans to snails

$$\lambda_{s,Q} = \beta_s \sum_{Q' \le Q} v_{(Q',Q)} C_{m,(Q',Q)}$$

Here, *Q'* runs *Q* and all the villages upstream above *Q*.

Miracidia and Cercariae

The amount of miracidia and cercariae at the riverbank of *Q'*

$$q_{m,Q'} = w_{h,n} \sum_{a=1}^{5} e_h^{(a)} H_{Q',3}^{(a)}, \quad q_{c,Q'} = \sum_{b=1}^{2} S_{Q',3}^{(b)},$$

A-C *villages that front a wide river*

The density (*C*) of cercariae or miracidia in the river that are drifting from *Q'* is expressed by the advection diffusion equation in the rectangular domain with the Neumann type boundary condition $(\partial C / \partial y) = 0$ on the riversides, where the origin, *x*-axis, *y*-axis are chosen as the riverbank of *Q'*, the direction of water flow and its

vertical direction, respectively, and velocity of the Mekong River flow and the diffusion coefficient are denoted as u and K, respectively.

$$\frac{\partial C}{\partial t} = -u\frac{\partial C}{\partial x} + K\left(\frac{\partial^2 C}{\partial x^2} + \frac{\partial^2 C}{\partial y^2}\right) + q, \quad \left(q = q_{m,Q'} \text{ or } q_{c,Q'}\right)$$

For $Q'<Q$, $C_{m,(Q',Q)}$ and $C_{c,(Q',Q)}$ denote the density of miracidia and cercariae in the riverbank of Q that are drifting from Q' that are determined the equation, respectively, while we put $C_{m,(Q,Q)} = q_{m,Q}$ and $C_{c,(Q,Q)} = q_{c,Q}$ for $Q'=Q$.

D-F *villages that front a narrow river*

The density of miracidia or cercariae in the riverbank of Q that are drifting from Q' for $Q' \le Q$ is simply set as $C_{m,(Q',Q)} = q_{m,Q'}$, $C_{c,(Q',Q)} = q_{c,Q'}$, respectively.

Longevity

The longevity (ν) of cercariae or miracidia in the river at a distance l (m) that are drifting from Q' at is expressed by the following formula, and $\nu_{(Q',Q)}$ denotes the longevity of miracidia or cercariae in the riverbank of Q that are drifting from Q' for $Q' \le Q$.

$$\nu(l) = \begin{cases} 1 & \cdots\ 0 \le l \le 100 \\ e^{-\delta(l-100)} & \cdots\ 100 < l < 1500 \\ 0 & \cdots\ l \ge 1500 \end{cases}$$

Caption

Table 1

The population size and number of schools in villages in the study areas in 2003

Table 2

Risk of transmission, intensity of infection and initial prevalence for each age category

Table 3

Estimated values of the model parameters

Legends

Fig. 1

Map of the Khong district of Lao PDR.

Fig. 2

Monthly average water level of the Mekong River for 2 years during 2004-2005 in Pakse [Mekong River Commission].

Fig. 3

The monthly variation of total snail population.

Fig. 4

The scheme of the transmission model for *S. mekongi*, (a) basic scheme of epidemiological classes and transfers among them, (b) concept of intra- and inter-village transmission. Deaths of both hosts are omitted in the figure (a). The solid and broken lines show infection through miracidia and cercariae, respectively (b).

Fig. 5

Variation of the prevalence of schistosomiasis mekongi in village A with yearly universal mass treatment (UT) at three coverage rates: 35% (dashed line), 55% (dotted line), 75% (solid line).

Fig. 6

Variation of the prevalence of schistosomiasis mekongi in villages B (a), C (b) and F (c)

in the situation of yearly universal mass treatment (UT) with 75% coverage for three years with (solid line) yearly UT of 75% coverage for three years and without (dotted line) any execution of UT on village(s) upstream.

Fig. 7

Variation of the prevalence of schistosomiasis mekongi in villages B (a), C (b) and F (c) in the situation of yearly (black line) or biyearly (gray line) targeted treatment (TT) with coverage of 85% after yearly universal mass treatment (UT) with 75% coverage for three years, with (solid line) yearly UT of 75% coverage for three years and without (dotted line) any execution of UT on village(s) upstream.

Table 1

Village	Population	Number of schools	Distance (m)
Thamaakheb, Thakhaam, Somveuntok			
A	656	1	
			510
B	326	1	
			720
C	625	0	
Det Ok, Khorn Neua, Khorn Tai			
D	494	1	
			280
E	587	1	
			330
F	537	1	

Table 2

Age category (years)	Risk of transmission	Intensity of infection (egg/g) *	Initial prevalence (%)
0	0	0	0
1-4	1.17×10^{-5}	105	6.5
5-9	8.31×10^{-5}	130	31.7
10-14	1.14×10^{-4}	195	43.4
15-	3.94×10^{-7}	97	0.2

*Estimated based on epidemiological data of Char Thnaol and Samraong in 1994-95 [31]

Table 3

Symbol	Interpretation	Estimated value	References
Human			
d_h	Death rate (/month)	0.0013	[32]
$e_h^{(a)}$	Intensity of infection (egg/g)	See Table 2	
$\tau_h=1/\sigma_h$	Latent period (month)	1.58	[33]
γ_h	Recovery rate (/month)	0.0167	[34]
$\beta_h^{(a)}$	Risk of transmission from snail to human	See Table 2	
Snail			
d_s	Basic mortality (/month)	0.087	[26]
$\phi_s^{(1)}$	Seasonal mortality for new-born snails (/month)	d_s (Mar-Oct) $4d_s$ (Nov-Dec)	[20,29]
$\phi_s^{(2)}$	Seasonal mortality for new-born snails (/month)	6 d_s (Jan-Mar) 12 d_s (otherwise)	[20,29]
b_s	Average number of eggs (/female/month)	0-15 (depending on season)	[20]
p_{ht}	Probability of egg hatching	0.8	[35]
ξ_s	Ratio of female to male	0.67	[35]
$\tau_{s,ht}$	Hatching period (month)	1	[20,36]
$\tau_{s,mt}$	Maturity period to participate in transmission (month)	1	[20]
$\tau_s=1/\sigma_s$	Latent period (/month)	1.25	[24]
β_s	Risk of transmission from human to snail	4.0×10^{-6}	See text
Transmission			
$w_{h,s}$	Water contact	0 (high-water period) or 1 (low-water period)	[20]

$w_{h,n}$	Water contamination	0 (high-water period) or 1 (low-water period)	[20]
δ	Decay rate of longevity of cercariae and miracidia (/m)	0.005 (100-1500m)	See text
Mekong River			
u	Velocity of flow (m/s)	3	–
K	Diffusion coefficient (m^2/s)	10^{-5}	[37]

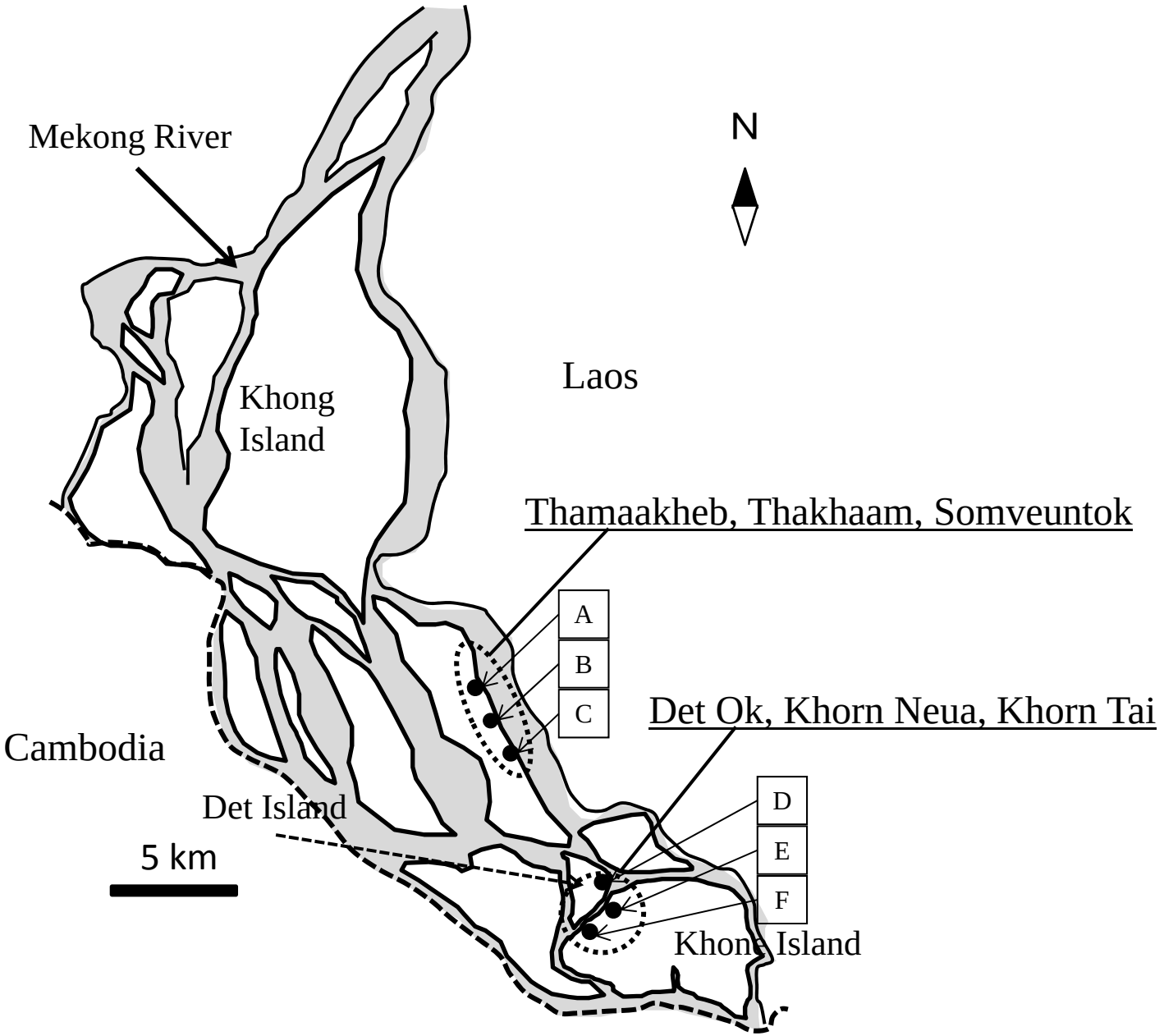
Mekong River
N
Laos
Khong
Island
Thamaakheb, Thakhaam, Somveuntok
A
B
C
Det Ok, Khorn Neua, Khorn Tai
Cambodia
Det Island
D
E
F
5 km
Khone Island

Fig. 1

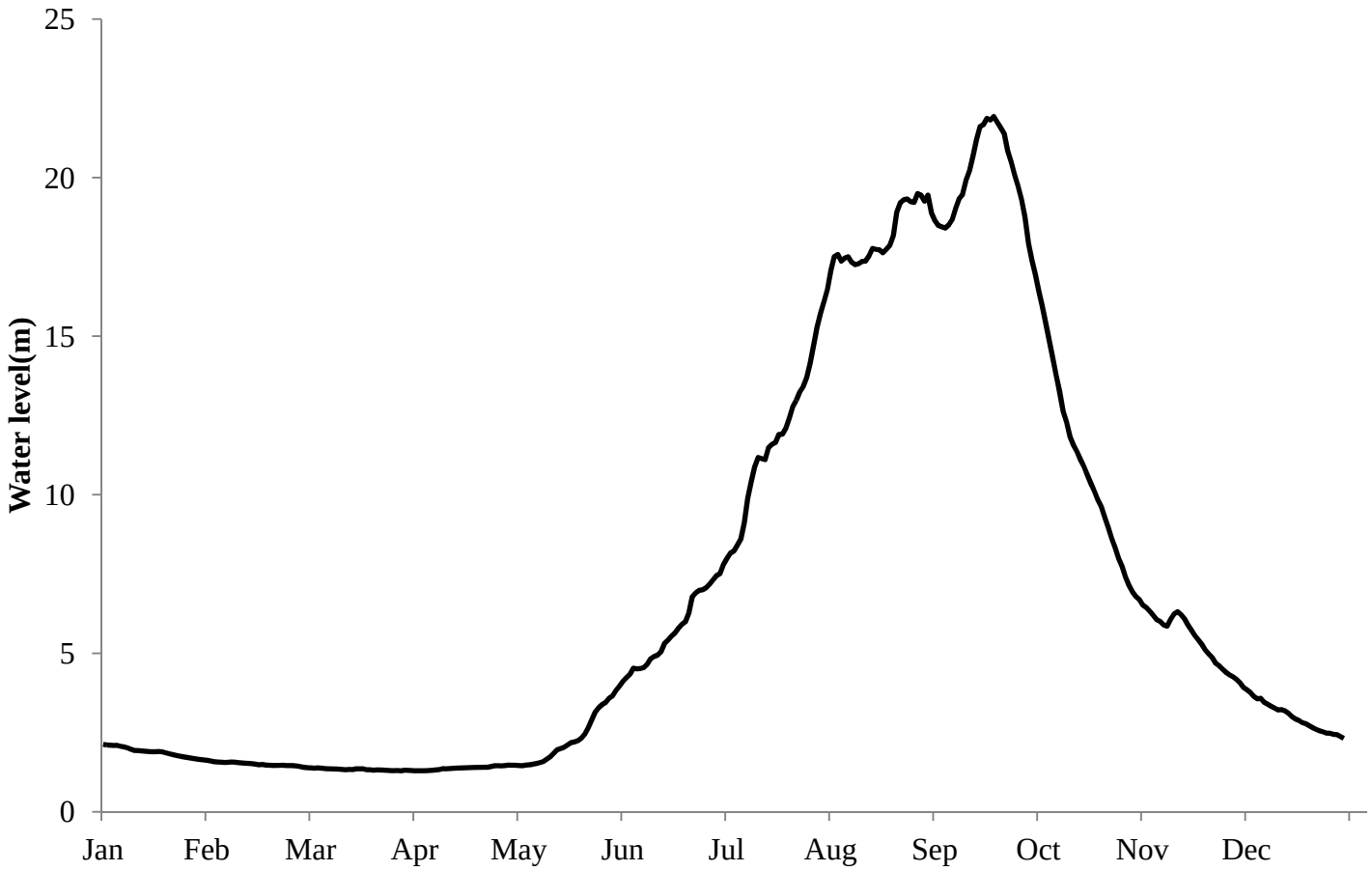
Water level(m)
25
20
15
10
5
0
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec

Fig. 2

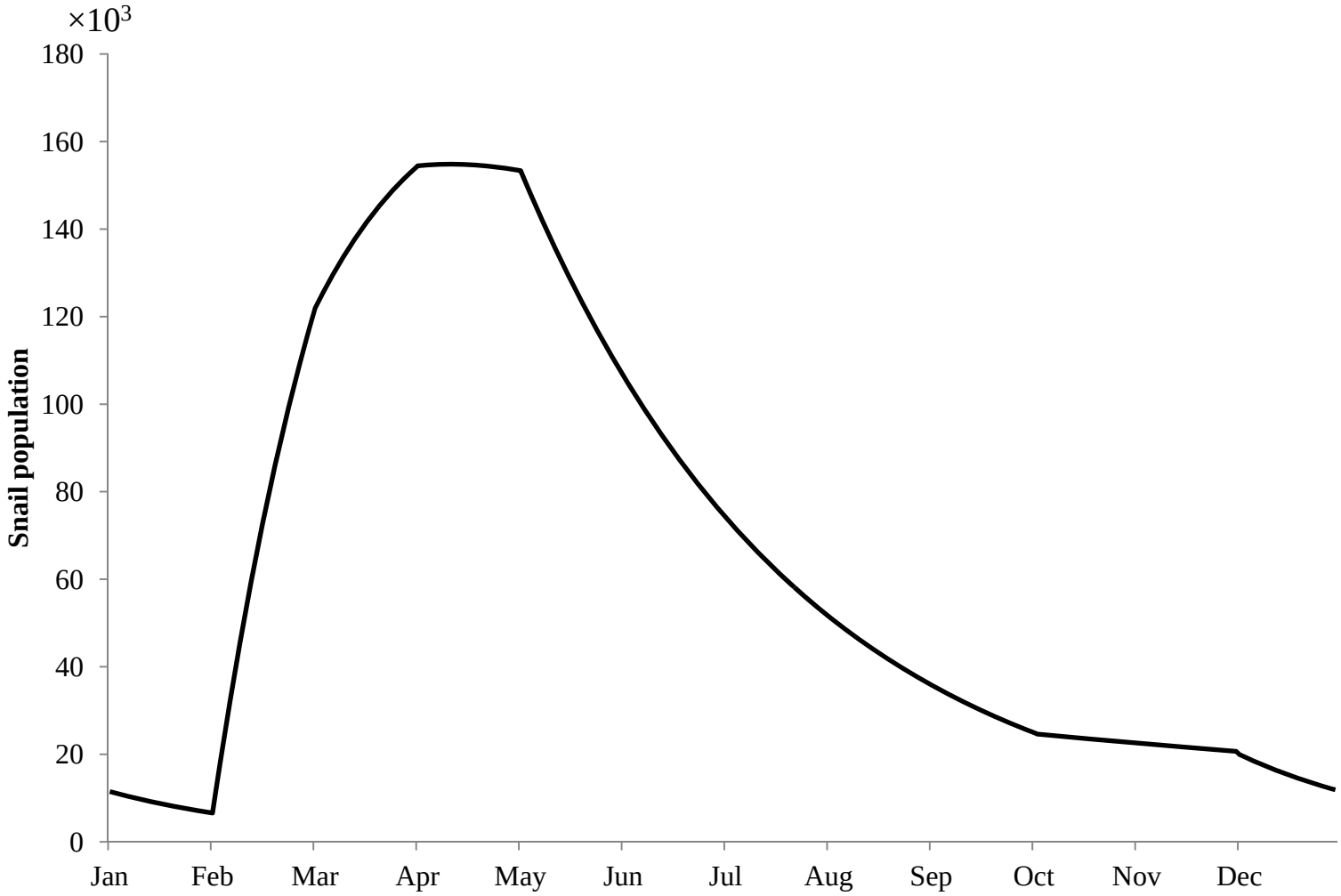
×10^3
180
160
140
120
100
80
60
40
20
0
Snail population
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec

Fig. 3

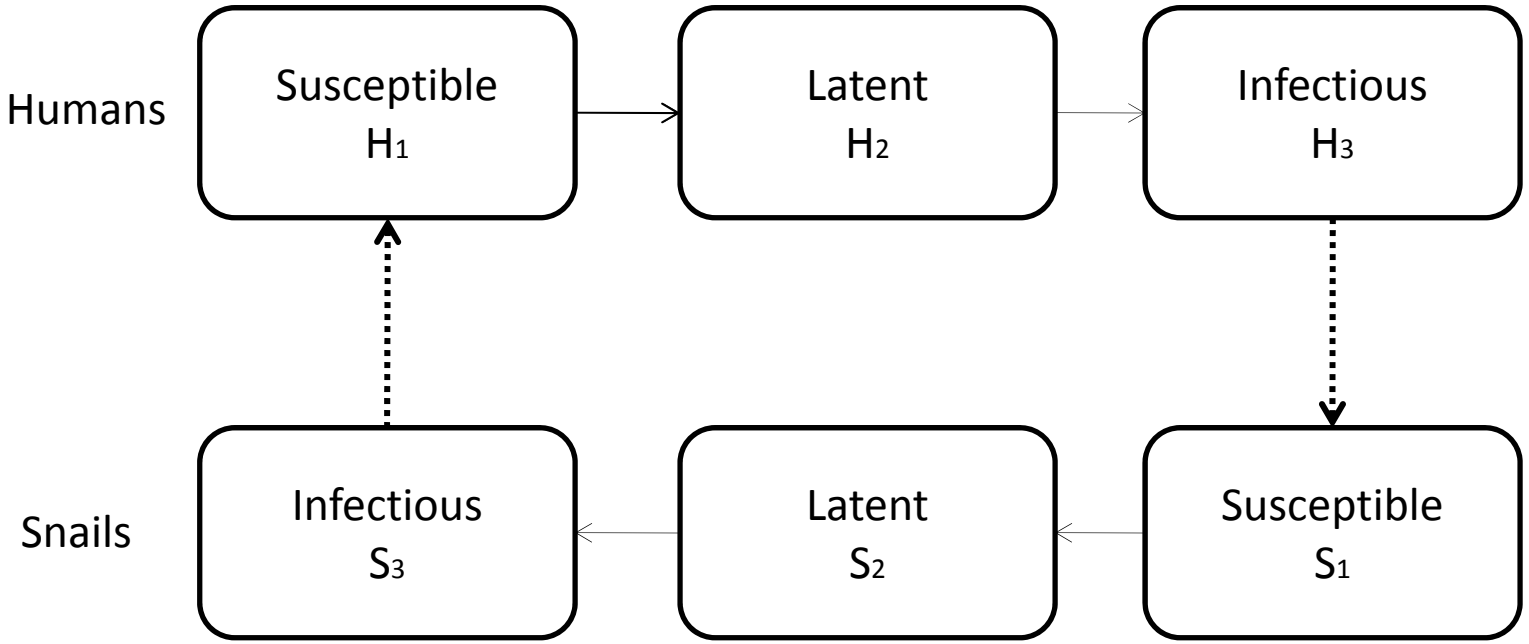
Humans
Susceptible
H1
Latent
H2
Infectious
H3
Snails
Infectious
S3
Latent
S2
Susceptible
S1

Fig. 4(a)

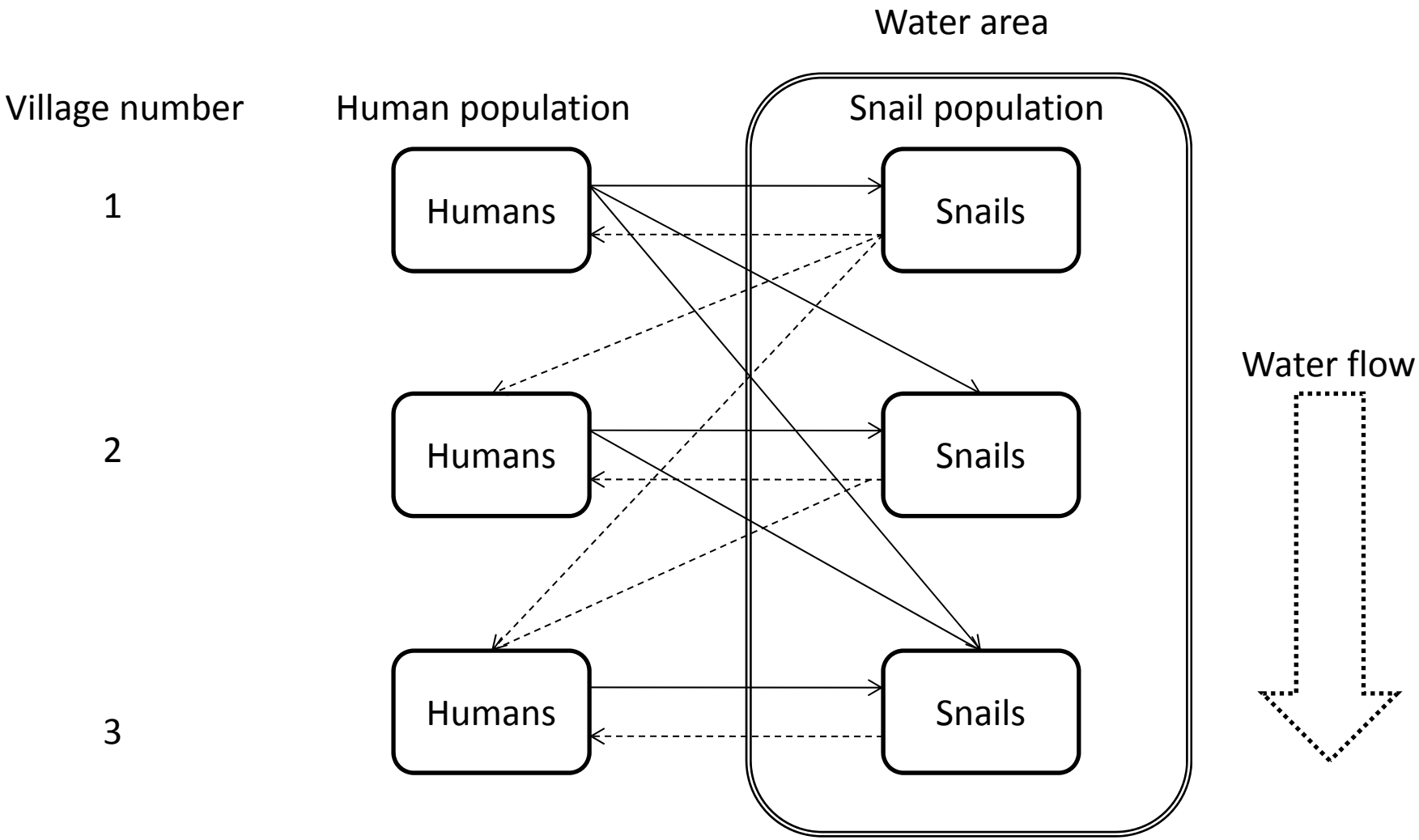
Water area
Village number
Human population
Snail population
1
2
3
Humans
Humans
Humans
Snails
Snails
Snails
Water flow

Fig. 4(b)

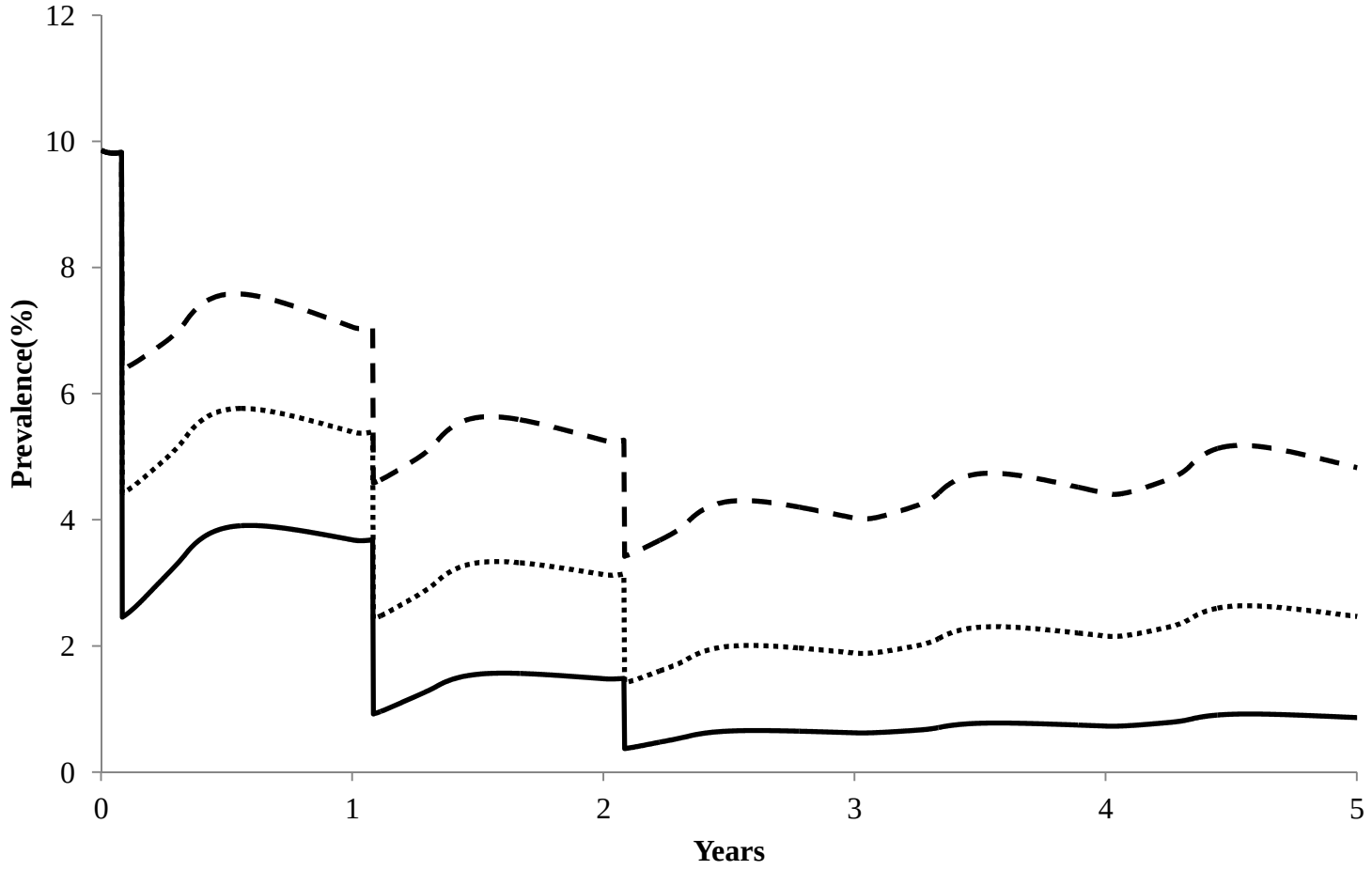

Fig. 5

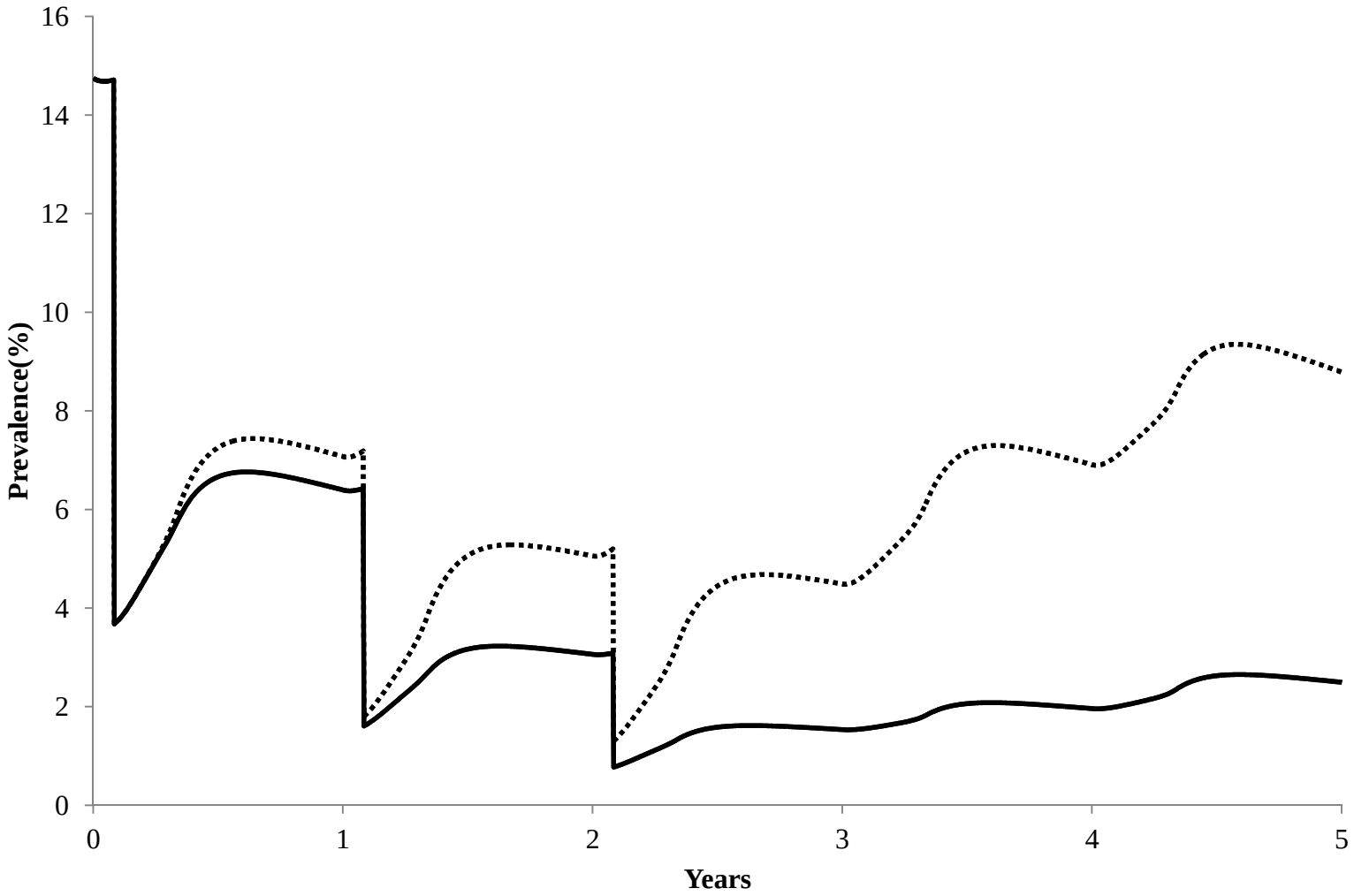

Fig. 6(a)

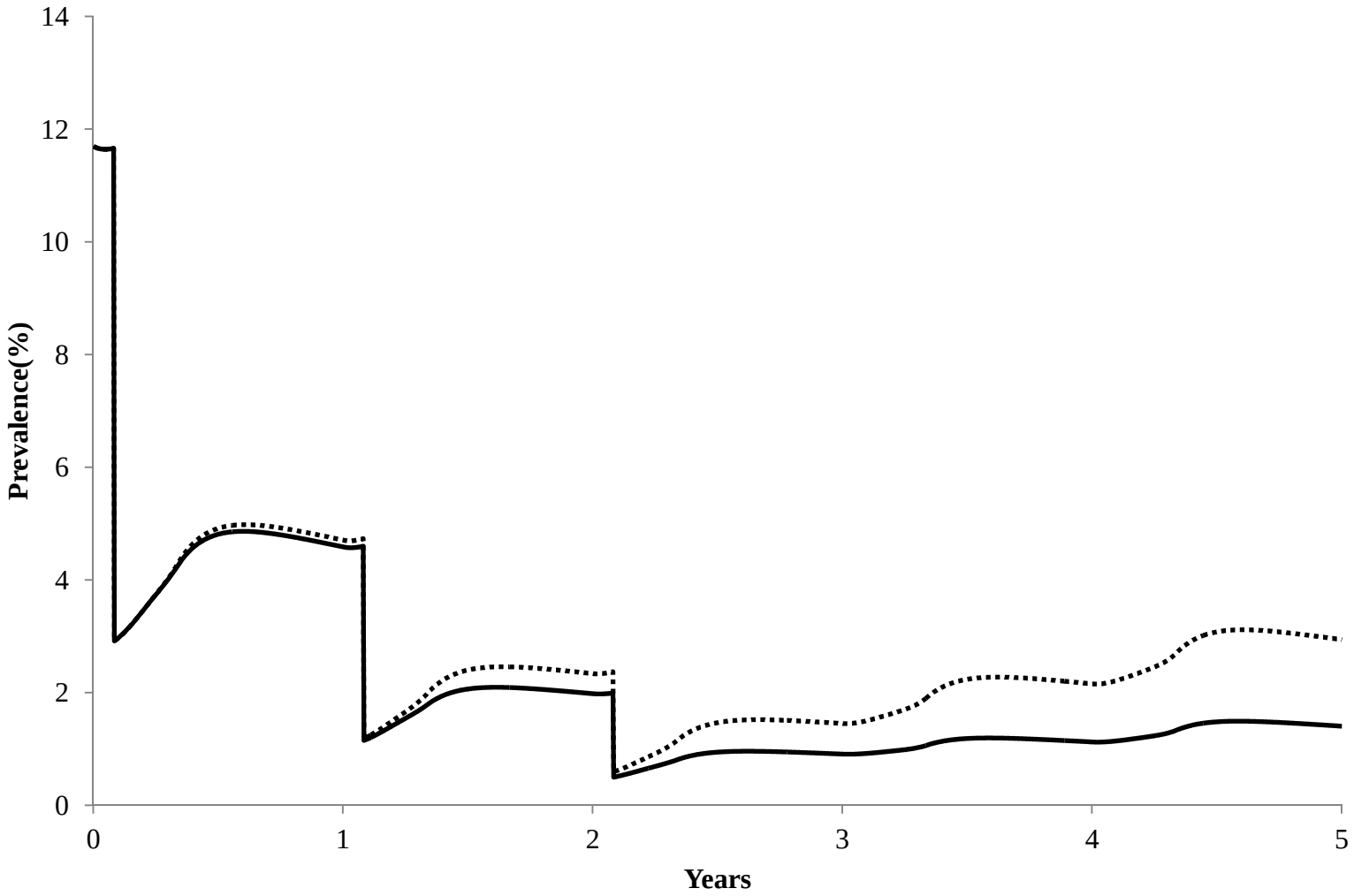

Fig. 6(b)

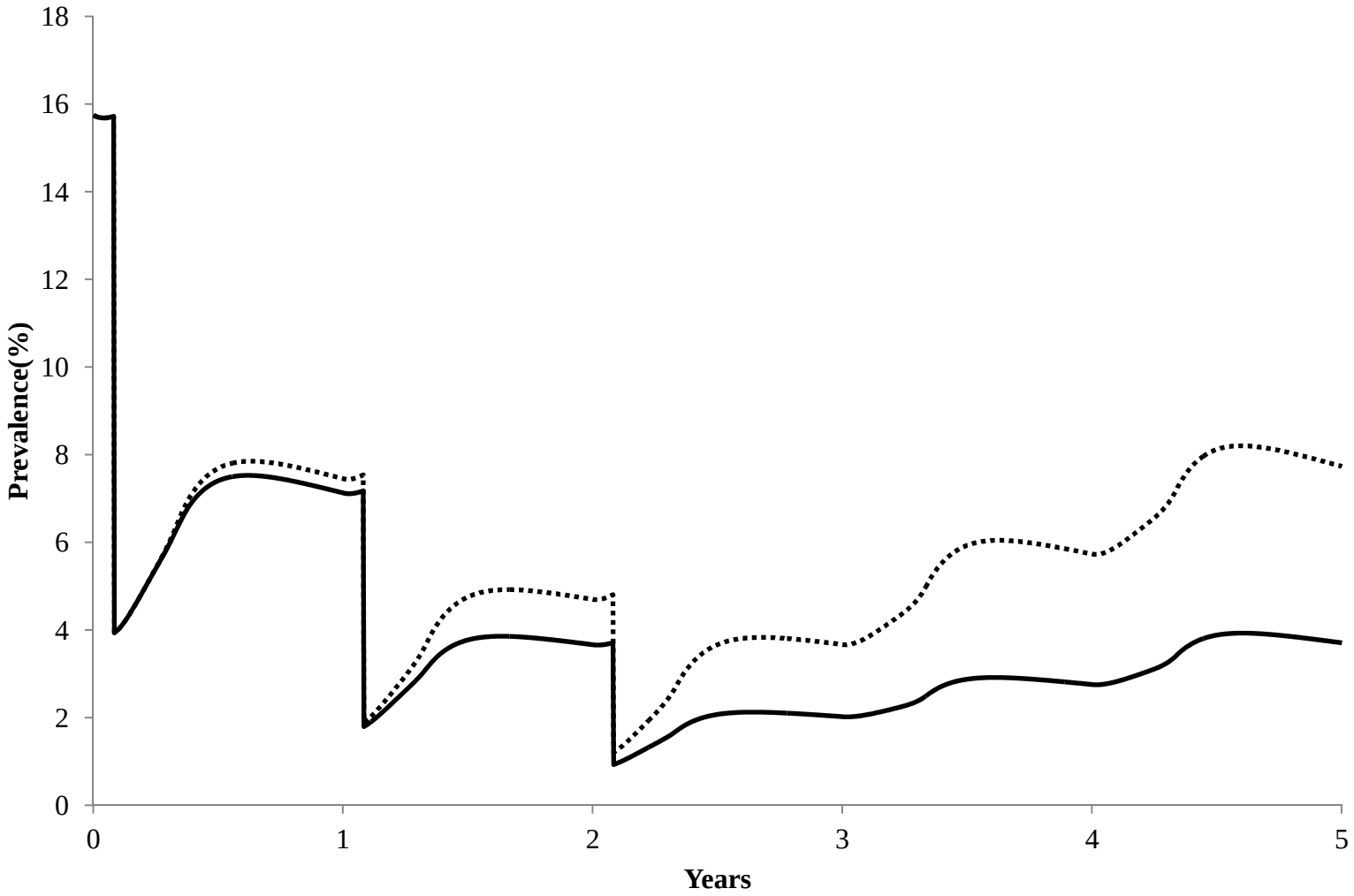

Fig. 6(c)

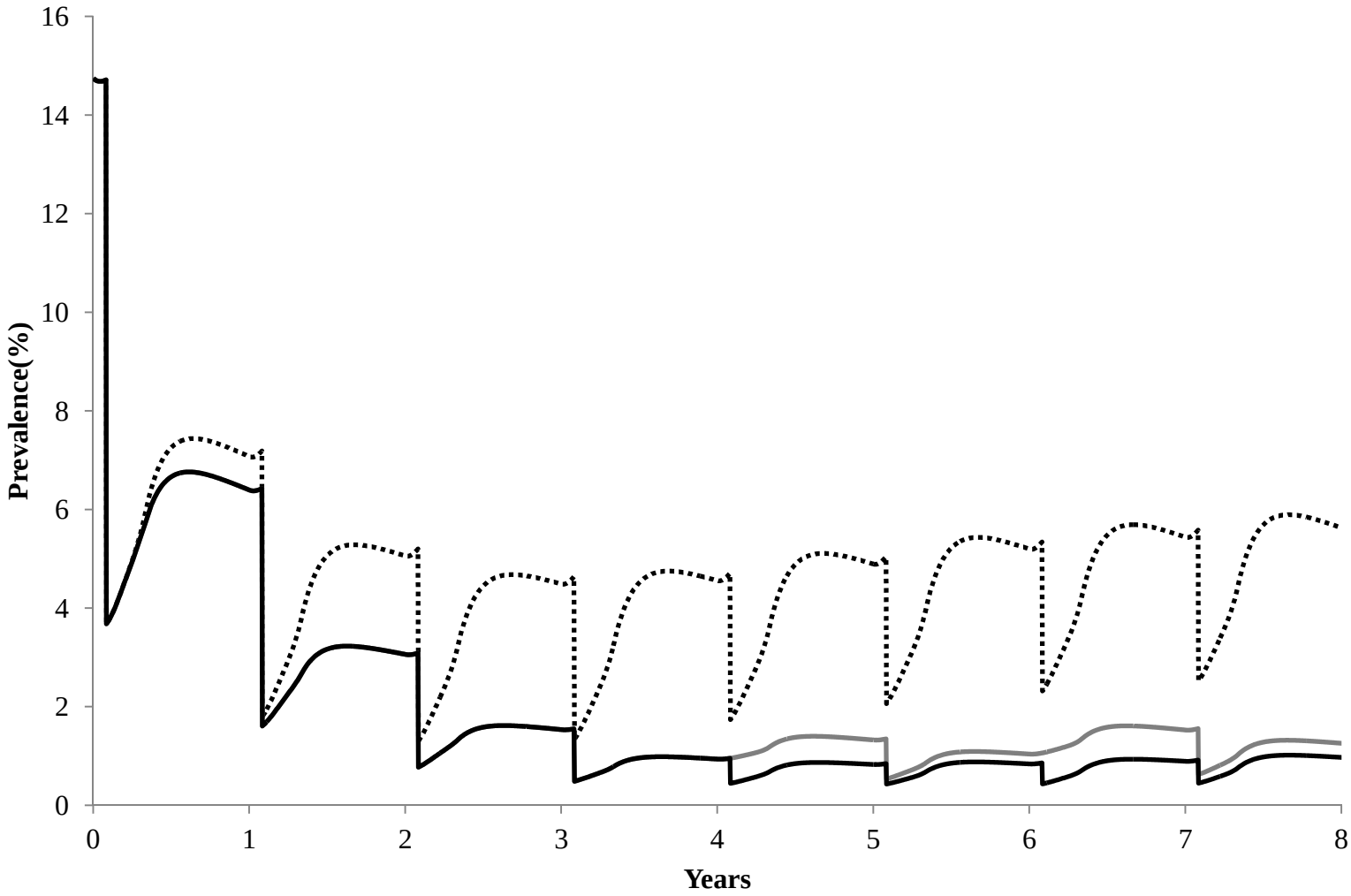

Fig. 7(a)

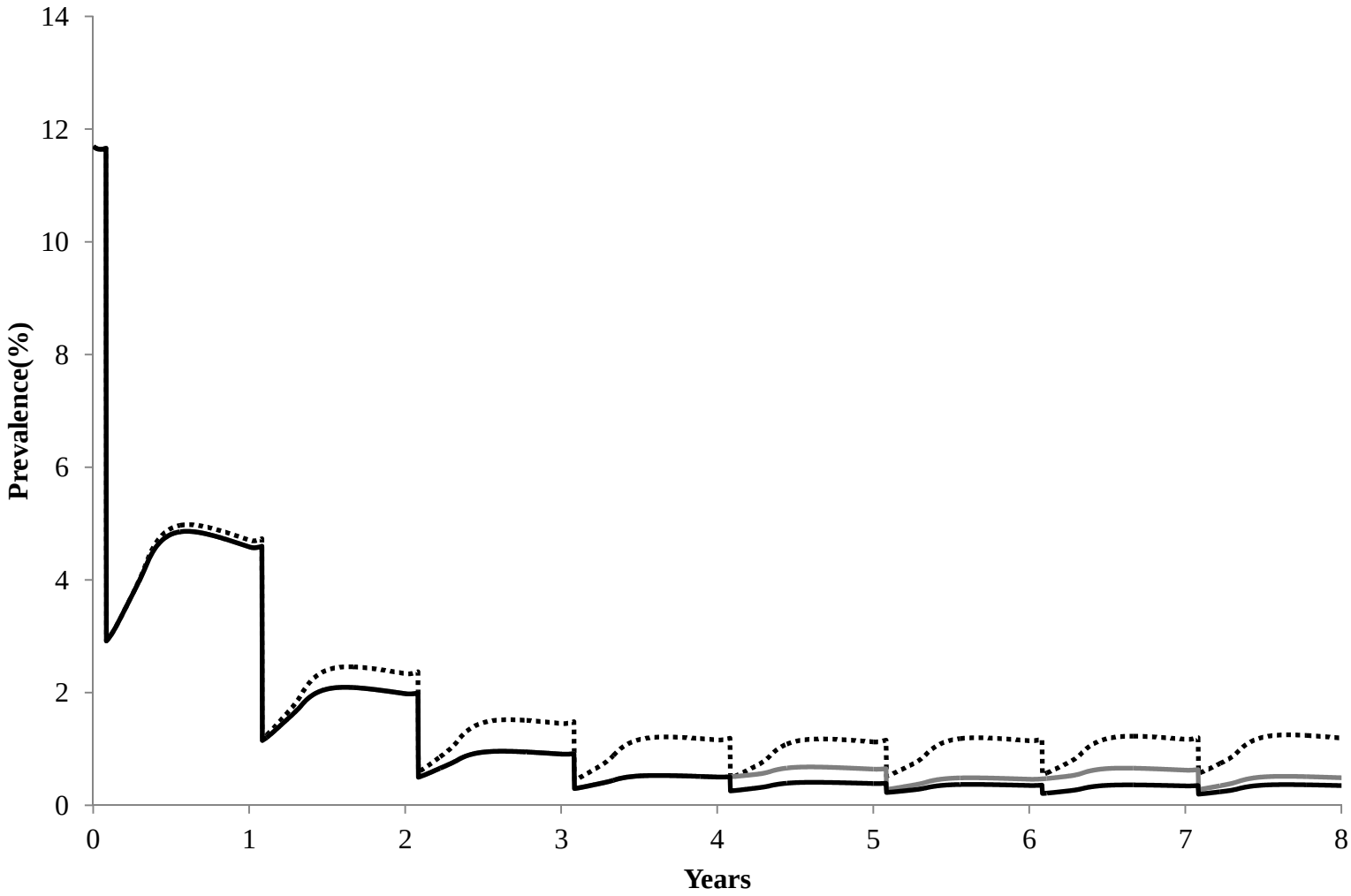

Fig. 7(b)

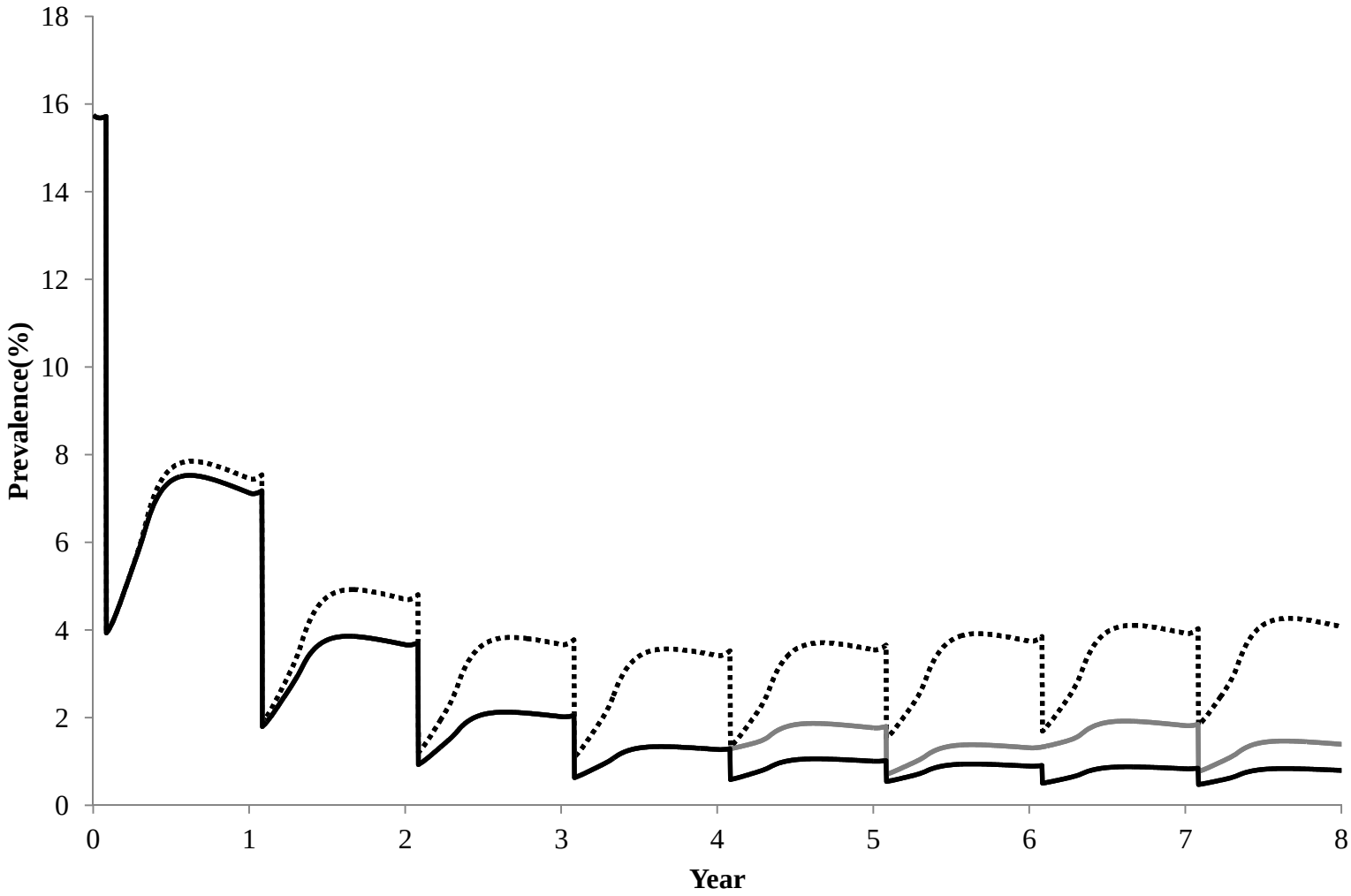

Fig. 7(c)