

REVIEW ARTICLE

Will integrated surveillance systems for vectors and vector-borne diseases be the future of controlling vector-borne diseases? A practical example from China

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SUMMARY

Vector-borne diseases are one of the world's major public health threats and annually responsible for 30–50% of deaths reported to the national notifiable disease system in China. To control vector-borne diseases, a unified, effective and economic surveillance system is urgently needed; all of the current surveillance systems in China waste resources and/or information. Here, we review some current surveillance systems and present a concept for an integrated surveillance system combining existing vector and vector-borne disease monitoring systems. The integrated surveillance system has been tested in pilot programmes in China and led to a 21·6% cost saving in rodent-borne disease surveillance. We share some experiences gained from these programmes.

Key words: Integrated surveillance vectors, vector-borne diseases.

INTRODUCTION

Vector-borne diseases, like plague, dengue fever, yellow fever, Japanese encephalitis, Lyme disease, and so on, are widely spread. Taking West Nile fever as an example, since the first isolation of West Nile virus (WNV) in 1937 in Uganda, it has spread to Egypt, Israel, South Africa, Asia, North America and parts of Europe, causing a significant disease burden [1]. In Louisiana, USA, the total cost of a WNV epidemic in 2002 was estimated at US \$20·1 million, 54·22% for illness and 45·78% for the public health response [1]. Continual autochthonous transmission of Chikungunya fever in Italy and France, autochthonous transmission of dengue fever in France, Croatia and Madeira, and autochthonous transmission of malaria in The Netherlands, USA, and Spain have been reported [2–10]. In China, vector-borne diseases are annually responsible for 5–10% of new cases of

reported infectious diseases and 30–50% of deaths reported to the national notifiable disease system [11]. Dengue fever broke out in Guangdong Province, China, in 2014, and over 45 000 cases were confirmed, causing huge losses in local economic development. Alongside the constant emergence of new diseases and the continuous expansion of epidemic areas, vector-borne diseases have become one of the most serious global public health threats [12]. Monitoring and controlling vectors undoubtedly plays an important role in preventing vector-borne diseases. There is an urgent need to develop efficient surveillance systems to help simultaneously monitor and control hosts, vectors and diseases.

SOME CURRENT SURVEILLANCE SYSTEMS

Different kinds of surveillance systems have gradually been established around the world, such as surveillance systems for WNV, rodents, plague, *Aedes aegypti*, dengue fever, etc. These systems can be divided into three categories: host surveillance, vector

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Table 1. *Examples of current worldwide surveillance systems for vector-borne diseases*

Publication year	Authors [ref.]	Country	Subjects of surveillance	Type of surveillance
2004	Watson <i>et al.</i> [13]	USA	Crows	Host
2003	Mostashari <i>et al.</i> [14]	USA	Birds	Host
2004	Yaremych <i>et al.</i> [15]	USA	Crows	Host
2006	Shuai <i>et al.</i> [16]	Canada	Birds	Host
2013	Mulatti <i>et al.</i> [17]	Italy	Horses	Host
2009	Regis <i>et al.</i> [18]	Brazil	Insects	Vector
2013	Schaffner <i>et al.</i> [19]	Europe	Mosquitoes	Vector
2013	Pautasso <i>et al.</i> [20]	Italy	Mosquitoes	Vector
2013	Calzolari <i>et al.</i> [21]	Italy	Insects	Vector
2012	Xiaoqing <i>et al.</i> [22]	China	Mosquito-borne disease	Disease
2013	Yongzhuang <i>et al.</i> [23]	China	Dengue fever	Disease
2014	Hongmei <i>et al.</i> [24]	China	Vector-borne disease	Disease

surveillance, and disease surveillance (Table 1). Both host and vector surveillance systems include density surveillance and pathogen carriage surveillance. Host surveillance is meaningful, especially when the data are combined with epidemiology of related diseases. For example, Mulatti *et al.* [17] carried out research on the relationship between serology screening based on an IgM test for WNV in equines and the prevalence of WNV in Italy in 2011, and found that the prevalence of IgM antibody was a sensitive marker for the prevalence of WNV. However, to reduce costs, only some host species tend to be included in surveillance systems [13, 14, 16, 25]. Vector surveillance focuses on establishing the density and pathogen carriage rate of vectors in a given area, which helps to identify how vectors spread infections to hosts and to determine the best intervention strategies to reduce the risk of infection. Disease surveillance includes early detection of infection in humans and the screening of pathogens in healthy people; the aim of which is to estimate pathogen diffusion through systematic analysis of newly emergent clinical cases and the prevalence of pathogens in the population.

In China, the aim of traditional vector surveillance is to monitor the density of traditional vectors such as mosquitoes, flies, rodents, ticks and cockroaches. There is no separate vector-borne disease surveillance system in China, and cases of vector-borne disease are reported via the national notifiable diseases reporting system. These two systems belong to two different agencies between which there is no direct link. Thus, one agency cannot take full advantage of the surveillance data of the other, which in turn causes repetition of work, and the loss of comprehensive monitoring of risk factors and disease prediction. Integrated surveillance systems can manage, efficiently share, and then

take advantage of, information on vectors and vector-borne diseases (Fig. 1). The aim is to provide comprehensive information related to all vector-borne diseases, including public education materials and targeted protective measures.

The concept of integrated surveillance

Integrated surveillance on vectors and vector-borne diseases combines host surveillance, vector surveillance and vector-borne disease surveillance. In mature integrated systems, a large website should be used to collate and disseminate information, and diseases should be the terminal output, connected with specific pathogens related to vectors and hosts. That is to say, if we look at one disease on the website, there should be information on the prevalence of that disease, the epidemiology of its hosts and vectors, and of the related pathogen in those hosts and vectors. At the same time, epidemiology of hosts and vectors can provide information on other diseases that share the same hosts or vectors.

Integrated surveillance has two parts: the primary stage is surveillance for a single disease or virus, such as plague or WNV. Such surveillance covers the whole chain of transmission. The next step – the advanced stage that distinguishes integrated surveillance from traditional single-disease monitoring – is integration of surveillance to cover multiple vector-borne diseases and vector-transmitted pathogens. Different kinds of tissue specimens from hosts and vectors are sampled to test for various pathogens, covering a variety of diseases. In this way, the cost of disease monitoring is much lower than the total for individual disease surveillance systems.

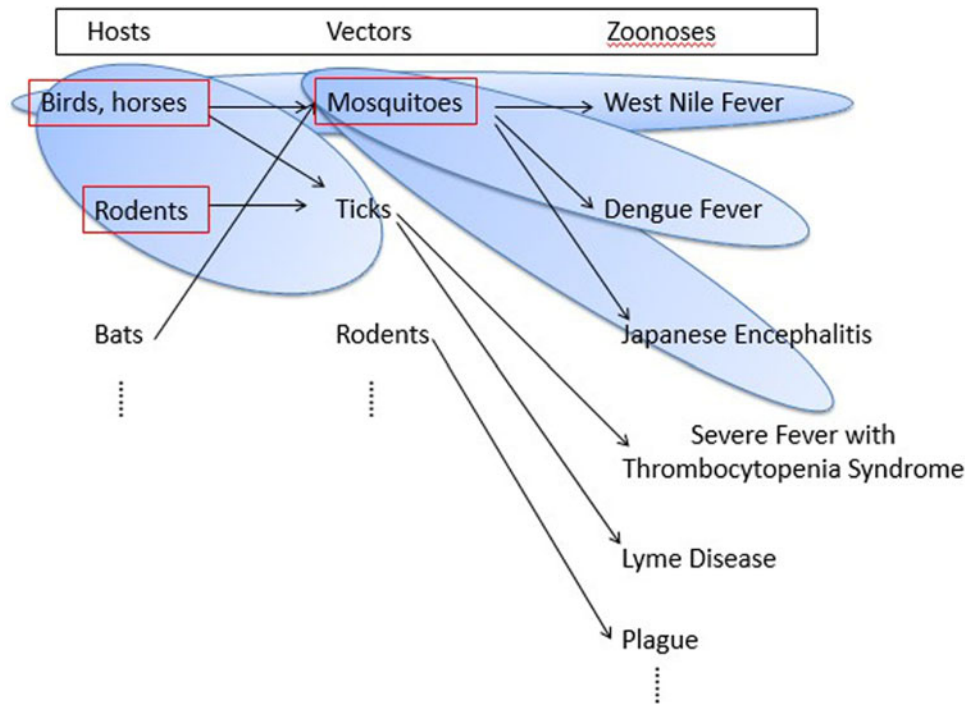


Fig. 1. The intersection among current host, vector and vector-borne zoonosis surveillance systems.

At present, the main monitoring systems in most of the world are primary stage. Only a few surveillance systems have been set up and these focus only on one disease or pathogen, such as the WNV surveillance systems in some countries [16, 21, 26, 27]. In other countries the focus is only on hosts and vectors, not on diseases [19, 20, 28].

Integrated surveillance pilot programmes in China

Development of an integrated surveillance system is at an early stage in China. Two pilot surveillance programmes have been carried out in Zhejiang Province: one on mosquitoes in Jiande City, and the other on rodents in Longyou City and Lishui City. These cities were chosen randomly from 11 cities undertaking traditional surveillance of mosquitoes and rodents.

Initially, a specific project team for integrated surveillance was established. The Vice-Director of Zhejiang Provincial CDC was appointed to coordinate different departments involved in the integrated surveillance, including laboratories, infectious disease surveillance departments at provincial, regional and county levels, and departments involved in entomological surveillance. Standard criteria for vector surveillance (see below) and for some specific diseases were established by Zhejiang CDC; only a few diseases of great concern were included in these pilot

programmes due to limited resources. Professional training of workers involved by Zhejiang CDC was performed on how to conduct standard integrated surveillance. Risk assessment was carried out regularly according to the surveillance data. If the data from routine surveillance predicted an epidemic (reaching the level of an alert event – see Table 2), emergency surveillance would be started (Fig. 2).

Vector surveillance

The light traps method was used for integrated adult mosquito monitoring by Jiande County CDC from June to October, 2009. The light traps were set in four farmhouses and four livestock sheds at the start, middle and end of every month, i.e. three times per month. Mosquitoes caught were killed by freezing and identified under a stereomicroscope using the identification keys of Ribeiro *et al.* and Hervy *et al.* [29, 30]. After classification, they were sent to Zhejiang Provincial CDC for pathogen testing. The container index (CI) was used for *Aedes* larvae.

Rodents were trapped overnight once per month from 2009 to 2011 and the fleas on their surface were collected. Serum, liver, spleen and lungs were removed from rodents to test for haemorrhagic fever with renal syndrome (HFRS) and plague. Combined with direct rodent surveillance, disease hosts (pigs,

Table 2. Criteria for suspected clinical cases and the definition of alert events in the integrated surveillance pilot programmes for mosquitoes and rodents

Disease	Criteria for suspected clinical cases	Alert events
Malaria	Fever (indiscipline in type and cycle of fever), feeling cold, sweating, any incidence of lodging or staying in an epidemic area during malaria transmission season	Cases exceed the average 3/4 cases per month in the preceding 5 years
Epidemic encephalitis B	Fever, headache, vomiting, drowsiness, various disturbances of consciousness, travel to an epidemic area within the last 25 days	Carriage of encephalitis B in <i>Culex tritaeniorhynchus</i> >0.1%
Dengue fever	Double quotidian fever, arthralgia, weakness, nausea, vomiting, decrease of blood platelets and white blood cells, travel to an epidemic area within the last 15 days, or lived in an epidemic area	Container index >10 %
Plague	Hyperpyrexia, severe toxæmia, shock syndrome without lymphadenectasis, severe headache, travelled to a plague epidemic area or touched animals or animal products from an epidemic area within the last 10 days	Index of rat fleas >1
Leptospirosis	Remittent fever, myalgia, weakness, gastrocnemius muscle tenderness, touched polluted water or animal urine/blood within the last 30 days	Carriage of pathogen in rodents >10% and the carriage of pathogen in pigs >7% or the carriage of pathogen in cows >6.5%
Haemorrhagic fever with renal syndrome	Fever, digestive tract symptoms such as weakness, nausea or vomiting, congestion, symptoms of blood capillary damage like exudation and bleeding, travelled to an epidemic area or directly/indirectly touched rodents or excreta within the last 2 months	Density of rodents in night trapping >15%. Carriage of pathogen in rodents >10%

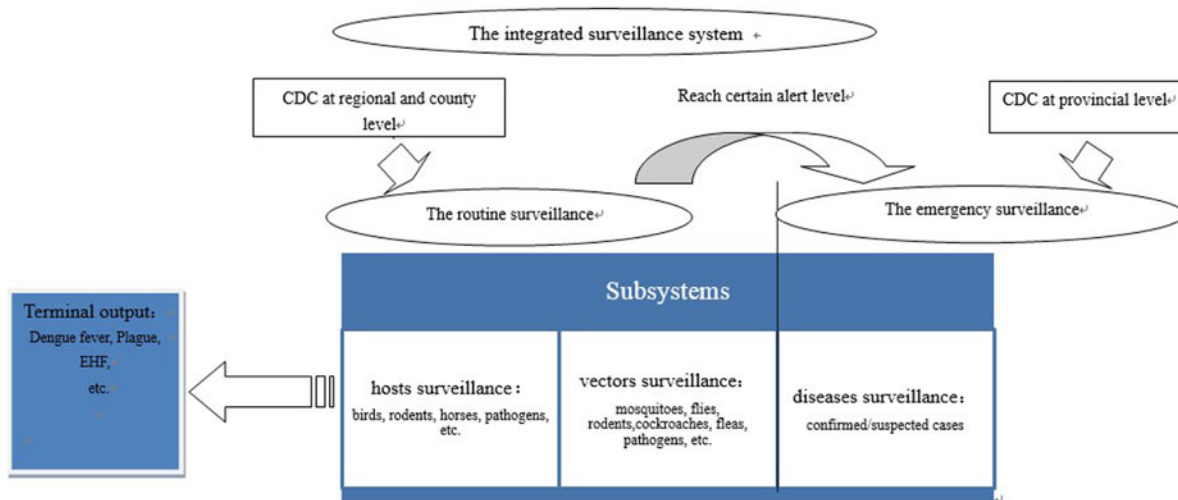


Fig. 2. The main programmes and groups involved in the Chinese pilot programme integrated surveillance system for vectors and vector-borne zoonoses.

cows, frogs, ducks) from Longyou and Lishui cities were also monitored. Kidneys from pigs, frogs, and ducks, and blood from ducks, were collected to test for leptospirosis. All samples were sent to Zhejiang Provincial CDC for testing.

Pathogen testing

Total DNA was extracted from mosquitoes and rodent organs. Epidemic encephalitis B virus, malaria parasites and flaviviruses were tested for using PCR assays on

Table 3. The composition of vector species and pathogens carried within them in two integrated surveillance pilot programmes

Pilot surveillance	Species	Pathogens carried									
		<i>Culex pipiens pallens</i>	<i>Culex tritaeniorhynchus</i>	<i>Aedes albopictus</i>	<i>Anopheles sinensis</i>	Others	Encephalitis B virus	Malaria parasites	Flaviviruses	HFRS virus	<i>Leptospira</i>
Mosquitoes	625	0	0	206	114	0	0	0	0	0	0
Rodents	120	122	610	32	6	0	22	6	0	26 (26/574, 4.5%)	1 (1/606, 0.17%)
		<i>Rattus norvegicus</i>	<i>Apodemus agrarius</i>	<i>Rattus confucianus</i>	<i>Rattus fulvescens</i>	<i>Suneus murinus</i>	<i>Rattus</i>	<i>Rattus</i>	<i>Yersinia pestis</i>	HFRS virus	<i>Leptospira</i>
							<i>musculus</i>	<i>fuscus</i>			

HFRS, Haemorrhagic fever with renal syndrome.

collected mosquitoes. Fleas and some parts of the liver and spleen of rodents were used to culture *Yersinia pestis*. The remaining liver and spleen material were tested for plague by reverse indirect haemagglutination assay (RIHA). The serum of rodents was tested by the indirect haemagglutination assay (IHA) and radiation immune precipitation test (RIP) methods for the F1 antibody to plague. Rodent lungs were tested by fluorescent antibody technique (FAT) for the HV antigen to HFRS, while serum was tested for the HV antibody by indirect fluorescent antibody technique (IFAT). The kidneys of rodents, pigs, frogs and ducks were used to culture *Leptospira*, and the blood of ducks was collected to detect antibody to leptospirosis by microscopy.

Human/disease surveillance

Human/disease surveillance was separated into two parts: passive (routine) surveillance and emergency surveillance. Passive surveillance of epidemic encephalitis B, malaria, dengue fever, plague, HFRS and leptospirosis was conducted using the national notifiable disease reporting system. For emergency surveillance, serum, blood, or cerebrospinal fluid samples were obtained from suspected clinical cases and analysed according to the diagnostic criteria for the six diseases being monitored. PCR assays and serum tests were conducted by Zhejiang Provincial CDC.

Alert events triggering emergency surveillance in the mosquito and rodent surveillance systems were discussed and triggered by an expert group including representatives of appropriate government departments, scientists and regional health authorities, using the method of Delphi (Table 2).

Outcomes

In the integrated mosquito surveillance pilot programme, a total of 945 mosquitoes were caught at a density of 4.92 mosquitoes per hour. Table 3 shows the composition of mosquito species and the pathogens they carried. The CI in Jiande City was monitored three times during the surveillance period; 111 containers were found with water, with CI = 2.70%. The carriage of encephalitis B virus in *Culex tritaeniorhynchus* was zero in Jiande City. No malaria, dengue fever or epidemic encephalitis B cases in Jiande City were reported to the national notifiable disease reporting system in 2009.

In the integrated rodent surveillance pilot programme, 1020 rodents were caught by night trapping,

with a density of 7.02%. Table 3 shows the composition of rodent species and the pathogens they carried. One hundred fleas were collected from 1020 rodents with a rat flea index (i.e. fleas per rat) of 0.098. Seven fleas were tested for plague and none was positive. Fifteen kidneys from pigs, 60 kidneys from ducks, 200 kidneys from frogs and 40 urine samples from cows were tested for leptospirosis, and none was positive. However, when testing duck blood (60 samples), 16 were positive for *Leptospira* antibodies. During 2009–2011, 11 leptospirosis cases (0.12/100 000), 198 HFRS cases (2.2/100 000) and zero plague cases were reported in Longyou and Lishui cities. No emergency surveillance was started because the density or pathogen carriage rate in hosts and vectors were within normal ranges in the two surveillance pilot areas, according to the definitions of alert events established before commencement (Table 2).

Comparison of cost between traditional surveillance and integrated surveillance

Taking the rodent integrated surveillance programme as an example, one integrated surveillance system could take the place of four traditional surveillance systems (for three diseases and one vector). Traditionally, the information obtained by these four surveillance systems was not shared. That is to say, when we wanted to know the density of rodents and of HFRS, two sets of 700 rodents were caught to perform the experiments, a huge waste of human labour. Table 4 shows that 155 778 yuan would be spent on the traditional rodent surveillance system, whereas the equivalent cost of the integrated programme was 122 178 yuan, a cost saving of 21.6%.

DISCUSSION

Many current surveillance systems combine monitoring of hosts, vectors and pathogens. However, they are mainly for a single disease, like plague, dengue fever, or West Nile fever [17, 18, 21, 28]. Thus, comprehensive surveillance of vector-borne diseases may still require repetitive work and waste resources. However, an integrated surveillance system can provide continual, comprehensive information in a more effective and economic way. In the integrated surveillance system pilot programmes in China that we report here, integrated surveillance combined traditional vector surveillance, surveillance of six specific diseases, and some parts of the national notifiable disease

reporting system. This is a reasonable approach, because some vector-borne diseases share the same vectors, and one type of host may bear many different kinds of vectors carrying different pathogens. Hosts, vectors and vector-borne disease-related pathogens represent a large system, which could and should be managed as a whole. The relative inefficiency of single disease surveillance systems can be illustrated by considering the traditional density, plague, leptospirosis and HFRS surveillance systems in China. Rodents (700, 600, 100 and 100, respectively) needed to be caught, and then a fixed number of rodents were dissected to obtain samples of serum, kidney, lungs, etc., according to the requirements of the national monitoring programme. Respectively, 48, 160, 48 and 96 person-days are needed to perform this work (352 person-days in total), while a total of only 240 person-days would be needed when using the integrated surveillance approach (Table 4); thus, 31.8% [(352–240)/352] of the labour was saved.

Development of an integrated surveillance system is just beginning in China. In pilot studies, three cities were chosen, one for mosquito surveillance and two for rodent surveillance. However, no malaria, dengue fever or epidemic encephalitis B cases were found in Jiande City in the study period and the carriage of encephalitis B virus in *C. tritaeniorhynchus* was zero. Thus, more cities should be included in integrated surveillance pilot programmes. In a mature integrated surveillance system, a real-time extranet website is needed to manage the large quantity of data and to make available the results of information surveyed, as is used by many single disease/pathogen surveillance systems such as the WNV monitoring system in Canada and the UK, and the dengue surveillance system in Thailand and Brazil [16, 18, 26, 27, 31, 32]. Such a website was lacking in our surveillance pilots because of resource limitations. The indicators for alert events must also be appropriate. For example, in our integrated mosquito surveillance, the CI was used for *Aedes* larvae monitoring, but the Breteau index is used more widely at present [33, 34].

The integrated surveillance system combined vectors, hosts and pathogens/diseases. It was consistent with an opinion – ‘one health’ – which emphasizes the unity of people, animals and the environment. A good integrated surveillance system could save much unnecessary, repetitive work and make information available more efficiently. However, such systems require contributions from WHO, OIE and FAO to establish standard criteria, valid programme design, and

Table 4. *The comparison of cost price between traditional surveillance and integrated surveillance of rodents*

Item of cost	Leptospirosis	Plague	HFRS	Density surveillance of rodents	Total cost (yuan)§
Traditional surveillance of rodents					
Number of rodents to be caught	100	600	100	700	
Other kinds of animals/vectors needed	Pig, cow, frog, duck	flea	–	–	
Labour needed (person-days)	48	160	48	96	105 600
Test items	Pathogen isolation	Pathogen isolation, IHA, RIP	FAT, IFAT	–	
Samples tested*	100	600	100		
Reagent kits and culture medium needed	Phosphate medium	Hiss agar, F1 antibody indirect hemagglutination kit, precipitation F1 antibody ria kit (RIP)	EHF direct fluorescent antibody, Sigma fluorescent rat antibody	–	
Cost price of reagent kits or culture medium (yuan/100 samples)	4000	493, 1500, 1500	160, 160	–	25 278
Labour needed (person-days)	60	18	5	–	24 900
Total (yuan)†	40 400	74 358	16 220	28 800	155 778
Integrated surveillance of rodents					
Number of rodents to be caught	1020				
Other kinds of animals/vectors needed	Pig, cow, frog, duck	Flea	–	–	
Labour needed (person-days)	240				72 000
Test items	Pathogen isolation	Pathogen isolation, IHA, RIP	FAT, IFAT	–	
Samples tested‡	100	600	100	–	
Cost price of reagent kits or culture medium (yuan/100 samples)	4000	493, 1500, 1500	160, 160	–	25 278
Labour needed (person-days)	60	18	5	–	24 900
Total (yuan)†	22 000	26 358	1820	–	122 178
Percentage of money saved (%)	21·6%				

HFRS, Haemorrhagic fever with renal syndrome; IHA, indirect haemagglutination assay, RIP, radiation immune precipitation test; IFAT, indirect fluorescent antibody technique; EHF, epidemic haemorrhagic fever.

* The number of samples quoted here for traditional surveillance is as recommended by the national plague, leptospirosis and HFRS monitoring programmes.

† The salary is 300 yuan per person per day.

‡ The number of samples in this table is the same for both traditional and integrated surveillance to make them comparable. In reality, more samples were tested in the integrated surveillance because of the range of experiments undertaken (see Table 3).

§ 100 yuan = ~10·5 British pounds.

coordination and/or training of professional staff. These organizations should collaborate with each other, and a specialized committee could be founded (like the specific project team in Zhejiang Province), whose members should include scientists, health authorities, animal authorities and insect authorities. Thus, a series of unified and standard criteria could be established, and a better way of dividing responsibility among agencies could be created. Regionally, the role of coordination should be played by the specific project team as in Zhejiang Province, while internationally, the role should be played by the specialized committee.

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DECLARATION OF INTEREST

None.

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