Universal Journal of Public Health 2(4): 111-117, 2014
DOI: 10.13189/ujph.2014.020401 http://www.hrpub.org

A Universal Model of Epidemic: Optimizing Interventions

Alexander G. Bachinsky, Lily Ph. Nizolenko*

The Theoretical Department, State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk 630559, Russia
*Corresponding Author: nizolenko@vector.nsc.ru

Abstract The outbreaks of infectious diseases caused by natural factors or bioterrorism acts are, unfortunately, quite real threats for the overall population. Planning of an efficient response to an outbreak of an infectious disease requires coordinated efforts of various services aimed to most efficiently utilize the limited resources. This paper describes a model that optimizes utilization of resources when preparing to counter the bioterrorism threats or responding to epidemics caused by epidemiologically dangerous or socially significant pathogens. The model computes the volume of limited resources as well as the particular control activities (isolation, ring vaccination, or mass vaccination) necessary to minimize the optimization criterion, comprising the total number of infected persons, number of lethal cases, and several other characteristics. The model is available remotely via WEB-interface at http://vector-epimod.ru.

Keywords Epidemy, Mathematical model, Limited resources, Optimizing Interventions

1. Introduction

Mathematical models have long been used when developing the strategies for control of infectious outbreaks (see, for example, [1]). Since it is impossible to perform epidemiological experiments in human populations, they have to confine ourselves to field studies, and mathematical modeling actually remains the only tool for studying the effects of particular factors on the dynamics of epidemics.

Numerous works have dealt with selection of the optimal strategies for responses to epidemics [2–8], including vaccination (mass, ring, or risk group vaccination), quarantine, isolation, and treatment. However, the "cost" of interventions, as a rule, is not estimated except for rare cases (for example, [9]). This suggests a need in optimizing the response activities taking into account the losses caused by epidemics and the cost for intervention. The cost for intervention may include the expenditures for maintaining certain resource stocks independently of whether an epidemic will take place or not, in particular, stocks of vaccines, preventive drugs, or therapeutics; specially equipped facilities for isolating infected cases and contacts; qualified medical and paramedical staff; systems for controlling emergency situations; and so on. The cost of interventions is also determined by the expenditures for the intervention activities per se, that is, in particular, search for and isolation of infected persons and cost of the used drugs and other tools necessary for abortion of an epidemic.

Principles for optimization of the anti-epidemic activities aimed to control outbreaks of some infections (mainly, caused by special pathogens) and some obtained results are discussed.

2. Materials and Methods

The State Research Center of Virology and Biotechnology Vector is developing a universal model for predicting scenarios of development of epidemics (outbreaks) of special and socially significant diseases [10, 11]. It is assumed that this model is able to describe the dynamics of any epidemics of an acute infectious disease caused by infection from a certain external source or via random contacts as the main transmission routes independently of sex, age, and other sociodemographic population cohorts.

A universal nature of this model consists in that all the computations utilize the same equations, the same code, and the same interface for all infections. The infections differ from one another only in the set of editable parameters.

Currently, the model is adapted to ten infections, mainly caused by special pathogens. The model provides a wide range of tools for studying local outbreaks and epidemics. User may interactively change all model parameters and thereby estimate the effects of particular pathogen characteristics, specific feature of localities or regions, resource availability, as well as the beginning and intensity of anti-epidemic activities on the prediction of epidemic dynamics. Moreover, an expert user may specify some other infection of interest, absent in the list of diseases already used for simulation.

The model considers several stages characteristic of each disease, differing in their symptoms, probability of correct diagnosing, and level of infectivity of the patients.

When computing the dynamics of an epidemic (outbreak),

three levels of anti-epidemic activities (AEA1-3), mainly determining the rate of detection and isolation (observation) of infected persons, their contacts, and suspects, may be specified [10]. In addition to these three modes, it is possible to specify quarantine, mass vaccination, and/or vaccination of risk groups (contacts and suspects) for some infections.

For some infections, one of the countermeasures in the case of an epidemic (outbreak) is preventive therapy with some drugs, such as immunomodulators, antibiotics, and so on. The model does not consider such intervention in a direct manner. However, it is possible to imitate this type of intervention. An emergency mass vaccination and vaccination of risk groups alter several characteristics, such as the sensitivity to disease, severity of the disease course in infected persons, and infectivity of patients. Prevention therapy gives approximately the same effect.

All these countermeasures are implemented if the corresponding resources are available; these resources comprise qualified medical and paramedical staff; facilities for isolation/observation of patients, contacts, and suspects; and stocks of preventive drugs and therapeutics. When resources are depleted, the levels of the corresponding AEA (detection, isolation, vaccination, treatments, etc.) may be decreased to a complete cessation. The "default" computation variant implies that implementation of the last "strict" AEA level cancels any resource limitations. This option is also user-changeable.

Initially, the model is deterministic and is mainly intended for describing mass epidemics. However, it provides the possibility to simulate an accidental infection and, thus, to obtain a certain range of outcomes in the case of many realizations of this random process.

The model is available remotely via WEB-interface at http://vector-epimod.ru. The user can specify any set of values of 89 parameters used in calculating dynamics of epidemics and assessment of losses from epidemics, as well as 81 factors that define values of the optimization criterion.

2.1. Optimizing Interventions

One of the options provided for by the model is optimization of interventions. Indeed, it is possible to manually select the values for factors that control an epidemic by analyzing the computed epidemic dynamics. However, the model allows for obtaining the values of factors that minimize a certain criterion after their initial values and permissible ranges are specified.

User may interactively specify the initial values and admissible ranges for each optimization factor, for example:

- rate of asymptomatic contacts, suspects and patients in infectious stage daily isolated with AEA1–3;
- bed capacity in provisional hospitals and in quarantine departments for contacts as well as for patients in infectious stage;
- number of vaccination stations and/or points for distribution of prophylactic drugs;
- reserve of drugs and/or vaccines and other.

For more details, see Tables 1 and 2.

It is assumed that maintenance of a certain level of preparedness to a biological threat as well as implementation of interventions requires certain expenditures, material and/or human. Correspondingly, user also specifies the "cost" for each unit factor; thus, the total expenditures for maintenance or use of specified factor values are also taken into account in the optimization criterion. In addition, user may specify a characteristic that canceling optimization of a factor. These data form the first constituent of the criterion.

The second constituent of the criterion is the total losses caused by epidemic, which depends on several characteristics of the epidemics such as total number of infected persons, lethal cases, quarantine days etc (for more details, see Tables 3 and 4). And the user-specified weights of these characteristics:

$$F = \Sigma v_i \cdot f_i + \Sigma L_j \cdot f_j, \quad (1)$$

where v_i is the value of the i-th optimization factor; f_i, unit cost for this factor; L_j, the characteristic determining results of epidemic, which contributes to the losses caused by the epidemic correspondingly to its weight, f_j.

Genetic algorithm [12, 13] is used for optimization. Its program implementation is as follows:

(1) An initial population of "genotypes" is constructed, where each genotype is the vector of values of all the optimized factors. When constructing a genotype, the initial values of each of the parameters are taken and subject to a "mutation" with a certain probability, that is, to a random change in the value having a Gaussian distribution with mathematical expectation equal to the initial value. If the new value in this case falls beyond the permissible limits, the corresponding value at the boundary is assigned to it. The population size is 100 genotypes.

(2) "Fitness" of each genotype is estimated, that is, the epidemic dynamics is calculated for the given set of factors and the value of optimization criterion is determined using the above equation.

(3) The genotypes are re-ordered according to the fitness so that the genotypes with a smaller value of the criterion have smaller ranking numbers in the population.

(4) The genotype with the minimal ranking number, that is, the genotype with the best fit, is taken to randomly select a "partner" for it from those not yet involved in generation of the progeny. Depending on the total fitness for the pair and mean fitness of the population, the number of progenies of this pair is determined. When determining the genotypes of the progenies, a random "recombination" may take place, when part of the "genes" (values of factors) is taken from one parent and the remaining "genes", from the other. A part of the genes of the progenies is also subject to mutations.

(5) The genotype next in fitness and its random partner are selected, both from the genotypes not yet involved in forming the progeny.

(6) The pairs are formed and the offspring is produced until the number of progenies reaches the specified population size. Thus, the genotypes displaying a higher fitness on the average give larger number of progenies.

(7) Then the fitness of the new-generation genotypes is estimated, new pairs are formed, and new progenies are produced. The process is continued until the number of generations is depleted or until the difference between the minimal and maximal fitnesses in generation becomes less than 1%.

(8) The genotype with the fitness maximal over all generations forms a new initial population without involvement of the remaining genotypes, and this cycle is repeated up to five times.

(9) The set of factors that give the minimal value of optimization criterion is regarded as "optimal" and used to compute the epidemic dynamics.

Table 1. Results of optimization of anti-epidemic activities for plague

.Factors of optimization	Default values, limits of permissible values	Costs of factors[1]	Values after optimization
Rate of asymptomatic contacts/suspects daily isolated with AEA2 (%), DolIz2	40 (0-50)	10	**50**[2]
Rate of asymptomatic contacts/suspects daily isolated with AEA3 (%), DolIz3	60 (20-70)	10	**70**
Rate of patients in infectious stage daily isolated with AEA1–3 (%); i, immune			
Iz_P1	20 (0–50)	10	**50**
Iz_P2	40 (0–70)	10	**70**
Iz_P3	60 (0–90)	10	**90**
Iz_Pi1	10 (0–20)	10	**0–20**
Iz_Pi2	20 (0–40)	10	**0–40**
Iz_Pi3	40 (0–70)	10	**80**
Minimal rate of symptomatic patients daily isolated with AEA1–3 (%), Iz_0	10 (0–10)	10	**0–10**
Maximal daily rate of having prophylaxis in risk groups (%), %, RiskVac	20 (0–30)	5	**0**–7
Number of medics/paramedics involved in AEA, NoMedPer	2000 (100–10000)	100	478–3177
Number of teams searching for and isolating infected cases and contacts, NoMedSt	100 (10–500)	200	48–215
Number of patients/contacts detected by one team per day, NoContSup	20 (5–100)	50	15–37
Number of points for distribution of prophylactic drugs, NoVacpoin	500 (0–500)	200	**0**–195
Number of persons treated at one point per day, NoVacPer	500 (0–500)	50	7–**500**
Reserve course doses of prophylactic drugs, NoVacSup	100 000 (0–1 000000)	2	**0**–96633
Reserve of drugs in hospitals (for one treatment course), DrugDoses, 3	100000 (1000–100000)	3	**1000**–93 381
Bed capacity for strict isolation, NoRemPl, 100	300 (100-1000)	100	647–780
Bed capacity in provisional hospitals, NoSupPl, 50	2000 (100–10000)	50	**100**–1130
Bed capacity in quarantine departments for contacts, NoContPl, 70	1000 (100–10000)	70	2653–3635
Values of optimization criterion	2427681331		412478590–414255942

[1] The third column in Table lists the minimal and maximal values for optimization factors obtained after five iterations of the procedure

[2] The limit permissible values are boldfaced.

Table 2. Results of optimization of anti-epidemic activities for smallpox

Factors of optimization	Default values, limits of permissible values	Costs of the factors[1]	Values after optimization
Rate of asymptomatic contacts/suspects daily isolated with AEA2 (%), DolIz2	20 (0-50)	10	**0**[2] - 3
Rate of asymptomatic contacts/suspects daily isolated with AEA3 (%), DolIz3	50 (0-70)	10	**0**
Rate of patients in infectious stage daily isolated with AEA1–3 (%), i – immune			
Iz_P1	20 (0-50)	10	**50**
Iz_P2	40 (0-70)	10	**0 - 70**
Iz_P3	60 (0-90)	10	**90**
Iz_Pi1	10 (0-40)	10	**0** - 7
Iz_Pi2	20 (0-70)	10	1 - 16
Iz_Pi3	40 (0-80)	10	**80**
Rate of patients in final stage (severe case), daily isolated with AEA1–3 (%)			
Iz_Ih1	40 (0-60)	10	**60**
Iz_Ih2	60 (0-80)	10	**0 - 80**
Iz_Ih3	80 (0-90)	10	**0** - 53
Rate of patients in final stage (mild case), daily isolated with AEA1–3 (%)			
Iz_Il1	20 (0-50)	10	48 - **50**
Iz_Il2	40 (0-60)	10	35 - **60**
Iz_Il3	60 (0-80)	10	**0 - 80**
Minimal rate of symptomatic patients daily isolated with AEA1–3 (%), Iz_0	10 (0-10)	10	**0 - 10**
Maximal daily rate of vaccinees in risk groups (%), RiskVac	20 (0-50)	5	**0 -** 32
Number of medics/paramedics involved in AEA, NoMedPer	2000 (100-10000)	100	332 - 2990
Number of teams searching for and isolating infected cases and contacts, NoMedSt	100 (10-500)	200	57 - 281
Number of patients/contacts detected by one team per day, NoContSup	20 (5-100)	50	8 - 68
Number of vaccination stations, NoVacpoin	50 (0-300)	200	1 **- 300**
Number of vaccinees immunized at one station per day, NoVacPer	500 (0-3000)	50	520 - 1056
Reserve of vaccine doses for mass vaccination, NoVacSup	100000 (0-1000000)	2	**0 -** 362075
Reserve of drugs in hospitals (for one treatment course), DrugDoses, 3	1000 (0-50000)	3	895 - 1684
Bed capacity for strict isolation, NoRemPl, 100	300 (100-1000)	100	420 - 771
Bed capacity in provisional hospitals, NoSupPl, 50	2500 (100-10000)	50	2197 - 6315
Bed capacity in quarantine departments for contacts, NoContPl, 70	1000 (100-10000)	70	**100 -** 1815
Values of the optimization criterium	92185380		43391115 - 46574888

[1] The third column in Table lists the minimal and maximal values for optimization factors obtained after five iterations of the procedure

[2] The limit permissible values are boldfaced.

3. Results and Discussion

When studying the effect of AEA optimization, the interventions were optimized for all the infections to which the model is adapted. All the default model parameters were used for computing the dynamics of epidemics. The costs for optimization factors were also equal in all the calculations as well as the weights for the losses caused by epidemics in the optimization criterion. Except for influenza, all computations started from the primary infected cohort of 500 persons, which, in principle, corresponds to a mass bioterrorism attack or a large-scale accident in a facility dealing with pathogens. The computations were performed on the server of the model. The parameters that characterize infections and their justification are available on the server.

One of the factors, namely, rate of immune persons, was

discarded from optimization since its influence is so great, that it took on the maximally permissible values for all infections. In the case of plague, the rates of isolated patients in the third noninfectious stage, initially amounting to zero, were also not optimized.

Since the genetic algorithm of optimization is based on random processes of mutations, recombinations, and selection of parental pairs, the optimization was repeated five times for each pathogen. In this process, the criterion values for each infection after optimization fell in a rather narrow range, thereby demonstrating stability of optimization, based on a random process (Fig. 1). The following value was used to assess the sensitivity to optimization:

$$S = 100*(1 - C_i/C_0), \quad (2)$$

where C_i and C_0 are the values of criterion after and before optimization, respectively.

Consider in more detail the results obtained by optimizing interventions for two infections, smallpox and plague (pneumonic form).

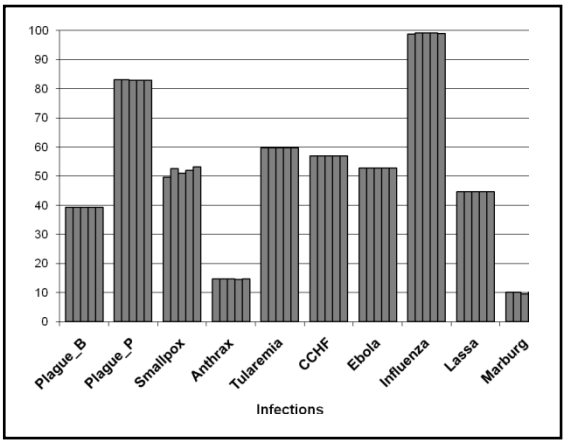

Figure 1. Sensitivity to optimization of interventions: Plague_B, bubonic form of plague; Plague_P, pneumonic form; and CCHF, Crimean-Congo hemorrhagic fever

In a sense, these two selected infections are opposite. The smallpox incubation and infectious periods are long enough versus very short periods of plague. Efficient preventive and emergency vaccinations are possible for smallpox, whereas there is no anti-plague vaccine for mass immunization; however, the latter is compensated for by preventive administration of therapeutics (antibiotics) in the case of a plague epidemic. A rather high average number of the persons infected from one smallpox patient ($R_0 \approx 8$; this estimate has been obtained by adapting the model to the data on smallpox outbreaks in European cities [11]) and a relatively low transmission potential for plague ($R_0 \approx 3$ [14]) are leveled by that the duration of "generations" in the case of plague is short, so that one plague patient over one month can have more following infected persons than a smallpox patient.

Both the plague and smallpox appeared to be rather sensitive to the optimization of interventions. In particular, the optimization criterion for smallpox decreases more than twofold over 43–112 generations and for plague, sixfold over 48–58 generations.

The sets of "optimal" values for the factors are listed in Tables 1 (plague) and 2 (smallpox). It is evident that the minimal values of the criterion in the case of plague are attained provided that most of the factors run into the boundaries of permissible values. As for the isolation rates, these are the maximal values. For the remaining factors, most diverse values minimizing the value of the criterion have been obtained in individual implementations.

Low optimal values of several factors (for example, reserves of prevention drugs) are explainable by that, according to default settings, all resource restrictions are removed in the case of strict AEA, which is launched for plague approximately on day 10. Thus, all resources from that moment on are obtainable "free of cost", so there is no need to maintain expensive mobilization preparedness for several factors. Note that all these reasoning is true only taking into account the "default" modeling parameters. Once a user considerably changes the time for implementation of AEA, costs for the factors, and weights of losses, the final conclusions may appear quite different.

As for the results of optimizing intervention in the case of local smallpox epidemics, the overall pattern is similar on the background of differences in absolute values, namely, close values of optimization criterion are attained at considerably different values of the parameters (Tables 1 and 2). Relative scattering of the epidemic (outbreak) parameters per se after several iterations of optimization procedure is only slightly higher than the relative scattering of optimization criterion (Tables 3 and 4).

Table 3. Indices of epidemics used for calculations of losses for plague

Indices	Weights of indices	Values for default parameters	Values after optimization
Total number of infected persons	100	31664	5001–5177
Person days of isolated patients	1	380615	42111–45543
Person days of observed contacts	0.5	171874	24886
Person days of observed suspects	0.5	1405548	169 358–184422
Quarantine (days)	100	90	35
Total number of lethal cases	10 000	21 709	4103–4229
Took preventive treatment	0.1	408838	288240–322180

Table 4. Indices of epidemics used for calculations of losses for smallpox

Indices	Weights of indices	Values for default parameters	Values after optimization
Total number of infected persons	100	5552	4539–4865
Person days of isolated patients	1	103378	87 536–94 575
Person days of observed contacts	0.5	71012	13777–17101
Person days of observed suspects	0.5	3104620	2 471357–411417
Quarantine (days)	100	53	42–44
Total number of lethal cases	10000	863	412–449
Total number of vaccinees	0.1	733933	770730–857717

When the optimal values of factors run into the permissible limits, a dilemma emerges whether the limits should be expanded or, if the limits are real, the values of the corresponding factors should be fixed to the boundaries, the factors should be discarded from optimization, and the optimization procedure should be repeated for the remaining factors.

3. Conclusions

The universal model for epidemics, constructed at the State Research Center of Virology and Biotechnology Vector, makes it possible to study in an integrated manner the effects of manifold parameters on dynamics of a local epidemic or an outbreak, the range of parameters spanning from characteristics of pathogens to availability of necessary resources, which is most important for timely and comprehensive implementation of anti-epidemic activities.

One of the provided options is optimization of interventions. In this procedure, user may change the initial values of optimization factors and their permissible limits as well as the "weights" for the contributions of the factors and some epidemic parameters to the optimization criterion. The weights should be specified most accurately, since underestimated weights actually exclude the influence of factors or parameters on the value of the criterion as compared with the others. On the contrary, overestimated weights level the effects of the remaining factors.

This is vividly demonstrated by the fact that the "optimal" values of several factors may coincide with their lower limits despite their evident importance for the dynamics of an epidemic. This is explainable by that a default condition implies that any resource restrictions on the scale of interventions are canceled when the third-level strict anti-epidemic activities are switched on. This allows the constant and expensive maintenance of preparedness for several factors to be canceled too.

In general, the computations demonstrate that the model allows for efficient optimization of interventions. The optimization leads to a considerable decrease in all the parameters contributing to estimation of the losses caused by epidemics, such as the total number of infected persons and lethality.

Individual infections display different sensitivities to the optimization procedure. It appears expectable that the more transmissive the infection, the more sensitive is the epidemic it causes to the optimization of anti-epidemic activities. Influenza has emerged to be the most sensitive to optimization of interventions (the criterion decreases almost 100-fold) as well as pneumonic plague (the criterion decreases by over 80%). Marburg hemorrhagic fever, a weakly transmissible disease, and nontransmissible anthrax are least sensitive to the optimization.

Thus, by specifying permissibility limits of the factors determining the intervention efficiency and the costs for their maintenance or implementation, it is possible to obtain close to optimal values of the factors and to estimate feasibility of a full-fledged implementation of the anti-epidemic activities for several acute infectious diseases and even any acute infectious diseases, provided by a user high qualified in epidemiology, for which it is possible to ignore sex-related differences, age, and other sociodemographic characteristics of population cohorts.

Acknowledgements

The work was partially supported by the Federal Target Program "National System of Chemical and Biological Safety of the Russian Federation for 2009–2014."

REFERENCES

[1] R. Anderson, R. May. Infectious diseases of humans: dynamics and control, Oxford, Oxford University Press, 1992.

[2] D. M. Prieto, T. K. Das, A. A. Savachkin, A. Uribe, R. Izurieta, S. Malavade. A systematic review to identify areas of enhancements of pandemic simulation models for operational use at provincial and local levels, BMC Public Health, vol. 12, No. 251, 2012. Online available from: http://www.biomedcentral.com/1471-2458/12/251 [cited 2013 24 Dec].

[3] P. Schumm, W. Schumm, C. Scoglio. Impact of Preventive Responses to Epidemics in Rural Regions, PLOS ONE, vol. 8,

No. 3, e59028, 2013.

[4] K. Ejima, K. Aihara, H. Nishiura. The Impact of Model Building on the Transmission Dynamics under Vaccination: Observable (Symptom-Based) versus Unobservable (Contagiousness-Dependent) Approaches, PLOS ONE, Vol. 8, No. 4, e62062, 2013.

[5] N. Arinaminpathy, A. R. McLean. Logistics of control for an influenza pandemic, Epidemics, Vol. 1, Issue 2, 83–88, 2009.

[6] J. Wallinga, M. van Boven, M. Lipsitch. Optimizing infectious disease interventions during an emerging epidemic, PNAS, Vol. 107, No. 2, pp. 923–928, 2010.

[7] N. Halder, J. K. Kelso, G. J. Milne. Analysis of the effectiveness of interventions used during the 2009 A/H1N1 influenza pandemic, BMC Public Health, Vol. 10, No. 168, 2010. Online available from: http://www.biomedcentral.com/1471-2458/10/168 [cited 2013 24 Dec].

[8] T. House, M. J. Keeling. Epidemic prediction and control in clustered populations, Journal of Theoretical Biology, Vol. 272, No. 1, 1–7, 2011.

[9] A. Kleczkowski1, K. Olesr, E. Gudowska-Nowak, C. A. Gilligan. Searching for the most cost-effective strategy for controlling epidemics spreading on regular and small-world networks, J. R. Soc. Interface, Vol. 9, No 66, 158–169, 2012.

[10] A. G. Bachinsky, L. Ph. Nizolenko, A Universal Model for Predicting Dynamics of the Epidemics Caused by Special Pathogens, BioMed Research International, vol. 2013, Article ID 467078, 7 pages, doi:10.1155/2013/467078, 2013. Online available from: http://www.hindawi.com/journals/bmri/2013/467078/cta/ [cited 2013 24 Dec].

[11] A.G. Bachinsky. 30 years after the smallpox eradication: research continues. 10.2. Mathematical model of the epidemic of smallpox. Evaluation of countermeasures. ed. by G. G. Onishchenko, I. G Drozdov, Koltsovo, Inform-Express, pp. 253-283, 2010 (in Russian).

[12] M. Mitchell. An Introduction to Genetic Algorithms, A Bradford Book The MIT Press, 1999.

[13] R. L. Haupt, S. E. Haupt. Practical genetic algorithms. Second edition. A JOHN WILEY & SONS, INC., PUBLICATION, 2004.

[14] H. Nishiura, M Schwehm, M Kakehashi, M. Eichner. Transmission potential of primary pneumonic plague: time inhomogeneous evaluation based on historical documents of the transmission network, J Epidemiol Community Health, Vol. 60, No7, 640–645, 2006.