

# Syndromic Surveillance

## — Toward the Early Detection of Infectious Disease Epidemics —

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### 1 Introduction

Infectious disease epidemics are one of the major crises faced by human society. Following the outbreak of diseases such as SARS (severe acute respiratory syndrome), an emerging infectious disease that shook the world from the end of 2002 to 2003, and the pandemic (H1N1) 2009, cross-border health crisis management has become more important. Mainly in Asia, avian influenza A (H5N1) infection in humans is still being reported, and emerging infectious disease epidemics is of concern.

The early detection of infectious disease outbreaks in order to minimize the spread of epidemics is central to countermeasures against the diseases. In recent years, “syndromic surveillance” has attracted attention as a new technology that meets these demands. The word “surveillance” is generally used when surveying trends in infectious diseases or the economy. It refers to the systematic collection, analysis and interpretation of data required for the planning, implementation and evaluation of countermeasures against diseases, through continuous monitoring of the situation and trend of disease occurrence, enabling the establishment of effective countermeasures based on the results of prompt and regular surveillance feed back to stakeholders.

Syndromic surveillance focuses on patient symptoms such as fever, diarrhea and vomiting. As syndromic surveillance spends less time than the diagnosis-based surveillance, it is said to enable the early detection of infectious disease epidemics and the taking of prompt measures to prevent their spread. In a situation where the “improvement and enhancement of surveillance” come at the top of the list of countermeasures against emerging and reemerging infectious diseases, including new influenza subtypes,

discussed at international conferences hosted by the World Health Organization (hereinafter referred to as WHO), expectations for syndromic surveillance are high.

In syndromic surveillance, technology to analyze information on patient symptoms epidemiologically using statistical methods, as well as technology for the efficient collection, processing and distribution of the information, play an important role. While allowing details of those technologies to be discussed in other reports, this article focuses on the positioning of syndromic surveillance in countermeasures against infectious diseases in humans, describes research and development trends and practical application examples in Japan and abroad, and extracts future challenges.

### 2 What is Syndromic Surveillance?

#### 2-1 Definition and Objective

Research and development and practical applications of syndromic surveillance have been promoted since the anthrax cases following the 9-11 terrorist attacks in the United States in 2001, as well as the SARS outbreak from the end of 2002 to 2003, with the aim of developing anti-bioterrorism measures and the early detection of epidemics of emerging and reemerging infectious diseases-in particular, unknown or rare diseases. With regard to the operation of syndromic surveillance, the U.S. Centers for Disease Control and Prevention (hereinafter referred to as the U.S. CDC) proposes the following definition as the most comprehensive and most accepted today<sup>[1]</sup>:

Syndromic surveillance is “an investigational approach where health department staff, assisted by automated data acquisition and generation of statistical alerts, monitor disease indicators in real-time or near real-time to detect outbreaks of disease earlier than would otherwise be possible with traditional public

health methods.”

In other words, syndromic surveillance is “an action that captures outbreaks of disease in real-time or near real-time by focusing on symptoms that serve as disease indicators, collecting information automatically and analyzing the information epidemiologically using statistical methods.”

According to the Japanese Ministry of Health, Labour and Welfare’s description of syndromic surveillance in its guidelines for measures against new influenza subtypes, syndromic surveillance is “a surveillance for the early detection of outbreak of an infectious disease, through the identification of rapid increases in patients with the target disease based on the number of patients with specified symptoms prior to a diagnosis confirmation from a physician”.<sup>[2]</sup> The Infectious Disease Surveillance Center of the National Institute of Infectious Diseases describes syndromic surveillance as “a surveillance of ‘symptoms’ with the aim of promptly engaging in the ‘early detection’ of epidemics of emerging and reemerging infectious diseases-in particular, unknown or rare diseases”,<sup>[3]</sup> a description which explains the objective of syndromic surveillance.

When the above points are taken together, it can be said that syndromic surveillance is “to collect information on patient symptoms, analyze the information epidemiologically by using statistical methods, make an early judgment as to any outbreaks and epidemics of disease, notify health professionals and government organizations of the results, and take early public health measures,” and “an effective action for preventing the spread of epidemics of man-caused (caused by bioterrorism) or naturally-occurring infectious diseases.”

## 2-2 Types

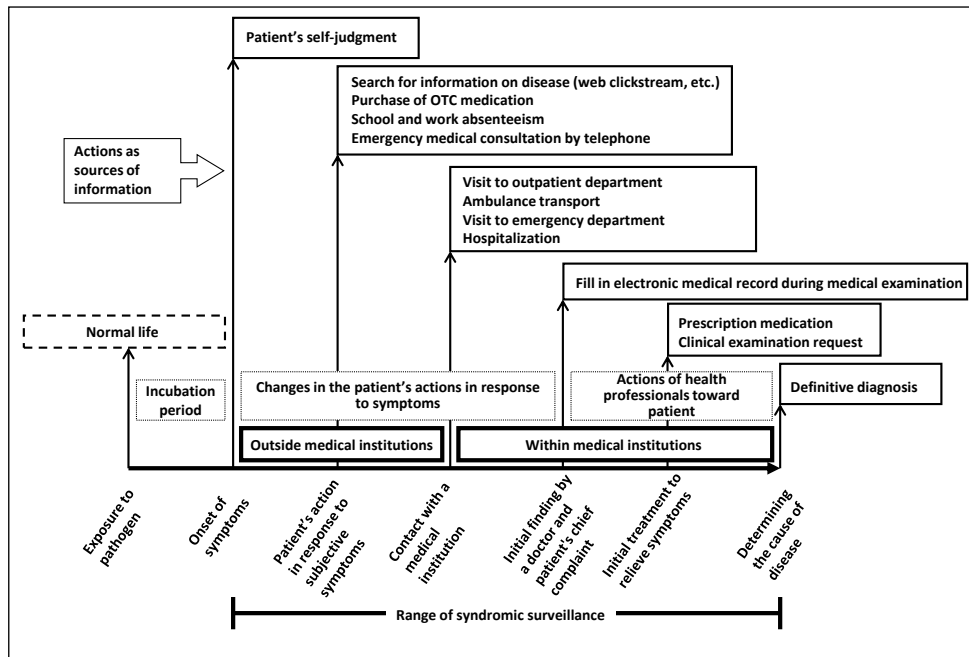
At the core of syndromic surveillance is information on patient symptoms. Symptoms vary, from fever to coughing, rashes, diarrhea, vomiting, and spasm. Patient symptoms are collected extensively, using as sources of information about outpatient visits, emergency department visits, medication sales, school and work absenteeism, and ambulance transportation. A worker, for example, wakes up one morning and feels unwell, so he takes his temperature and finds that it is just over 37°C. He buys and takes over-the-counter medication (hereinafter referred to as OTC medication)<sup>[NOTE 1]</sup> such as antipyretics and a

combination cold remedy at the pharmacy on his way to work and during his lunch break, and sees how he feels for the day while continuing to work. After he comes home, he checks the flu epidemic situation on the Internet. When his temperature goes up the next day, he takes a day off work and visits a doctor. His symptoms get worse quickly, and he cannot go to a medical institution by himself due to severe vomiting and diarrhea, so he is transported by ambulance and is hospitalized. Syndromic surveillance focuses on each behavior that becomes evident with such progression of a patient’s symptoms, and uses this as the information source for the collection of information on many patients’ symptoms.

Figure 1 shows examples of the sources of information on patient symptoms in syndromic surveillance.<sup>[4]</sup> Naturally, these actions of a patient or health professionals are not unique to infectious diseases, and can be observed in other diseases. Specifically, it is conceivable that many people might develop similar symptoms to those described above in a short period of time due to food poisoning, toxic gas or radiation exposure. Therefore, in order to determine whether a symptom is caused by an infectious disease and to make a final judgment as to the occurrence of an epidemic, it is necessary to check the syndromic surveillance results against the diagnosis-based surveillance results (see also 2-3).

Syndromic surveillance is divided into cases where surveillance is based on information sources from medical institutions and cases where it is based on other information sources. Information sources of the former type include outpatient and emergency department visits, and surveillance using these sources consists of collecting information on the outpatients’ subjective symptoms and objective symptoms (symptoms that can be observed by the doctor, such as a rash, jaundice or bleeding) at the clinic, counting the number of patients for each specific symptom, and analyzing the information epidemiologically (this is referred to as syndrome surveillance for outpatient visits). In syndromic surveillance for outpatient visits, electronic medical records are being

[NOTE 1] : OTC (over-the-counter) medication medication that is available at pharmacies, drugstores, etc. without a prescription. The term derives from the way a pharmacist hands medication to a patient over the counter at pharmacies and drugstores.



**Figure 1 :** Sources of Information on Patient Symptoms Subject to Syndromic Surveillance  
Prepared by the STFC based on Reference<sup>[4]</sup>

**Table 1 :** Major Types of Syndromic Surveillance

	Type	Surveillance target
Within medical institutions	Surveillance for outpatient visits	Number of outpatients for each specific subjective and objective symptom (fever, coughing, vomiting, diarrhea, rash, etc.), counted based on patients' answers to the doctor's questions during their visit to an outpatient or emergency department and the doctor's observations
	Surveillance for prescription medication	Number of out-of-hospital prescriptions of specific therapeutic classifications processed at pharmacies (antipyretics, painkillers, antibiotics, Tamiflu, Relenza, etc.)
	Surveillance for ambulance transport	Number of transported patients (by symptom) based on records of ambulance dispatches
Without medical institutions	Surveillance for OTC medication sales	Sales of OTC medication at pharmacies and drugstores (by type of medication, such as combination cold remedy)
	Surveillance for school absenteeism	Number of people absent from school (by symptom)
	Surveillance for internet search	Number of searches for specific key words (e.g.: Influenza)

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used increasingly in recent years in order to collect information on patient symptoms efficiently (see also 2-5). Other information sources from medical institutions include prescriptions (out-of-hospital prescriptions) processed at dispensing pharmacies, ambulance transportation and hospitalization. On the other hand, information sources of the latter type include OTC medication sales and school and work absenteeism, as well as Internet searches for influenza information, which have attracted attention as a new source of information. The major types of syndromic surveillance based on the information sources described above are shown in Table 1.

While attempts have been made to carry out various types of syndromic surveillance up to now, multiple types of surveillance are often conducted concurrently

at the practical application stage following verification tests for each type. For measures against bioterrorism and the pandemic (H1N1) 2009 to be described in chapter 3, several types of syndromic surveillance are conducted concurrently and, based on the results, a comprehensive judgment is made as to the occurrence of an infectious disease epidemic.

Meanwhile, it has been reported that the usage frequency of each type of syndromic surveillance varies depending on each country's medical practices. According to a questionnaire survey of U.S. public health departments, of the syndromic surveillance types shown in Table 1, surveillance for outpatient visits, and in particular, surveillance for emergency department visits, was conducted the most frequently.<sup>[5]</sup> The survey showed that

84% of the 43 public health departments conducting syndromic surveillance have introduced surveillance for emergency department visits. This was followed by surveillance for outpatient department visits (49%), surveillance for OTC medication sales (44%), and surveillance for school absenteeism (35%) (as of 2007). The cost of the maintenance of syndromic surveillance, according to responses from 18 health departments, ranged from 5,500 dollars to 1,000,000 dollars (median of 95,000 dollars), varying widely among institutions. The survey was conducted by the International Society for Disease Surveillance (ISDS) in 2007. Between August 2007 and February 2008, 59 U.S. public health departments nationwide funded by the U.S. CDC through its cooperative agreement for emergency preparedness were surveyed, of which 52 responded (a response rate of 88%). Of the 52 health departments that responded, 43 reported having experience of conducting syndromic surveillance.<sup>[5]</sup>

### *2-3 Comparisons with Diagnosis-based Surveillance*

The characteristics of syndromic surveillance can be understood well when compared with those of diagnosis-based surveillance. Diagnosis-based surveillance is based on the names of diseases diagnosed by a doctor, such as “influenza” or “measles.” It has been used for many years in international surveys of infectious disease outbreaks led by WHO and national surveys in the public health administration by various countries. In the case of Japan, the surveillance of infectious disease patients provided in the “Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients with Infections” (Law No. 73, last revised as of June 18, 2008; hereinafter referred to as the Infectious Disease Control Law) falls under this category (this is called an “Trend survey on infectious disease outbreaks”). Since it is based on a definitive diagnosis, it offers superior reliability but poor timeliness and flexibility.

By contrast, syndromic surveillance excels in timeliness as it was developed in order to detect infectious disease epidemics at an early stage. In addition, as it involves information on patient symptoms, investigations are possible even in cases where the name of the disease has not been determined. Even unknown infectious diseases can be detected if any symptoms are present, indicating a high level of flexibility. However, while syndromic

surveillance can suggest the possibility of an epidemic of some kind of infectious disease, it cannot determine the actual disease. In addition, since fever, coughing and gastrointestinal symptoms are not unique to infectious diseases, there is a risk of capturing a mass outbreak of diseases other than infectious diseases (see also 2-2). In terms of reliability, therefore, syndromic surveillance is inferior to diagnosis-based surveillance.

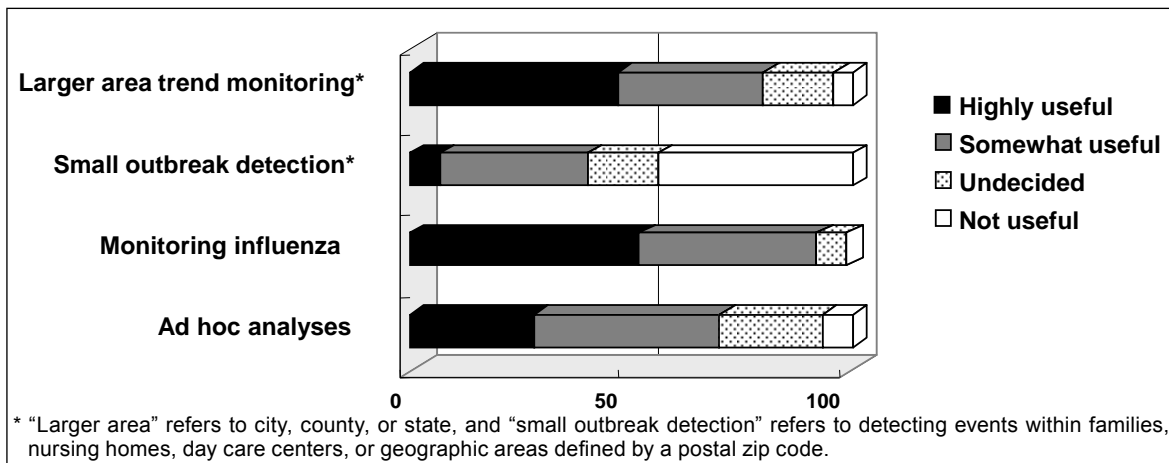
The two types of surveillance described above are mutually complementary from the three standpoints of timeliness, flexibility and reliability. When taking measures against infectious diseases, it is essential that syndromic surveillance is conducted hand in hand with diagnosis-based surveillance.

### *2-4 Utility and Effectiveness*

The utility and effectiveness of syndromic surveillance, in reality, are likely to be largely affected by the public health management systems of each country or region. However, there are few reports of systematic analysis methods which measure the utility value of syndromic surveillance and their results. Here, I will refer to part of the results of the questionnaire survey of U.S. public health departments described in 2-2 as an example that demonstrates the practical capability of syndromic surveillance (Figure 2).<sup>[5]</sup>

Looking at Figure 2, in terms of monitoring larger areas and monitoring influenza, 80% and 92% of the respondents, respectively, reported that syndromic surveillance was “highly useful” or “somewhat useful.” This indicates that U.S. public health departments evaluate highly the utility of syndromic surveillance in monitoring larger areas and monitoring influenza. On the other hand, their evaluations of syndromic surveillance for small outbreak detection were low. The ratings were similar for areas with four years or more of experience in conducting syndromic surveillance and those with fewer years of such experience. Therefore, it is likely that the results reflect the intrinsic adequacy of syndromic surveillance, regardless of the amount of skill required.

The utility and effectiveness of syndromic surveillance also differ depending on the types of syndromic surveillance described in Table 1. While various evaluations are available, here, the findings based on a report by Yan et al. are summarized in Table 2.<sup>[6]</sup> Since the advantages and weaknesses in



**Figure 2 :** Results of Questionnaire Survey of U.S. Public Health Departments on the Utility of Syndromic Surveillance

Prepared by the STFC based on Reference<sup>[5]</sup>

**Table 2 :** Characteristics of Each Syndromic Surveillance Type

	Specificity*	Timeliness*	Advantages	Weaknesses
Surveillance for outpatient visits (outpatient and emergency departments)	High	Medium to High	Routinely generated; often available in electronic format	Difficulty of searching keywords of symptoms (due to misspellings and abbreviations, deletions of negative words, and vocabulary differences across medical institutions for the same symptoms)
Surveillance for OTC medication sales	High to Medium	High	Providing early signs and indications more timely than patient visits; data routinely generated and available in electronic format	Additional information about medication purchasers is unknown (inquiry and investigation after a symptom has been found are difficult)
Surveillance for school or work absenteeism	Low to Medium	High	Timely	Lack of disease characterization

\* These are comparisons among syndromic surveillance types indicated in the left column, not comparisons with surveillance based on definitive diagnosis.

Prepared by the STFC based on Reference<sup>[6]</sup>

the table are provided from a feasibility perspective, please check against the operation overview described in 2-5 below with respect to surveillance for outpatient visits.

### 2-5 System Organization and Operation Overview

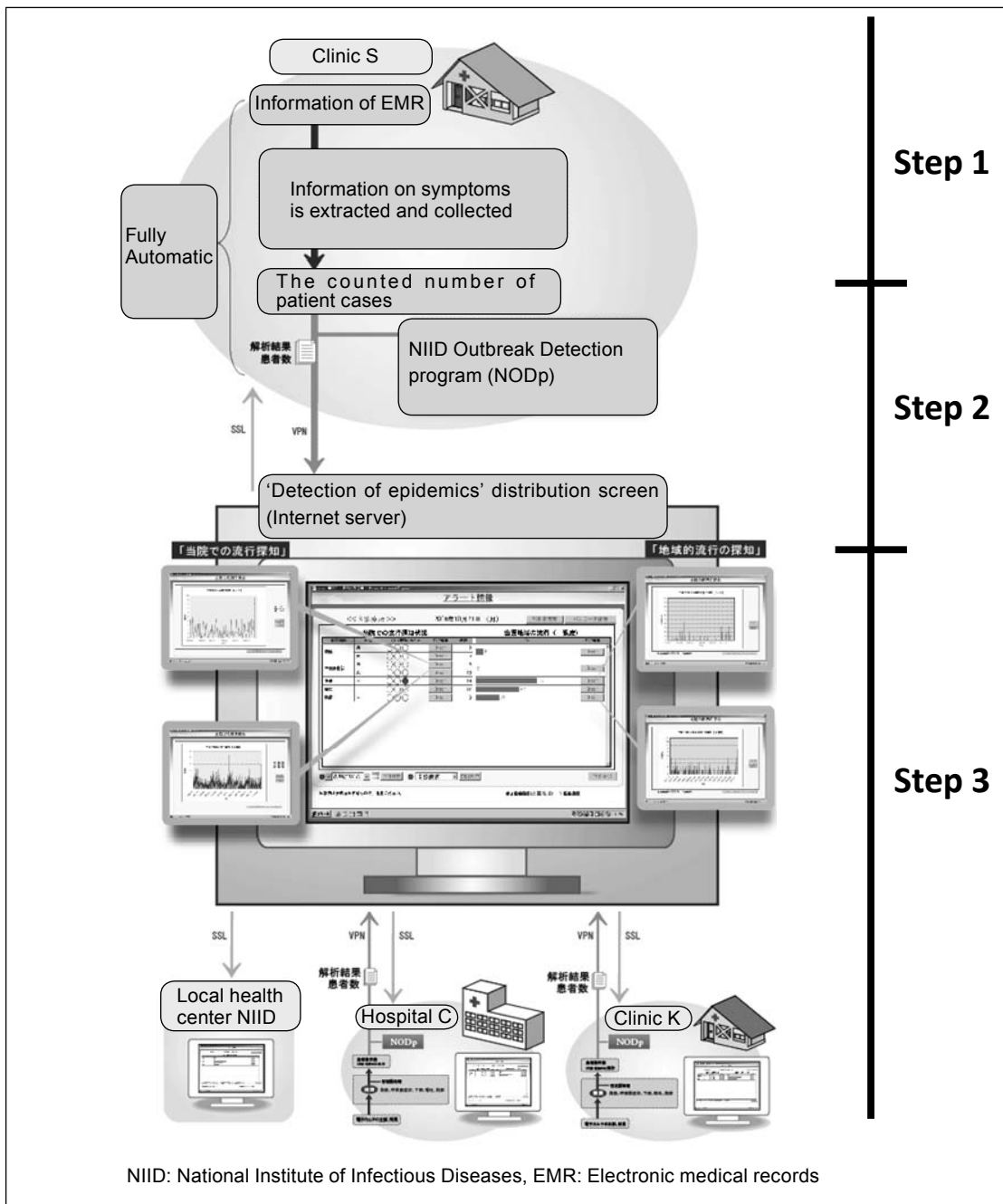
The operational process of syndromic surveillance consists of three steps: 1) selecting the information source of symptoms and collecting information; 2) analyzing the collected information and, based on the results, judging the likelihood of an infectious disease epidemic; and 3) notifying health professionals and government organizations in charge of measures against infectious diseases of the result of 2). These steps are common to all types of syndromic surveillance.

However, since infectious disease epidemics come in various forms depending on the microbiological characteristics of pathogens and the environment of the outbreak area, and since syndromic surveillance

utilizes various information sources, the information collection and analysis algorithms are diverse. The main objective of basic research on syndromic surveillance is to establish these algorithms, and various research findings have been reported in Japan and abroad.

In the following, I will outline the operations involved by taking the example of surveillance for outpatient visits under trial operation by the National Institute of Infectious Diseases (Figure 3).<sup>[7]</sup>

In the example of Figure 3, information is collected for symptoms of fever, respiratory symptoms such as coughing and breathing difficulties, diarrhea, vomiting, and rashes. In Step 1, information on these symptoms is extracted and collected from medical data entered in the electronic medical records of designated medical institutions. If the information on symptoms is stored in text format in electronic medical records, words describing symptoms can be extracted by using the full text search function.



**Figure 3** : System Chart of Syndromic Surveillance for outpatient visits

Source: Infectious Disease Surveillance Center, National Institute of Infectious Diseases<sup>[7]</sup>

If symptom words are included, they are extracted as one patient case. The removal of negative words is important; for example, in the case of fever, by processing negative phrases such as “fever: none,” “no fever,” “no fever either,” and “fever (-),” only those patients who have the symptom are counted. Patient data other than symptom information are limited to age and gender, and other information that leads to the identification of the individual, such as name, address and health insurance card number, are not collected. Furthermore, information collection and extraction are conducted within the medical institution, and only the data of the counted number of patient cases are

used for analysis in the following steps. Thus, this operational process is based on the concept of personal information protection.

In Step 2, the collected data are analyzed. Figure 3 uses an analysis program developed in basic epidemiological research.<sup>[8]</sup> Based on various past infectious disease outbreak trends, this program sets past epidemic patterns as a baseline by applying a multivariate analysis that adds seasonal and day-of-the-week factors (it also takes into consideration whether the day falls after a holiday). Cases where the number of patients who have actually developed symptoms is significantly higher than the baseline are

considered abnormal and are indicated in three alert levels: low, medium and high. As can be seen from the program, the objective of this analysis is to detect at an early stage epidemics that deviate from past infectious disease epidemic patterns. Explained in terms of a specific infectious disease, the annual epidemic of seasonal influenza, for example, is not considered an abnormal infectious disease epidemic as it does not show deviations from past epidemic patterns.

In Step 3, only the number of patients obtained in Step 1 and the alert information obtained in Step 2 are automatically extracted and sent to an Internet server. The number of patients, alert information and epidemic detection information gathered in the server are posted on the website. The system developed by the National Institute of Infectious Diseases uses a VPN (Virtual Private Network) for data transmission and reception, and an SSL (Secure Socket Layer) for sending out information.

After Step 3, based on the epidemic detection information described above, public health department officials will judge whether to collect more detailed information and, in some cases, will make inquiries at medical institutions. Depending on the response to the inquiry, concrete action may follow, such as local institutes of health taking patient specimens and conducting microbiological examinations. If further epidemics are confirmed, the relevant government organizations will take steps to prevent a spread of the epidemic, such as issuing requests to refrain from using and operating public transport and from holding meetings. Since these judgments and measures cannot be automated, it is necessary to seek the judgment of infectious disease experts.

### 3 Research and Development of Syndromic Surveillance and Attempts toward Its Practical Application : Domestic and International Developments

Here, I will introduce research and development of syndromic surveillance and practical examples in Japan and abroad, and consider its utility and effectiveness with respect to measures against infectious diseases.

#### 3-1 Global Trends

Research and development in syndromic

surveillance was triggered by the anthrax cases following the 9-11 terrorist attacks in the United States in 2001, as well as the SARS outbreak from the end of 2002 to 2003. Furthermore, WHO's revised International Health Regulations (hereinafter referred to as IHR2005), which entered into force in June 2007, require timely reporting and action in the event of public health emergencies of international concern, including infectious disease epidemic and mass outbreaks of disease caused by chemicals and radioactive materials,<sup>[9]</sup> and expectations of syndromic surveillance are growing as a way of meeting this requirement.

By country, efforts being made in the United States toward practical applications are prominent. Yan et al. reviewed about 200 publications released between 1997 and 2006, and found that 12 syndromic surveillance systems, including the U.S. CDC's BioSense and EARS (Early Aberration Reporting System), and RODS (Real-time Outbreak and Disease Surveillance), run jointly by the University of Pittsburgh and Carnegie Mellon University, were reported as nationwide-level syndromic surveillance systems as of 2008.<sup>[6]</sup> According to the nationwide questionnaire survey conducted by Lori et al. in the United States in 2009 (to which 41 of the 50 states responded), of the above systems, the most widely adopted system was BioSense (20.61%), followed by RODS (13.39%).<sup>[10]</sup> At local and state levels, 18 syndromic surveillance system implementations, such as projects run by New York City and the State of Michigan, have been reported.<sup>[6]</sup>

Syndromic surveillance in the United States, overall, is mainly aimed at fighting bioterrorism. Following the above-mentioned anthrax cases in 2001, a nationwide campaign against bioterrorism has been implemented, based on the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, and Biodefense for the 21<sup>st</sup> Century, a homeland security executive order issued in April 2004. In the latter executive order, in particular, "Surveillance and Detection" is one of the pillars of the biodefense program, and practical application of syndromic surveillance has been promoted as part of efforts to improve relevant systems. Additionally, in recent years, syndromic surveillance applications have expanded to include measures at state, local and city levels against norovirus infection, which is raising concerns about an epidemic in the United States, as

**Table 3** : Major National and International Syndromic Surveillance Systems (Except the United States and Cases in 3-2 and 3-3)

	Surveillance	Responsible body	Network	Surveillance target
National level	QSurveillance®	British Health Protection Agency, Egton Medical Information Systems Ltd., University of Nottingham	Over 3,000 practices nationwide (as of 2009)	Influenza-like symptoms, respiratory symptoms, gastrointestinal symptoms, etc.
	French Syndromic Surveillance System	French Institute for Public Health Surveillance (Institut de Veille Sanitaire, InVS)	98 hospitals in France and four overseas departments (OSCOUR Network; as of 2007)	Influenza-like symptoms, respiratory symptoms, and gastrointestinal symptoms
	Alternative Surveillance Alert Project (ASAP)	Health Canada	Canadian Association of Chain Drug Stores (CACDS) member stores	Sales of antidiarrheal and antinausea OTC medication (gastrointestinal symptoms)
	Australian Sentinel Practices Research Network (ASPREN)	Royal Australian College of General Practitioners (RACGP), University of Adelaide	More than 100 general practitioners nationwide (as of 2009)	Influenza-like symptoms, gastrointestinal symptoms and other specific symptoms
	Emergency Department Information System in Korea	Korea Centers for Disease Control and Prevention (Korea CDC)	125 sentinel hospitals (as of 2008)	Acute respiratory symptoms
	Taiwan's Respiratory Syndromic Surveillance System (RSSS)	Centers for Disease Control (Taiwan) (Taiwan CDC)	189 hospitals (as of 2005)	Influenza-like symptoms, respiratory symptoms, etc.
International level	Early Warning Outbreak Recognition System (EWORS)	U.S. Naval Medical Research Unit Two (NAMRU-2)	Public health departments and medical institutions of Indonesia, Cambodia, Vietnam, Laos and South Korea	Symptoms of infectious disease registered in ICD* <sup>1</sup> or arbitrarily-found symptoms
	DISTRIbUTE (Distribute Syndromic Surveillance Project)	International Society for Disease Surveillance (ISDS)	U.S. CDC, U.S. Public Health Informatics Institute (PHII), Markle Foundation	Influenza-like symptoms
	SIDARTHa (the Emergency Data-based System for Information on, Detection and Analysis of Risks and Threats to Health)	European Commission co-funded project (June 2008 - December 2010)	Public health departments and medical institutions of 12 European countries (project group), as well as an advisory body comprising officials of the European Centre for Disease Prevention and Control (ECDC) and WHO	Influenza-like symptoms and symptoms of other infectious diseases

\*<sup>1</sup> The International Classification of Diseases (ICD), recommended by the WHO, was first created in 1900 in order to establish an international standard of classification for causes of death, and has since been revised approximately every 10 years (the latest is ICD-10). "Certain infectious and parasitic diseases" are registered and are classified into intestinal infectious diseases, tuberculosis, sepsis, viral hepatitis, human immunodeficiency virus (HIV) disease and other diseases.

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well as measures against new influenza subtypes. National, local and state public health departments are conducting multiple syndromic surveillance systems concurrently to make a comprehensive judgment on the occurrence of an infectious disease epidemic.

Other than the United States, practical applications or trial operations of syndromic surveillance have been launched in the UK, Canada, South Korea, Taiwan, Australia, France, Japan, etc. Like the United States, they have conducted various syndromic surveillance systems with the chief aim of fighting bioterrorism, new influenza subtypes, and infectious diseases that present gastrointestinal symptoms such as norovirus

infection. Examples of syndromic surveillance as anti-bioterrorism measures that have been published in implementation reports and academic papers include: the G8 Hokkaido Toyako Summit in Japan in July 2008; U.S. President Barack Obama's visit to Japan in November 2009; the FIFA World Cup held in Japan and South Korea from May to June 2002; and the G8 summit in Gleneagles, Scotland, in July 2005. Table 3 summarizes syndromic surveillance systems other than those related to anti-bioterrorism measures (except for the United States and cases described in 3-2 and 3-3). These are conducted at national or international levels.



Most syndromic surveillance systems are run by government organizations in charge of public health management and national research institutes, or jointly conducted between those organizations and universities. A certain degree of involvement from government organizations is considered to be necessary in order to take steps as promptly as possible, based on the results of syndromic surveillance, to prevent the spread of an infectious disease epidemic, such as issuing requests to refrain from using and operating public transport.

### 3-2 *Syndromic Surveillance for prescription medications and School Absenteeism*

In the following, I will refer to cases of syndromic surveillance conducted in Japan during the pandemic (H1N1) 2009 outbreak and analyze how the surveillance led to the early detection of the epidemic. I will also evaluate the consistency of the results between syndromic surveillance and diagnosis-based surveillance. Furthermore, I will introduce surveillance for Internet search as an example of recently developed syndromic surveillance. While syndromic surveillance, as described previously, is used widely as an anti-bioterrorism measure, this article, instead of referring to cases based on hypothetical infectious disease epidemics, will look at cases of infectious disease epidemics that actually occurred.

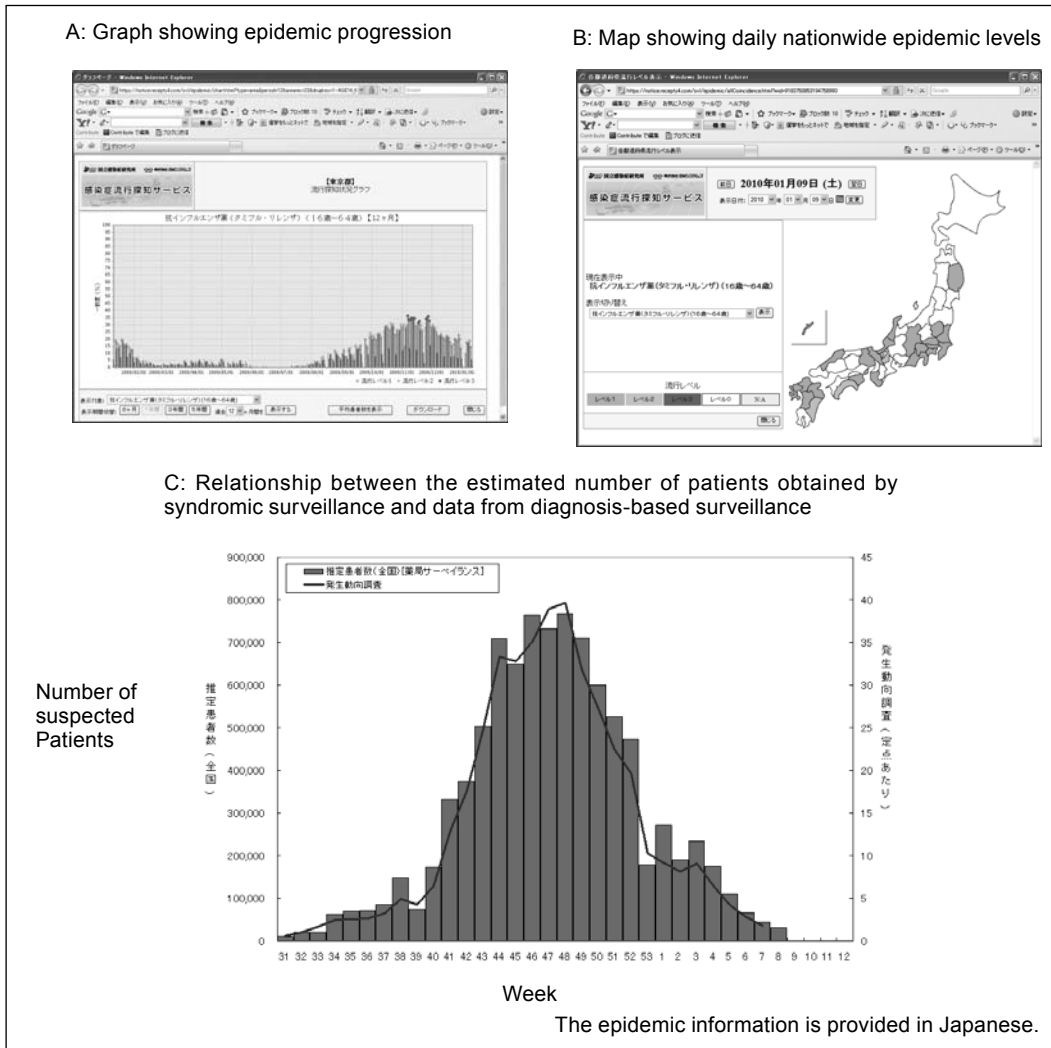
In April 2009, a new influenza subtype, whose outbreak was first reported in Mexico, spread rapidly across the world and, on June 12, 2009, WHO raised its alert level to Phase 6, the pandemic phase. Since an influenza pandemic is believed to occur in 10- to 40-year cycles from past cases of the Spanish flu, Asian flu and Hong Kong flu, WHO member countries had prepared an action plan for countermeasures even before the pandemic (H1N1) 2009.

In Japan, the Pandemic Influenza Preparedness Action Plan was formulated by the Inter-ministerial Avian Influenza Committee in December 2005, followed by the enforcement in May 2008 of the Law on Partial Revision of the Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients with Infections and the Quarantine Act (Act No. 30 of 2008). The amended law created a new classification called “Pandemic human influenza and relevant infections,” enhancing surveillance systems for a possible influenza pandemic. The above

action plan, revised in February 2009, places great importance on the role of syndromic surveillance<sup>[11]</sup>: “It is extremely important to detect an outbreak of new influenza subtype as early as possible through surveillance, and prevent the spread of infection to minimize damage.”

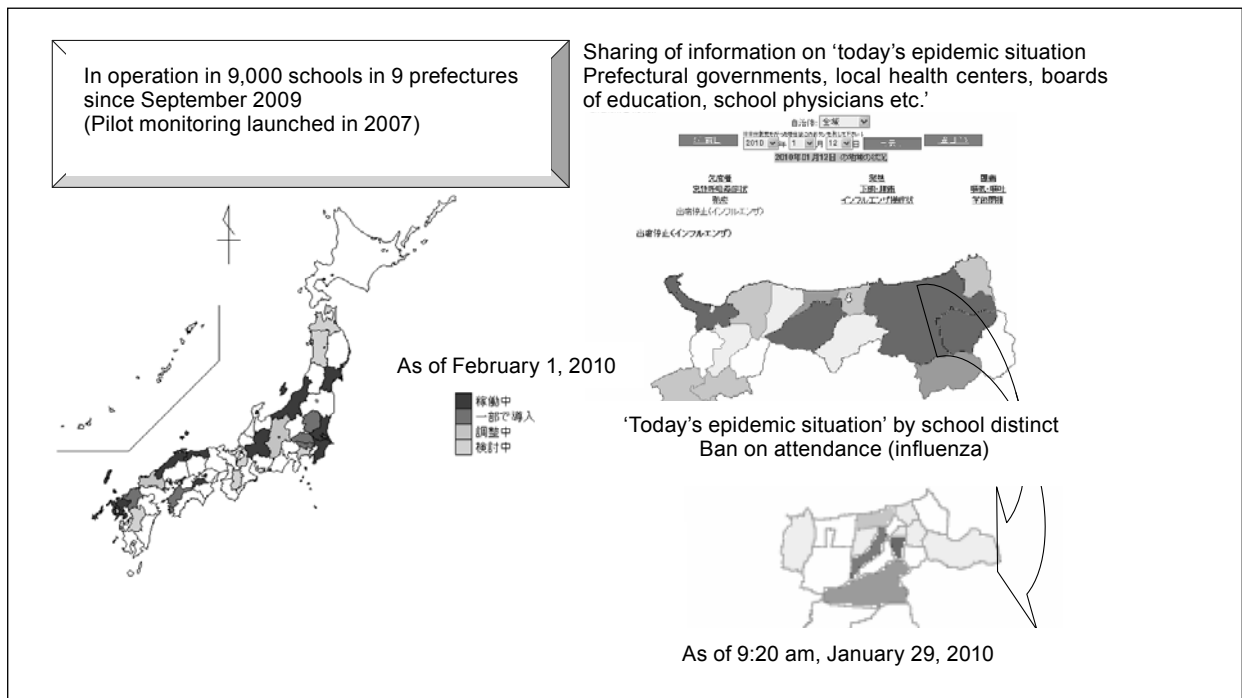
During the pandemic (H1N1) 2009 outbreak in Japan, syndromic surveillance was put to practical use by the National Institute of Infectious Diseases. The institute had been conducting research and development in surveillance for outpatient visits, ambulance transport, prescription medication, OTC medication sales, and school absenteeism prior to the pandemic as measures against various public health crises of international concern required by IHR2005 (FY2007-FY2009; “Empirical study on early detection of local health crisis management information and information sharing systems including government organizations” as part of a multidisciplinary research project on health and safety crisis management measures under the health science and labour research grant from Ministry of Health, Labour and Welfare; research representative Dr. Yasushi Ohkusa). As part of the research and development effort, surveillance systems for prescription medication and school absenteeism attributable to new influenza subtype were established and their effectiveness and utility were tested during the pandemic H1N1 2009 outbreak (as of March 2010, both of the surveillance systems are in progress).

Surveillance for prescription medication, as described in Table 1, is based on the number of prescriptions issued for each specific therapeutic classification. In Japan, the out-of-hospital prescription rate exceeds 50% and the computerization rate of dispensing pharmacies is high. The out-of-hospital prescription rate was 59.3% in a 2008 survey (2008 Social healthcare survey by medical action; Social Statistics Division, Statistics and Information Department, Minister’s Secretariat, Ministry of Health, Labour and Welfare), and the computerization rate of dispensing pharmacies stood at 98.9% as of July 2009 (the Trend of Medical Care Expenditures Pharmacies (Pharmacies dispensing expenditures); Actuarial Research Division, Health Insurance Bureau, Ministry of Health, Labour and Welfare). By using prescription data, information on many patients can be obtained and, since the data are mostly computerized, automatic data collection is possible.



**Figure 4 : Information Provided in Surveillance for prescription Medication**

Source: Infectious Disease Surveillance Center, National Institute of Infectious Diseases<sup>[12]</sup>



**Figure 5 : Information Provided in Surveillance for School Absenteeism**

Source: Infectious Disease Surveillance Center, National Institute of Infectious Diseases (Group conference material pertaining to the research project of Reference<sup>[13]</sup>)

When the therapeutic classification of antiviral drugs for influenza is selected, for example, the number of prescriptions will correspond one on one to the number of suspected influenza patients, thus it is likely to provide a highly accurate surveillance result. Surveillance for prescription medication as a countermeasure against the pandemic (H1N1) 2009 has been conducted in earnest by the National Institute of Infectious Diseases since April 20, 2009. Specifically, the number of prescriptions of, mainly, Tamiflu® and Relenza®, both antiviral drugs for influenza, is being monitored at 4,042 pharmacies nationwide (as of April 10, 2010; equivalent to approximately 9% of all pharmacies in Japan) that gathers out-of-hospital prescription data by ASP (Application Service Provider). The monitored data are distributed to health professionals next day in the form of information collection and analysis results. Thus, it can be said that this enables almost real-time detection of an infectious disease epidemic. Figure 4 shows examples of information distributed to health professionals.<sup>[12]</sup>

According to the results up to the end of December 2009, 38 prefectures reported a high positive correlation between the estimated number of patients obtained by surveillance for prescription medication and the actual number of patients obtained from diagnosis-based surveillance (a correlation coefficient of 0.9 or higher). These results have led to an evaluation that the surveillance conducted was able to present indicators of the pandemic (H1N1) 2009 ahead of diagnosis-based surveillance.<sup>[13]</sup>

Meanwhile, the National Institute of Infectious Diseases has conducted surveillance for school absenteeism in earnest since September 2009.<sup>[13]</sup> In the surveillance for school absenteeism, the absenteeism situation of all students suffering from fever, headaches, acute respiratory symptoms, diarrhea and abdominal pain, nausea and vomiting, rashes, and influenza-like symptoms were monitored in a total of 9,000 elementary, junior high and high schools, equivalent to 19% of all schools in Japan (covering nine prefectures as of February 2010) (Figure 5).

In January 1-15, 2010, a questionnaire survey of participants in the surveillance for school absenteeism was conducted. Responses were obtained from 2,218 respondents including school officials, board of education officials and public health department officials of local governments, and views such as on

the usefulness of surveillance in making a decision on temporary school closures were heard.<sup>[13]</sup> However, the FY2009 project report notes that there remain problems in the surveillance system for school absenteeism (see also 4-2).<sup>[13]</sup> It seems that it will be necessary to examine further the intrinsic effectiveness and utility of surveillance for school absenteeism through future research and development and verification tests.

### 3-3 Surveillance for Internet Search

In recent years, surveillance of seasonal influenza that utilizes Internet search information has attracted attention. Such systems enabling the early detection of seasonal influenza epidemics in the United States were made public in 2008 by the University of Iowa and other U.S. academic institutions and Yahoo! Research,<sup>[14]</sup> and by Google.org and U.S. CDC.<sup>[15]</sup> The former used search query logs in the United States from March 2004 through May 2008 and demonstrated that the number of searches containing the terms “influenza” or “flu” was strongly linked to the percentage of influenza-positive cases in clinical tests and death attributable to pneumonia and seasonal influenza. In other words, they found a positive correlation between the number of influenza-related searches and the number of patients who actually displayed symptoms of seasonal influenza. Based on this result, Google.org developed a more comprehensive and automated Internet search surveillance system, and released an experimental version of Google Flu Trends on November 11, 2008 (U.S. local time; the same shall apply hereinafter) (available in Japan by the service name of “Influtrend”).<sup>[16]</sup> It has been reported that, whereas the U.S. CDC’s traditional Influenza Sentinel Providers Surveillance Network takes one to two weeks for information collection, analysis and publication of results, the two systems described above are able to process information faster. In other words, by analyzing the number of search query data related with influenza, it is possible to estimate an epidemic of seasonal influenza prior to a definitive diagnosis.

Google Flu Trends<sup>[16]</sup> is similar to the Internet search surveillance system of the University of Iowa et al. in that they are both based on influenza-like illness (ILI)-related search queries. However, Google Flu Trends covers a wider variety of search terms (according to Ginsberg et al., 45 queries related to influenza

complications and remedies were established at the initial stage of system development),<sup>[15]</sup> divides the epidemic level into five phases, and shows the estimated epidemic level by means of maps by country or by region and temporal transitional graphs. In particular, in deciding on the epidemic level, Google Flu Trends compares the estimates based on search data against a historic baseline level of influenza activity for that area. Data are updated on the Internet on a daily basis, and Google Flu Trends releases visualized information on the seasonal influenza epidemic situation in almost real-time. In addition, Google Flu Trends verifies estimated data from each country by using diagnosis-based surveillance data officially released by the respective public health management institutions.

With regard to the handling of personal information, Google.org says “we are keenly aware of the trust our users place in us, and of our responsibility to protect their privacy. Google Flu Trends can never be used to identify individual users because we rely on anonymized, aggregated counts of how often certain search queries occur each week.”

The effectiveness of Google Flu Trends has been demonstrated by comparisons with data from the above-mentioned traditional influenza surveillance conducted by the U.S. CDC. Ginsberg et al.<sup>[16]</sup> compared the data from weekly reports on the proportion of patients suffering from influenza-like symptoms in nine U.S. regions over five years (2003-2007) with estimated data obtained from Google Flu Trends, and found that the two showed a strong positive correlation (a correlation coefficient of 0.80-0.96). In addition, when surveillance using Google Flu Trends was conducted in the same nine regions on a trial basis during the seasonal influenza epidemic in 2007-2008, Google Flu Trends reportedly succeeded in detecting the epidemic one to two weeks earlier than the U.S. CDC’s data release. Furthermore, in New Zealand, it has been reported that the peak period for the seasonal influenza epidemic in 2009 was indicated by Google Flu Trends one week earlier than reports from general practitioners.<sup>[17]</sup>

Google Flu Trends, only available in the United States when first launched in November 2008, has since extended its coverage to countries such as Mexico, New Zealand and Australia, adding Japan and certain European countries on October 8, 2009, and covering a total of 20 countries as of March 2010.

## 4 | Issues Regarding Future Development

As shown in Figure 1 and Table 2, syndromic surveillance has a broad information source and an extensive coverage area. It can be conducted at national or international levels and, as in the U.S. case described in 3-1, it can be conducted at local, state and city levels within a country. In addition, as shown in Table 2, differences in utility and effectiveness have been reported depending on the type of syndromic surveillance. Here, I will attempt to capture syndromic surveillance in its entirety and identify what is required for the future development of domestic and international syndromic surveillance systems.

### 4-1 Issues Common to All Systems

As described in Chapter 3, syndromic surveillance has been conducted worldwide in recent years, and the types of syndromic surveillance have become increasingly diverse. With such widespread use, however, various issues with regard to syndromic surveillance systems have also been pointed out.

Chretien et al., responsible for the U.S. Department of Defense Global Emerging Infections Surveillance and Response System (DoD-GEIS), raised four important issues-1) technical, 2) financial, 3) political, and 4) ethical, social and cultural considerations-in building syndromic surveillance systems.<sup>[18]</sup> In the following, issues will be extracted in line with these considerations.

From technical and financial perspectives, the key is to collect information on patient symptoms as efficiently and effectively as possible to maintain the operation of syndromic surveillance systems. While issues regarding information collection, analysis and distribution technologies and cost-related issues vary depending on the surveillance target, location and system, there is room for improvement, in particular, with regard to software. Chretien et al., referred to above, has proposed the introduction of open-source software to replace the commercial software used in many existing syndromic surveillance systems in order to reduce operational costs.<sup>[19]</sup> The proposed software should be compatible with various information sources and be equipped with a function that can automatically collect, analyze and distribute data. In other words, since a high level of usability is

required, software developers and persons conducting syndromic surveillance need to collaborate for software creation.

From a political standpoint, coordination between administrative departments of national and local governments, as well as cooperation with stake holders, is important. In the case of Japan, the National Institute of Infectious Diseases, quarantine stations, local institutes of health, local health centers, medical institutions, and organizations involved with the information sources of each syndromic surveillance system need to work closely together to build a framework for syndromic surveillance, under jurisdiction of the departments of national and prefectural governments in charge of public health administration, school health administration, and occupational health administration.

With respect to ethical, social and cultural issues, greater public understanding of syndromic surveillance as a countermeasure against infectious diseases is necessary. In particular, understanding with regard to information disclosure is crucial. While syndromic surveillance is based on personal and medical information regarding symptoms, information that can identify the individual is not released from institutions that possess the information source. Persons responsible for conducting syndromic surveillance are obliged to be accountable to the public in adhering to the privacy policies of syndromic surveillance. In addition, when building syndromic surveillance systems, it is also necessary for the public to cooperate in maintaining the flexibility of such systems by refraining from overestimating or underestimating specific methods and tools. Google Flu Trends, for example, is gaining worldwide recognition and is prospective for a useful countermeasure against infectious diseases; in Japan, however, public awareness of medical services serves as a hurdle to its full-scale introduction. Considering the differences between Japan and other countries in their outpatient care systems, internet search patterns of Japanese people may not always be the same as those of people from other countries. It is necessary to select information sources and verify systems by keeping in mind that the utility and effectiveness of syndromic surveillance may vary according to its location and social influences. In the following, I will describe more specific issues concerning Japan.

#### *4-2 Domestic Issues*

In Japan, several syndromic surveillance systems have been developed mainly by the National Institute of Infectious Diseases and are at the stages of experimental demonstration, trial operation and practical application. The following are issues that have been highlighted through conducting syndromic surveillance.

From a technical standpoint, the need for further consideration with respect to the compatibility of data management software has been pointed out in surveillance for outpatient visits and ambulance transport (sourced from group conference materials pertaining to the research project of Reference<sup>[13]</sup>). The two current surveillance systems have been developed for software for specific electronic medical records or records of ambulance dispatches, and are not compatible with software that differs among medical institutions or fire departments. With respect to electronic medical records, in particular, there are cases where different software systems are used at different medical institutions or, in university hospitals, at different departments, and technological development is required to enable the necessary information to be extracted from the various software systems. To this end, cooperation is needed among the National Institute of Infectious Diseases, which is leading surveillance efforts, medical institutions and vendors of electronic medical records. In addition, since information collection is not automated in the current surveillance system for school absenteeism, the school needs to enter data for each event of absenteeism. According to Ohkusa et al.,<sup>[13]</sup> an average of 7-8 minutes is reportedly required for entering data under the current system, and further technological development is necessary in the future to reduce the operation.

In view of their future widespread use, national and local governments should consider measures to incorporate surveillance for prescription medication and school absenteeism, which are at the practical application stage, into public health administration at an early date. Also, in surveillance for outpatient visits, the widespread use of electronic medical records is essential. According to the Ministry of Health, Labour and Welfare's survey of medical facilities (static survey), as of 2008, electronic medical records were introduced in the entire facility in 10.8% (948 facilities) of hospitals and 13.1% (12,939 facilities)

of clinics. While the figure rose 5.6% for hospitals and 6.8% for clinics from the results of the same survey three years ago,<sup>[19]</sup> the situation is far from being ready for conducting a full-scale operation of syndromic surveillance. The New IT Reform Strategy compiled by the government's Strategic Headquarters for the Promotion of an Advanced Information and Telecommunications Network Society (IT Strategic Headquarters) calls for the widespread use of electronic medical records and other medical information systems in order to improve the quality and efficiency of medical services.<sup>[20]</sup> Thus, the spread of electronic medical records is also desirable from the perspective of contributing to improving the quality of medical services as a whole through countermeasures against infectious diseases.

Meanwhile, with regard to surveillance for school absenteeism, it is hoped that verification of its utility and effectiveness will make progress through future verification tests. Sites where group activities take place, such as schools, are prone to become hotbeds for infectious diseases and, at the same time, may trigger a spread of the epidemic to the home and the community. It is considered to be meaningful, from the perspective of public health management, to measure the utility value of surveillance for school absenteeism.

#### 4-3 International Issues

Expectations for syndromic surveillance are growing with respect to international public health measures promoted by IHR2005. IHR2005 calls for an enhancement of measures against large-scale infectious diseases, irrespective of whether they are man-caused or naturally-occurring.<sup>[9]</sup>

In considering measures against emerging infectious diseases, it is particularly important to conduct syndromic surveillance in Africa's tropical regions, Asia and Latin America where infectious diseases are epidemic frequently. Public health infrastructure is generally underdeveloped in these areas, and they typically lack the experimental facilities for clinical research and tests. Therefore, in many cases it is difficult to conduct diagnosis-based surveillance, and syndromic surveillance would become an effective measure against infectious diseases. In introducing syndromic surveillance, it is necessary to minimize the costs of installing and maintaining a surveillance system by making use of low-cost netbook PCs,

mobile phones, and smartphones as a means of the collection, processing and distribution of information. At the same time, it is important to ensure that conducting syndromic surveillance does not interfere with existing medical systems. Creating community-based syndromic surveillance programs and seeking the participation of volunteers equipped with public health knowledge should be considered so as not to place an excessive burden on the limited number of medical staff. The consideration of syndromic surveillance systems that involve lower financial burdens and do not waste human resources are under way, and trial surveillance cases of malaria, food-borne infectious diseases and sexually transmitted diseases are being accumulated in the above-mentioned areas.<sup>[21]</sup>

In order to disseminate syndromic surveillance globally in the future, including in the above-mentioned areas, it is necessary to make greater use of the syndromic surveillance skills in developed countries and existing achievements of international syndromic surveillance. It is desirable to strengthen the network of experts of WHO and the International Society for Disease Surveillance (ISDS), and to provide venues for exchanging views and information on ways to overcome technical, financial, political, ethical, social and cultural issues. In order to advance Asia's public health management system as a whole, Japan needs to deepen further its partnership with WHO's Western Pacific Regional Office (WPRO) and the Asia-Pacific Economic Cooperation (APEC), and take action such as being more active in providing the above-mentioned venues for exchanging views and information.

## 5 | Other Important Perspectives

Syndromic surveillance offers superior timeliness and flexibility than diagnosis-based surveillance. While its timeliness is obvious considering its primary objective, its flexibility is noteworthy in that it can also accommodate unknown infectious diseases since the name of the disease is not required. In addition, the diversity of syndromic surveillance systems should also be noted. Various information sources are available for capturing a patient's symptoms, and the utility and effectiveness of syndromic surveillance change depending on the information source and the surrounding social environment. The

expected outcome of syndromic surveillance is also diverse. Surveillance for outpatient visits, by linking information on infectious diseases with that on other diseases through the use of electronic medical records, is considered to be useful for improving the quality of medical services as a whole. Conducting syndromic surveillance on sites of group activities such as in schools is expected to improve public health knowledge, understanding and management skills within the local community to which the site belongs. Furthermore, Internet search surveillance is considered to contribute to enhancing Internet users' awareness of the public health situation at national and international levels. In general, since syndromic surveillance is diverse, the required approach is to select the information source in accordance with the objective, target, scale, location and changes in the social environment, without adhering to specific methods or tools, and to constantly explore new information sources and embrace them as necessary. Considering the need to select valuable information sources rationally among a wide variety of sources, I would like to emphasize that the flexible selection

of information sources and a swift evaluation of their utility and effectiveness are the two key points of promoting syndromic surveillance.

While the National Institute of Infectious Diseases is taking the initiative in conducting syndromic surveillance in Japan, it is desirable that other related research institutes, private organizations and enterprises also take part at the system development stage. With regard to the National Institute of Infectious Diseases, which has led efforts in organizing syndromic surveillance systems, analyzing information, making a comprehensive judgment and taking public health responses to prevent the spread of epidemics, a further enhancement of its role is required in the future.

While this article discusses syndromic surveillance for humans, it is also necessary to look at monitored data of animals in the future when considering measures against emerging infectious diseases. This is because it has been reported that more than 60% of emerging infectious diseases are zoonotic infections.<sup>[22]</sup> Syndromic surveillance for humans should be promoted with the aid of data regarding

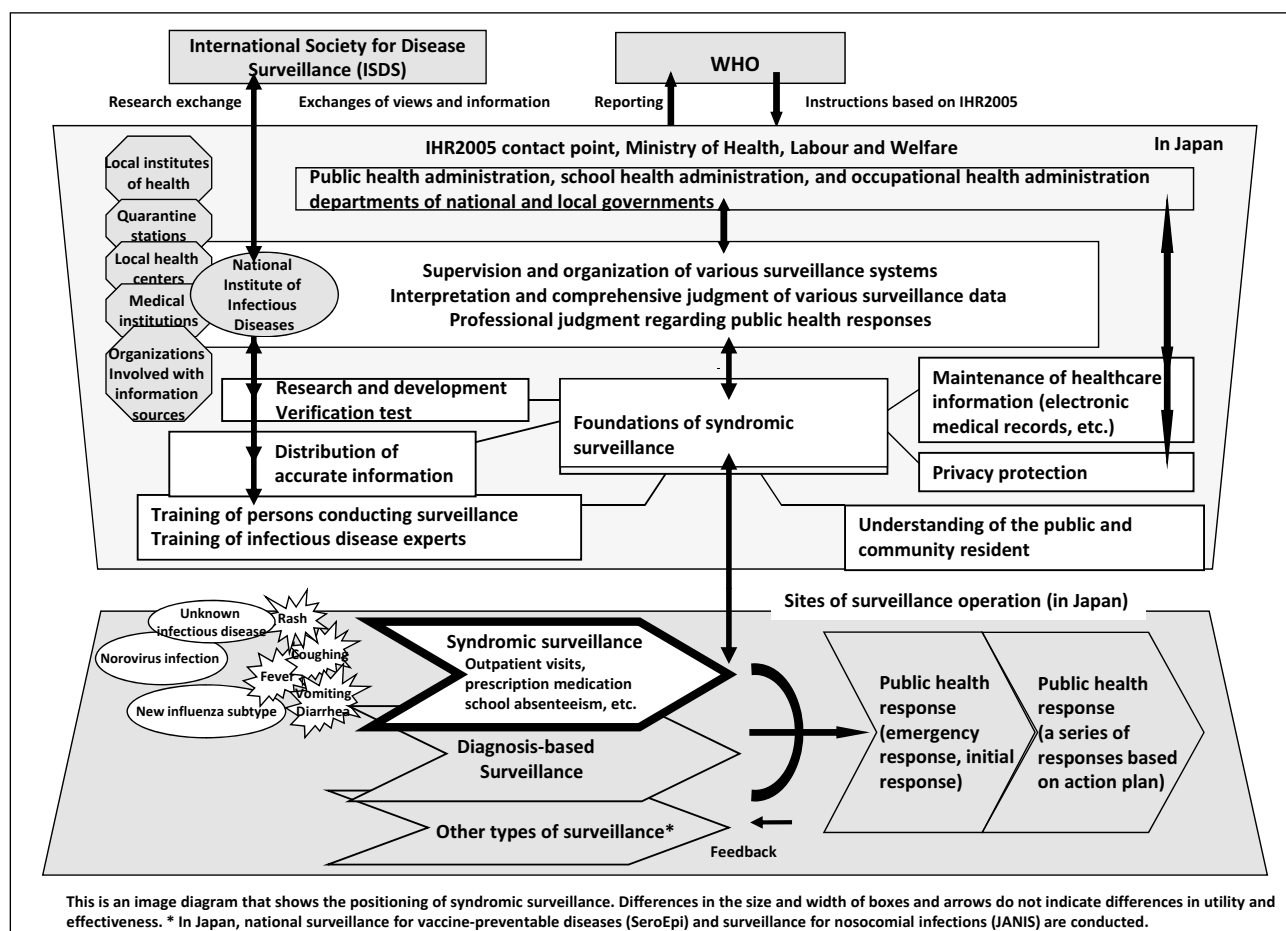


Figure 6 : Framework for Syndromic Surveillance in Japan

Prepared by the STFC.

behavioral abnormalities, diseases and mass deaths of migratory birds, arthropods, wild mammals and livestock.

Figure 6 sums up the positioning of syndromic surveillance among measures against infectious diseases as a whole as well as its future framework, and it is clear that syndromic surveillance is applied at a very early stage. While it is considered to be possible to fully automate the information collection, analysis and distribution operations of syndromic surveillance in the future, human judgment is necessary for taking concrete measures to prevent the spread of an epidemic based on that information. In other words, it

is essential to train infectious disease experts who are able to interpret and understand data obtained from syndromic surveillance appropriately and swiftly prompt public health-related responses.

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## Profile

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