表2. 学級閉鎖の効果的な条件の検討(ロジスティック回帰分析)

	Adjusted Odds Ratio	95% CI
学年群		
1−3 年生(低学年)	2.10	(1.00-4.41)
4−6 年生(高学年)	Ref.	
学級閉鎖を実施した月		
9 月	0.41	(0.03-5.27)
10 月	Ref.	
11 月	5.97	(2.66-13.42)
クラス人数		
20 人〜29 人	0.90	(0.42-1.95)
30 人以上	Ref.	
学級閉鎖期間		
3 日間	Ref.	
4 日間	2.70	(1.18-6.15)
5 日間	4.41	(1.39-13.98)
6 日間	2.37	(0.48-11.78)

III　研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ

論文

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Tamie Sugawara, et.al	Real-time Prescription Surveillance and its Application to Monitoring Seasonal Influenza Activity in Japan	JMIR	14(1)	1-9	2012
菅原民枝、他	薬局サーベイランスによるバイオテロ対策のためのアシクロビル製剤モニタリング	感染症学雑誌	85(6)	632-637	2011
大日康史、他	学校欠席者情報収集システムの構築と評価	学校保健研究	53(4)	312-319	2011
大日康史、他	学校の業務簡素化と有効な活用に向けて－アンケート報告「学校欠席者情報収集システム」の活用状況－	学校保健	292 (9)		2012
大日康史、他	「学校欠席サーベイランス」と急性感染症流行の把握	小児科臨床	64	1540-1556	2011
大日康史、他	症候群サーベイランス	臨床と微生物	38(4)	335-340	2011

Ⅳ　研究成果の刊行物・別刷

Original Paper

Real-time Prescription Surveillance and its Application to Monitoring Seasonal Influenza Activity in Japan

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Abstract

Background: Real-time surveillance is fundamental for effective control of disease outbreaks, but the official sentinel surveillance in Japan collects information related to disease activity only weekly and updates it with a 1-week time lag.

Objective: To report on a prescription surveillance system using electronic records related to prescription drugs that was started in 2008 in Japan, and to evaluate the surveillance system for monitoring influenza activity during the 2009–2010 and 2010–2011 influenza seasons.

Methods: We developed an automatic surveillance system using electronic records of prescription drug purchases collected from 5275 pharmacies through the application service provider's medical claims service. We then applied the system to monitoring influenza activity during the 2009–2010 and 2010–2011 influenza seasons. The surveillance system collected information related to drugs and patients directly and automatically from the electronic prescription record system, and estimated the number of influenza cases based on the number of prescriptions of anti-influenza virus medication. Then it shared the information related to influenza activity through the Internet with the public on a daily basis.

Results: During the 2009–2010 influenza season, the number of influenza patients estimated by the prescription surveillance system between the 28th week of 2009 and the 12th week of 2010 was 9,234,289. In the 2010–2011 influenza season, the number of influenza patients between the 36th week of 2010 and the 12th week of 2011 was 7,153,437. The estimated number of influenza cases was highly correlated with that predicted by the official sentinel surveillance ($r = .992$, $P < .001$ for 2009–2010; $r = .972$, $P < .001$ for 2010–2011), indicating that the prescription surveillance system produced a good approximation of activity patterns.

Conclusions: Our prescription surveillance system presents great potential for monitoring influenza activity and for providing early detection of infectious disease outbreaks.

(J Med Internet Res 2012;14(1):e14) doi:10.2196/jmir.1881

KEYWORDS

Surveillance; influenza; real-time surveillance; prescriptions; pharmacy; anti-influenza virus; automatic surveillance; early response

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Introduction

In Japan, the official sentinel surveillance reports the number of influenza patients per health care provider after collecting information from approximately 5000 clinics and hospitals. The intensity of influenza activity is assessed according to the number of influenza patients per clinic or hospital. Influenza is regarded as highly active if the ratio exceeds 1. In 2009, the number of patients per clinic or hospital approached 1 in the 32nd week, earlier than in any of the preceding 10 years, mainly because of the influenza pandemic A (H1N1), which started in April 2009 [1]. Accordingly, the vast majority of the reported cases were H1N1 novel influenza [1]. The number of influenza patients per health care provider declined below 1 in the 13th week of 2010. The total number of weeks during which influenza was highly active was 29, a longer active period than in any of the prior 10 years. In 2010, the reported number of influenza patients per clinic or hospital exceeded 1 in the 50th week [2]; a second peak week was detected in March 2011. Because of these irregular patterns of influenza activity, it is necessary that both policy makers and clinicians follow influenza activity closely to implement effective control of an influenza outbreak throughout the year.

Syndromic surveillance is a useful tool for seasonal influenza monitoring [3]. In Japan, the official sentinel surveillance of infectious diseases is implemented by the National Institute of Infectious Diseases. It reports the estimated number of influenza patients weekly as the *Infectious Diseases Weekly Report* [2]. The official sentinel surveillance collects the number of influenza cases from approximately 5000 hospitals and clinics all over the country and then estimates the number of influenza patients based on the reported cases [4]. The entire process of collecting information from health care providers, estimating the number of clinical influenza cases, and reporting them to the public usually takes 7–10 days. Furthermore, the cases are reported by health care providers as a weekly aggregate number. Some diseases spread rapidly, and the weekly aggregates might not provide sufficiently detailed information reflecting the complete character of disease activity. In addition, the official sentinel surveillance updates influenza activity less frequently during major holidays. In Japan, seasonal influenza activity usually starts to become active during the New Year holidays. Constant monitoring and reporting of activity during that period is necessary.

Syndromic surveillance is in widespread use for monitoring diseases, but usage of prescription drug sales as a source of information is fairly limited. In the United States, the most common source of syndromic surveillance reported by health officials is emergency department visits (84%), followed by outpatient clinic visits (49%) and over-the-counter medication sales (44%); less than 10% of health departments reported prescription medications as a source [3]. In the context of influenza, emergency department surveillance is used to monitor the impact of influenza by age [5]. For more rapid feedback, the Web recently has become a powerful tool for syndromic surveillance [6]. For example, health surveillance using a Web-based self-reporting daily questionnaire is applied to monitor influenza activities [7]. Google Flu Trends, a Web-based surveillance, tracks the rate of influenza using query logs [8]. In addition to monitoring disease activities, syndromic surveillance helps monitor bioterrorism-related disease [9] or health consequences of natural events [10].

Real-time information related to influenza activity is fundamentally important for better preparation of countermeasures against a sudden increase of influenza activity. Therefore, daily updates of influenza activity are indispensable for improved understanding and control of an influenza epidemic. We developed an automatic real-time prescription surveillance system with the collaboration of EM Systems Co. Ltd. (Tokyo, Japan) to provide timely information related to a disease outbreak. We applied the surveillance system to monitor influenza activity during the 2009–2010 and 2010–2011 influenza seasons to examine the magnitude and trajectory of an outbreak more closely and to share that information with public health authorities, as well as participating pharmacies.

We used prescription drug purchase data for surveillance of influenza activity for three reasons. First, prescribing anti-influenza drugs such as oseltamivir or zanamivir is a common clinical practice for diagnosed influenza cases in Japan. Japan has the highest annual level of oseltamivir usage in the world [11]. Therefore, prescription drugs can serve as a good indicator of the overall number of influenza patients. Physicians often perform rapid influenza diagnostic tests on patients who have a fever or report other influenza-like symptoms. If the test result is positive or, alternatively, if the physician clinically diagnoses influenza even when the test result is negative, then anti-influenza drugs are often prescribed. This contrasts to practices in some other developed countries, where anti-influenza drugs are recommended for those who are at high risk [12-14] or who have severe conditions from influenza infections [13,14]. In such circumstances, surveillance of prescriptions of anti-influenza drugs would trace influenza patients with severe symptoms [15].

Second, many pharmacies have adopted the electronic prescription record system (EPRS), which enables automatic, continuous, and constant information collection, and real-time analysis of prescriptions and patients. In Japan, the utilization rate of the EPRS among pharmacies was 99.0% in 2009 [16]. Japan also has a high rate of outpatient or office-based clinician visits in cases where people feel ill [17], partly because of the universal health insurance system. Therefore, one might infer that the number of influenza patients collected through the EPRS would closely approximate the number of symptomatic influenza patients.

Third, in contrast to the United States or Taiwan [18], in Japan electronic medical record (EMR) systems are not yet well established. In the United States, surveillance for influenza activity is based on data on outpatient visits along with data related to sales of over-the-counter drugs, school absenteeism, and ambulatory care encounters [3,9,19-21]. Surveillance for influenza activity using the EMR has been intensively discussed and widely applied [22-24]. By contrast, the Survey of Medical Institutions by the Ministry of Health, Labour and Welfare in Japan showed that the share of health care providers using EMRs

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was just over 10% in 2008, or 948 hospitals (10.8% of all hospitals) and 12,939 clinics (13.1% of all clinics) [25].

We developed the surveillance system to collect the number of prescriptions together with patients' characteristics from the EPRS automatically, to analyze the data simultaneously to estimate the number of influenza cases, and then to provide real-time information of influenza activity to health care providers and policy makers. The system was tested for a limited time at the G8 Summit meeting in Toyako, Hokkaido in July 2008 for 1 month [26]. The present report summarizes details of our prescription surveillance system and presents an evaluation of its performance in the first two influenza seasons, those of 2009–2010 and 2010–2011, since the start of the nationwide operation of the system. The evaluation of surveillance performance, particularly outbreak detection performance, is challenging and few studies conduct such analyses [27]. A study showed that weekly variation in visits for lower respiratory tract infections approximated the national mortality data for pneumonia and influenza [28]. Similarly, our retrospective evaluation analyzed how closely the estimates of influenza cases followed the trajectory of influenza epidemics reported by two other sources.

Methods

Prescription Surveillance

We started collecting and analyzing data related to prescriptions automatically through the application service provider of the EPRS in April 2009 (Figure 1 [29]). As of March 2011, the number of participating pharmacies was 5275. In the application service provider, data related to prescriptions from all participating pharmacies were collected and deposited in a single server, making the data collection secure, efficient, and nearly cost-free. Medications covered by the surveillance system included drugs for relief of fever and pain, drugs for common colds, antibiotics, and antiviral drugs including anti-influenza virus drugs and antivaricella-zoster virus drugs. The current study specifically addressed prescriptions for anti-influenza virus medication. The neuraminidase inhibitors oseltamivir, zanamivir, and laninamivir were included, but amantadine was excluded because it is not commonly prescribed for influenza in Japan.

The original prescriptions contain information related to patients' sociodemographic and social security information, as well as the health care providers' information. The automatic surveillance system aggregated the number of prescriptions for each type of drug and provided tabulations by age and by geography at both national and prefectural levels. The number of influenza patients was then estimated from the aggregated number of prescriptions for anti-influenza drugs by adjusting the number of prescriptions for anti-influenza drugs with the proportion of participating pharmacies and of prescriptions purchased through pharmacies. The analysis and estimation were conducted overnight and the report of the analysis was sent automatically at 7:00 AM on the next day to the registered recipients, including participating pharmacies and public health authorities. In addition, figures showing the number of prescriptions for each type of drug and of the estimated number of patients were created and posted on the website for public access.

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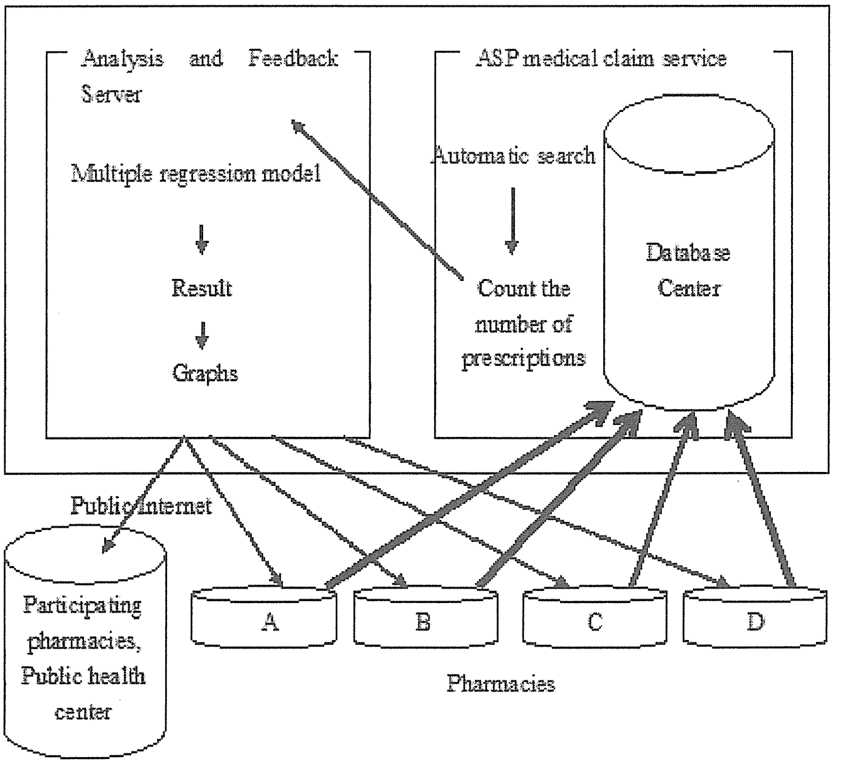
Figure 1. Prescription surveillance. Pharmacies A–D use the application service provider's (ASP) medical claims service. All data are stored in a central database. The surveillance system automatically counts oseltamivir, zanamivir, and laninamivir prescriptions at the data center. The information is analyzed using multiple regression models. The results are presented as figures and tables and feedback to participating pharmacies as well as public health authorities.



Performance Evaluation

We evaluated our surveillance system from two perspectives for the 2009–2010 and 2010–2011 influenza seasons. First, we compared the estimated number of influenza patients with the estimates provided by the official sentinel surveillance [2]. The official sentinel surveillance estimates the number of influenza patients based on the number of influenza patients reported by 5000 health care providers, including 3000 pediatricians, in Japan. We chose the evaluation period to include the period when influenza activity was high for the 2009–2010 influenza season. The epidemiological threshold of seasonal influenza activity is determined by the number of influenza patients per hospital or clinic. If the ratio is equal to or greater than 1 based on the official sentinel surveillance, activity is *high* by the definition that is accepted and widely used throughout Japan [2]. This corresponds to the period between the 28th week of 2009 (the week starting on July 6, 2009) and the 12th week of 2010 (the week starting on March 21, 2010) for the 2009–2010 influenza season. For the 2010–2011 season, the performance was evaluated between the 36th week of 2010 (the week starting on September 6, 2010) and the 12th week of 2011 (the week starting on March 21, 2011). Second, for the 2009–2010 influenza season, we also compared our estimates with the number of influenza patients estimated by the Gifu Medical Association, where the total number of influenza patients in the prefecture was calculated and reported publicly [29]. The number of influenza patients in Gifu Prefecture was surveyed during November 16–22, 2009 by the local public health authority as a response to the A/H1N1 influenza pandemic. A survey questionnaire asking for the number of influenza patients who visited health care providers was sent to all hospitals and clinics located within the prefecture (total of 1677 health providers); 1033 providers responded to the survey (response rate 61.6%) [29].

The Internal Review Board at the National Institute of Infectious Diseases approved the current study (approval number 57, "Development and application of real-time surveillance system to monitor syndromic and symptomatic cases using electronic record system").

Results

For the 2009–2010 influenza season, the total number of influenza patients estimated by the prescription surveillance system between the 28th week of 2009 and the 12th week of 2010 was 9,234,289 (Table 1). The largest number of influenza patients, 234,519, was reported on November 24, 2009. For the 2010–2011 influenza season, the number of influenza patients between the 36th week of 2010 and the 12th week of 2011 was 7,153,437 (Table 1). The largest number of influenza patients, 230,288, was reported on January 24, 2011. The official sentinel

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surveillance estimated the total number of patients for the same periods as 20,660,000 (95% confidence interval 20,460,000–20,860,000) for the 2009–2010 and 13,680,000 (95% confidence interval 13,350,000–14,010,000) for the 2010–2011 influenza seasons [2], indicating that the sentinel estimates were approximately double our estimates.

Table 1. Number of influenza cases estimated by the prescription surveillance, the official sentinel surveillance, and the Gifu Medical Association in Gifu Prefecture, 2009–2010 and 2010–2011 influenza seasons[a]

	2009–2010 influenza season: July 6, 2009–March 28, 2010 (28th week 2009–12th week 2010)	2010–2011 influenza season: September 6, 2010–March 27, 2011 (36th week 2010–12th week 2011)
Estimate by the prescription surveillance	9,234,289	7,153,437
Estimate by the official sentinel surveillance	20,660,000	13,680,000
Adjusted estimation by the survey in Gifu Prefecture	9,931,200	Not applicable[b]

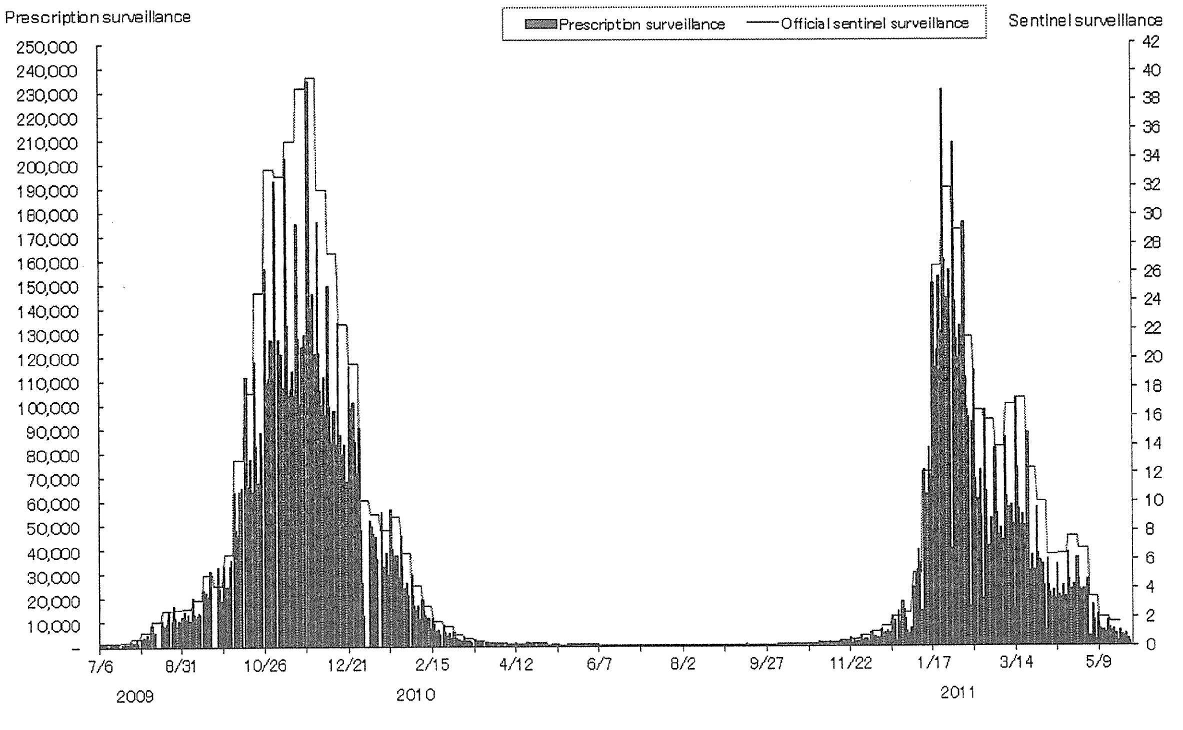
[a] Sources: the official sentinel surveillance [2]; Kawai et al [29].

[b] Adjusted estimation by the survey in Gifu Prefecture is shown only for the 2009–2010 influenza season because the data are available only for that year.

Pearson correlation coefficient (r) of time-series data on influenza patients between our estimates and the official sentinel estimate was .992 (P < .001) for the 2009–2010 influenza season, and .972 (P < .001) for the 2010–2011 influenza season (see Figure 2). A similar analysis was conducted at the prefecture level. The correlation was.950 or greater in 33 prefectures, .900–.949 in 5 prefectures, and .770–.899 in 8 prefectures. The correlation was the lowest in Akita Prefecture (r = .689).

The estimated number of influenza cases in the 2009–2010 influenza season was also compared with that ascertained from the survey of the number of influenza patients at all clinics and hospitals conducted in Gifu Prefecture. The estimated number from the survey collection in the prefecture based on the prescription surveillance was 127,568, whereas the number of influenza cases reported by the survey conducted by Gifu Medical Association was 132,474. The official sentinel surveillance estimated the number as 277,890.

Figure 2. Number of influenza cases, 2009–2011, estimated by the prescription surveillance and reported by the official sentinel surveillance. The estimated number of influenza cases by prescription surveillance was calculated based on the number of oseltamivir, zanamivir, and laninamivir prescriptions adjusted by the proportion of participating pharmacies and extramural dispensing percentage. See text for details. The reported number by the official sentinel surveillance shows the number of influenza patients per clinic or hospital, calculated with the reported number of influenza patients from 5000 sentinel clinics and hospitals.



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Discussion

Our analyses showed that the time-series pattern of influenza activity reported by the prescription surveillance system in the first two influenza seasons was highly correlated with the pattern reported by the official sentinel surveillance, showing that pharmacy surveillance can be a good indicator of influenza activity in Japan. Although the estimated number of influenza patients was double that of the official sentinel surveillance, it was close to the estimate by Gifu Prefecture, where the total number of influenza patients was collected in a survey.

The significance of our prescription surveillance is threefold. First, the syndromic surveillance system collected, analyzed, and reported data related to influenza patients simultaneously. Therefore, clinicians and policy makers were able to obtain the estimated number of influenza patients of the previous day. This meant that the estimates were available 1 week ahead of those reported by the official sentinel surveillance, enabling predictions of influenza activity for the immediately following week. This was particularly important at the outset of a seasonal epidemic, when the trajectory of a quickly spreading disease would have changed. Though the Google Flu Trends tool, another real-time surveillance, has been shown to perform well in the United States [8] and European countries [30], the results may be sensitive to variations in patients' behavior across countries.

Second, our prescription surveillance was national and observed regional variations in influenza activity at the prefecture level, although the precision of surveillance varied somewhat between prefectures. This provided helpful information to public health services to plan for the allocation of medical, pharmaceutical, and human resources for influenza control, shifting limited resources to the most affected regions.

Third, our surveillance runs constantly, maintaining the method of counting and estimating influenza cases at all times, and thus we were able to obtain the complete trajectory of the influenza pandemic in the 2009–2010 season. Initially during the pandemic, the law required hospitals and clinics to report all influenza cases, but that practice was terminated on July 24, 2009, after which activity was tracked only by the official sentinel surveillance.

Our surveillance system also promises great potential for future application to the early detection of an infectious disease outbreak or bioterrorism attack, which could happen potentially anywhere at any time. When we started operating a prescription surveillance system in 2009, all other surveillance systems running in Japan covered only specific regions of the country for practical reasons [31]. Furthermore, because influenza outbreaks do not necessarily occur during winter, the time that is covered by the sentinel surveillance, continuous monitoring of influenza activity is necessary to detect outbreaks early in their course. Our automatic prescription surveillance system uses the same standard for detection of a disease outbreak and runs continuously, providing an important complementary role in support of existing surveillance systems in Japan.

If EMRs were widely kept, then information related to influenza patients could be collected even faster and possibly more accurately. However, the share of health care providers that have adopted the EMR system was slightly above 10%. Under such circumstances, purchases of anti-influenza drugs can serve as an alternative indicator of influenza activity.

Limitations to this study exist. First, the total number of influenza cases was estimated as almost half of the estimate based on the official sentinel surveillance, although it approximated estimates based on a survey collecting the total number of influenza cases in Gifu Prefecture. One reason for this gap might lie in the choice of health care providers participating in the official sentinel surveillance. The sentinel health care providers have, on average, a larger number of patients than others, potentially resulting in an overestimation of the overall number of influenza patients. Second, anti-influenza drugs are also prescribed for prophylaxis in addition to treatment, which might engender overestimation of the total number of influenza cases. However, in Japan the preventive usage of oseltamivir is limited to household members of influenza patients who are 65 years or older or who are high-risk individuals [32]. Third, the prophylactic usage of anti-influenza drugs for health care providers and for the public was most intensive at the beginning of the H1N1 pandemic outbreak. We did not include those prescriptions in our surveillance data because they were not prescribed through health care providers. Fourth, 60% of the prescriptions were purchased through pharmacies in 2008. The other prescriptions were purchased directly through health care providers and were not included in our surveillance [33]. This is still much higher than the rate of adoption of the EMR system in hospitals and clinics. Fifth, the participation rate of pharmacies is low, particularly in certain areas. If the number of participating pharmacies were increased, then estimating influenza cases would be possible even for smaller geographical units.

Despite these limitations, pharmacy surveillance provided an approximation of the trend of influenza activity in the first two influenza seasons after the start of its nationwide operation. It provided both clinicians and policy makers with helpful real-time information related to influenza activity. Our pharmacy surveillance system has great potential for detection as well as for monitoring of infectious disease outbreaks in the population and in cases of significant political or cultural events.

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and the American Council of Learned Societies in cooperation with and with funds provided by the Japan Foundation Center for Global Partnership.

Conflicts of Interest

None declared.

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Abbreviations

EMR: electronic medical record
EPRS: electronic prescription record system

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アシクロビル製剤処方数に関する薬局サーベイランスによる水痘患者数推定とバイオテロ対策

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原　著

アシクロビル製剤処方数に関する薬局サーベイランスによる水痘患者数推定とバイオテロ対策

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Key words: syndromic surveillance, prescription, bioterrorism, chickenpox

要　旨

【目的】健康危機事案・バイオテロはいつどこで起こるか事前に探知することはできないので，できるだけ早期に探知することによって早期対策に結びつくことができる．天然痘（痘瘡）ウイルスによるバイオテロが行われた場合，診断不明の段階で個別の医療機関を受診した患者に対しては，水痘疑いでアシクロビル製剤が処方される可能性が大きい．そこで，電子化の進んでいる薬局の院外処方せんによるリアルタイム薬局サーベイランスの中で，アシクロビル製剤についてモニタリングしその有用性を評価することを目的として本研究を行った．

【方法】全国で ASP 型（Application Service Provider）のレセプトコンピューターを使っている 5,138 薬局から自動的にアシクロビル製剤の処方を毎日収集し，処方を受けた患者数を算出した．サーベイランスの評価は，15 歳以下の患者数のデータと，感染症発生動向調査による水痘報告数との比較とした．

【結果】薬局サーベイランスのアシクロビル製剤による推定患者数と感染症発生動向調査による水痘報告数は近似し，季節変動があり，相関係数は 0.8575 であった．16 歳～64 歳，65 歳以上のアシクロビル製剤の推定患者数は季節変動が少ないことが明らかになった．

【考察】アシクロビル製剤処方数を用いた薬局サーベイランスは，通常時からアシクロビル製剤の患者数のベースラインが策定できており，水痘の流行及びバイオテロで天然痘ウイルスが用いられ急に成人へのアシクロビル製剤処方数が増加し，かつ小児や高齢者では増加しなかった場合，水痘の流行あるいは天然痘発生を早期探知できる可能性があると示唆された．このようなサーベイランスは世界で始めての試みである．

〔感染症誌　85：632～637，2011〕

序　文

健康危機事案・生物製剤による攻撃（バイオテロ）は，発生すれば被害は大きいと想定されるので，できるだけ早期に探知することで，早期に対策を行い，被害を最小にすることが課題である．しかし，「いつ」「どこで」起こるかを事前に探知することはできないので，毎日全国で危機事案の発生をサーベイランスしておかなければならない．2000 年米国での同時多発テロ以来，諸外国ではこうした健康危機事案の早期探知サーベイランスが行われており，日本においても沖縄サミット[1]，日韓共同開催のワールドカップ[2]では医療機関で手入力によって行われたが，医療機関の負担が大きく継続して行われていない．

バイオテロでは，天然痘ウイルスが想定されているが，日本での種痘は，1976 年に定期接種が中止されたので，ワクチン接種をしていない世代がいる．そこで天然痘ウイルスによるバイオテロが行われた場合，ワクチン接種をしていない世代が発熱・発疹の症状が発現すると，天然痘の患者発生が世界的にみられなくなって以降，臨床診断で天然痘という早期診断は難しく，おそらく発生当初は原因不明のまま一般の医療機関を受診し，水痘などの疑いでアシクロビル製剤の処方を受ける可能性が大きい．アシクロビル製剤は，単

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純ヘルペスウイルス感染症の発症抑制に用いられており，小児の場合であれば水痘，高齢者であれば帯状疱疹の場合に処方されることが多い．バイオテロで天然痘ウイルスが放出された場合，主に成人がターゲットにされることを念頭に置けば，小児の水痘あるいは高齢者での帯状疱疹の増加を伴わない，成人でのアシクロビル製剤の処方が異常に多くなったときは，天然痘発生のシグナルである可能性が高い．

アメリカではバイオテロの早期探知として，救急外来の電子カルテや救急車要請における症状のモニタリング「症候群サーベイランス」が行われ[3)~5)]，発熱・発疹の患者の急増の探知が試みられている．日本においても同様の研究がされているが[6)~11)]，電子カルテは普及率や標準化の問題から全く進んでいない．救急車搬送も東京都をはじめ若干数の消防本部で実施されているが，APEC等の際には手入力で実施されることも多い．

そこで本研究は，電子化のすすんでいる薬局の院外処方せんによる薬局サーベイランスにおいて，アシクロビル製剤の処方数を常時モニタリングする方法を確立し，バイオテロ対策として有効に活用することを検討することを目的とした．薬局サーベイランスは，2009年の新型インフルエンザにおいて活用され[10)]全国運用でリアルタイム情報として有用である．2008北海道洞爺湖サミットやAPEC2010横浜においては，サミット前後の1カ月間この薬局でのサーベイランスを実施したが，実施地域が限定的であった[11)]ので，本研究では全国を対象として毎日モニタリングを行った．

材料と方法

アシクロビル製剤の処方せん件数の収集及び解析は，抗インフルエンザウイルス薬の解析と同じ方法で[11)]，院外処方せんのレセプトコンピューターの共同利用型であるASP型（Application Service Provider）をつかう5,138薬局（2010年12月末）から自動的に収集した．

外来の院外処方率は，年々増加しており，平成21年の社会医療診療行為別調査結果の概況によると62.0%である．かつ，ひとつの薬局が複数の医療機関からの処方せんを受け取る面分業が勧められている．調剤薬局の電子化は，調剤医療費（電算処理分）の動向によると，平成22年6月で99.3%である．

システムは，薬局からデータベースセンターにあがってくる情報のうち，年齢別，都道府県別，政令指定都市別のアシクロビル製剤の件数のみを抽出して解析用のサーバーに転送した．解析用のサーバーでサーベイランスの情報還元まで行った．

情報還元は，その日の集計分について，翌日7時とした．情報提供は2通りとし，薬局にはアシクロビル製剤の処方せん枚数及びグラフ作成を自動で行い，その結果を専用のホームページで提供した．公衆衛生行政担当者にはアシクロビル製剤を処方された推定患者数を3年齢層（15歳以下，16～64歳，65歳以上）で算出し，グラフ作成をし，専用のホームページで全国及び都道府県，政令指定都市別に提供した．水痘の推定患者数は，サーベイランス参加薬局の都道府県別のアシクロビル製剤の処方件数に，参加薬局率，院外処方せん率で調整し合計した．

サーベイランスの評価は，感染症発生動向調査による全国約3,000小児科の定点からの報告に基づく．水痘報告数と15歳以下のアシクロビル製剤の推定患者数の比較をした．期間は2010年1月1日から12月31日までとした．

アシクロビル製剤は，水痘と診断された患者に処方される以外に，帯状疱疹の患者にも処方される．帯状疱疹の患者の疫学調査はないため患者数は明らかではないが，多くは高齢者に発現があるとされている．そこで，16～64歳，65歳以上の年齢別にアシクロビル製剤推定患者数をモニタリングとした．

成　績

Fig. 1に，感染症発生動向調査による水痘報告の11年間を示した．縦軸は定点あたり報告数で，横軸は1週～53週を示している．春先から季節的には毎年12～7月に多く，8～11月には減少している．発生動向調査は，水痘の場合7日に一度の定点医療機関からの報告となっているため，患者が受診してから公表までにおよそ2週間あるので，薬局サーベイランスでは2週間先行して動向を把握することができた．

Fig. 2に，薬局サーベイランスのアシクロビル製剤による推定患者数の日ごと集計数と感染症発生動向調査による水痘報告数を組み合わせたグラフを示した．左縦軸はアシクロビル製剤による推定患者数で，右縦軸は定点あたり報告数を示している．推定患者数の多い月は12月で，疫学週では，51週（2010年12月20日～26日），ついで前週の50週，次いで21週（2010年5月24日～30日），次いで23週であった．発生動向調査においては，21週が最も多く，次いで23週，次いで51週，50週で，2つの動向は近似していた．相関係数は0.8575であった．都道府県別での相関係数は，0.9以上の都道府県が33，0.8～0.9が5であった．アシクロビル製剤の推定患者数は15歳以下で1,236,534人であった．

Fig. 3に16歳～64歳，Fig. 4に65歳以上のアシクロビル製剤の推定患者数のグラフを示した．いずれも18週（2010年5月3日～9日）が減少傾向であるが，この週は連休が続くゴールデンウイークの週なので，医療機関が休診になっている．他の週では，だいたい

平成23年11月20日

Fig. 1 Official sentinel surveillance of Chikenpox

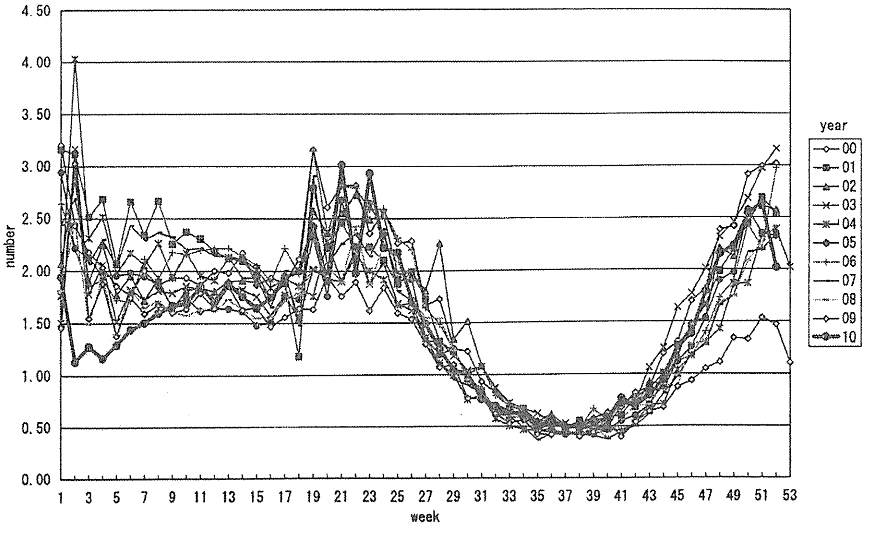
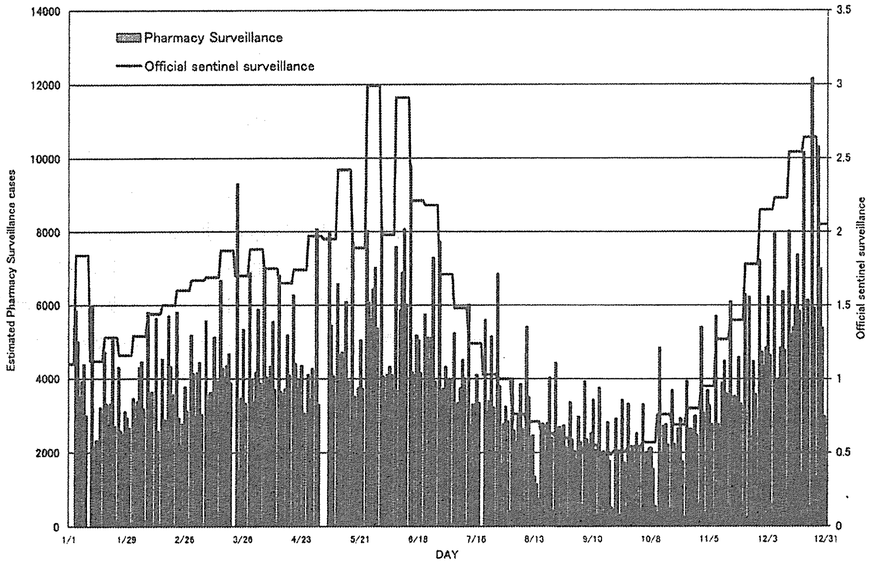


Fig. 2 Chickenpox cases estimated under Pharmacy Surveillance of those under 15 years old and official sentinel surveillance

Note: Cases estimated under Pharmacy Surveillance is calculated as the number of Acyclovir prescriptions adjusted by the proportion of corporate pharmacies and percentage of extramural dispensing. Official sentinel surveillance collects weekly reports from 3000 sentinel pediatric clinics and hospitals



平均前後を均等に推移していた．15歳以下に比べて季節変動が少ないことが明らかになった．アシクロビル製剤の推定患者数は65歳以上で961,002人であった．

考　察

健康危機事案の早期探知のために効率よくデータ収集する方策として院外処方せんに着目し，アシクロビル製剤処方数モニタリングの常時運用を実現できた．また水痘の推定患者数を算出し，2010年は約124万人であると推定された．

諸外国ではこのような薬局サーベイランスを全国単位では実施しておらず，さらにアシクロビル製剤のモニタリング実施しているところはなく世界で初めての試みである．16歳から64歳に対するアシクロビル製剤処方数をモニタリングすることは，バイオテロ発生時のベースライン処方数として使用できる可能性があり，かつ15歳以下のアシクロビル製剤処方数の把握により，水痘の流行を早期に探知できる．

Fig. 3　Cases estimated under Pharmacy Surveillance of those aged 16-64 years old

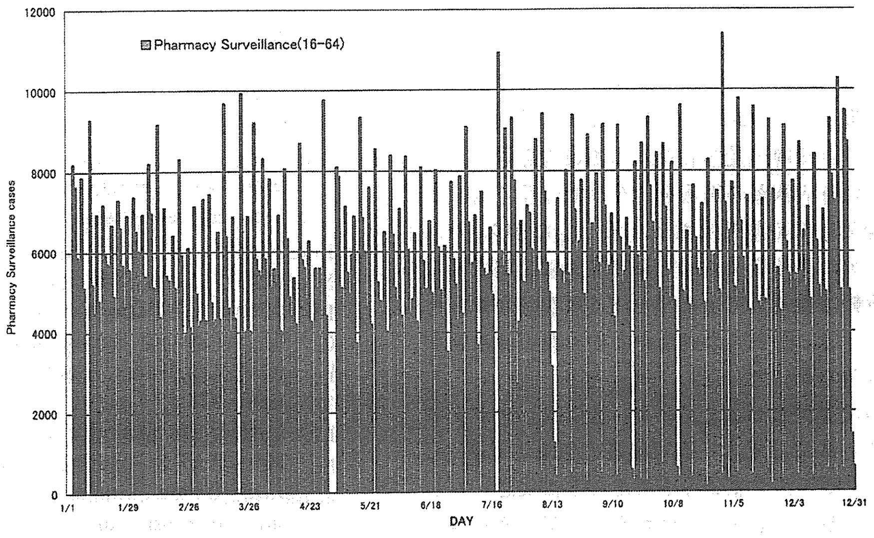
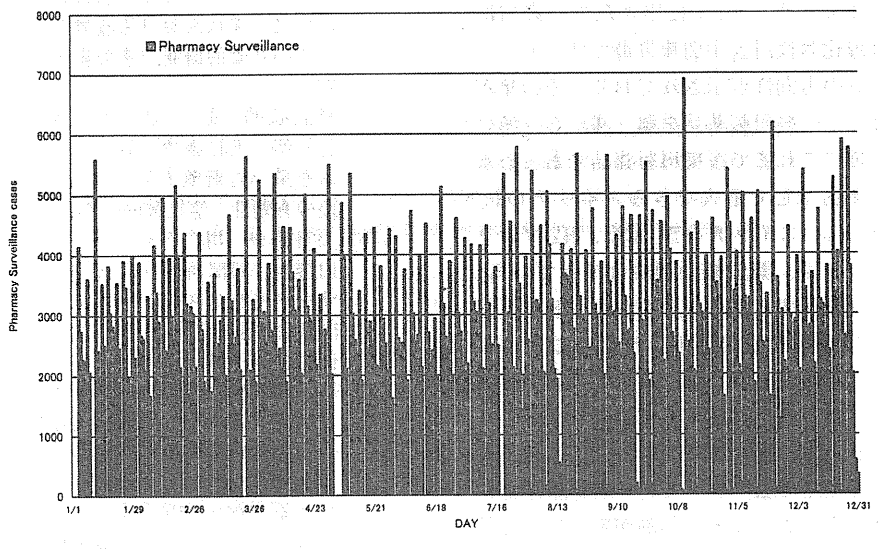


Fig. 4　Cases estimated under Pharmacy Surveillance of those aged 65 and over



本研究では，実際にバイオテロが発生した場合に有用であるかどうかの検証は不可能であるが，万が一，バイオテロとして天然痘ウイルスが用いられた場合，通常時から16歳～64歳のアシクロビル製剤の処方のベースラインが策定できているので，急にベースラインを超える増加がみられた場合，特に小児の水痘あるいは高齢者での帯状疱疹の増加を伴わない，成人のみでのアシクロビル製剤の処方が異常に多くなったときは，天然痘の可能性を早期探知できると示唆された．将来的には成人を未接種世代である40歳未満とそれ以上に分割することも，より特異性を増すという意味で有意義であると考えられた．

15歳以下のアシクロビル製剤の推定患者数と水痘の報告数は高い相関があり，水痘の流行を早期に探知できることが明らかになった．感染症発生動向調査は週ごとの報告であるため，日ごとの状況把握はできない．今後，水痘ワクチンの定期接種に向けた取り組みがなされるときにも，水痘患者の発生動向を知る疫学情報の一つとして有用であると思われる．一方で，高齢者における帯状疱疹の推定患者数の算出も試みたが，水痘の場合に比べて，帯状疱疹の場合は，治療が長期化することもあり，処方回数が複数回になる可能性もあることから，その頻度が不明であることから，今後の課題として残った．

こうした電子化されたデータを利用するサーベイランスは，米国や台湾では，電子カルテを用いたサーベイランスが実施[12][13]されており日本でも検討が進められてきた[9]．しかし，日本の電子カルテの普及率は，医

療施設調査によると，病院は平成20年948施設（病院総数の10.8%），一般診療所は平成20年12,939施設（一般診療所総数の13.1%）と増加しているものの，これまでのところ，全体では1割を超えたところである．将来的には電子カルテからの自動的な情報提供が開始されれば，医療機関へ受診した水痘の患者を含めて，発熱，発疹の有症状者の情報を，翌日ではなく当日に状況が把握できる可能性もある．しかしながら，現在の電子カルテの普及状況を勘案すれば，現段階では薬局からの情報提供によるサーベイランスが最も早く，最も正確で，労力をかけないという点で有用性が高いことが明らかになった．

本研究の限界は2つ考えられた．1つは，アシクロビル製剤は，多くは水痘，帯状疱疹に処方されるが，単純ヘルペスウイルス感染症等のその他の疾患に対しても処方されることもあることから，推定患者数は過大であると思われる．もう一つは，近年アシクロビル製剤のうち軟膏がスイッチOTC（Over The Counter）化されたことである．平成14年に出された一般用医薬品承認審査合理化等検討会中間報告書では，セルフメディケーションの方向性が示されており，その後薬事法が改正されて，一般用医薬品を第一種から三種に分類して，第一種にこれまで医療用医薬品であったものが，一般用医薬品として購入できるスイッチOTCが含まれている．このスイッチOTCには，H2ブロッカーや抗ヒスタミン剤，禁煙補助剤が含まれている．したがって，発疹の症状を訴える患者が，一般用医薬品を用いた場合は今回の推定に含まれないことになり，過少評価の可能性がある．これまでに一般用医薬品のサーベイランスの検討もしてきているが[14]，こうしたスイッチOTC化の動向にあわせて，処方せん情報による医療用医薬品に加えて，一般用医薬品についても常時モニタリングできる体制が望ましいと思われた．

今後はさらに薬局数が増え，例えば1万の薬局（全薬局の20%以上）を目標に整備できれば，保健所単位あるいは市町村単位での流行状況を把握することが可能となる．情報還元体制の構築で全国を監視するのと同時に，サミットやAPEC（Asia-Pacific Economic Cooperation：アジア太平洋経済協力）といった国際的，政治的に重要イベントに対して，地域や期間を限定して，より注意深く情報を精査する活用も期待される．

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Chickenpox Case Estimation in Acyclovir Pharmacy Survey and Early Bioterrorism Detection

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Objective : Early potential health hazards and bioterrorism threats require early detection. Smallpox cases caused by terrorist could, for example, be treated by prescribing acyclovir to those having fever and vesicle exanthema diagnosed as chicken pox. We have constructed real-time pharmacy surveillance scenarios using information technology (IT) to monitor acyclovir prescription.

Methods : We collected the number of acyclovir prescriptions from 5138 pharmacies using the Application Server Provider System (ASP) to estimate the number of cases. We then compared the number of those given acyclovir under 15 years old from pharmacy surveillance and sentinel surveillance for chickenpox under the Infection Disease Control Law.

Results : The estimated number of under 15 years old prescribed acyclovir in pharmacy surveillance resembled sentinel surveillance results and showed a similar seasonal chickenpox pattern. The correlation coefficient was 0.8575. The estimated numbers of adults, older than 15 but under 65 years old, and elderly, older than 65, prescribed acyclovir showed no clear seasonal pattern.

Discussion : Pharmacy surveillance for acyclovir identified the baseline and can be used to detect unusual chickenpox outbreak. Bioterrorism attack could potentially be detected using smallpox virus when acyclovir prescription for adults suddenly increases without outbreaks in children or the elderly. This acyclovir prescription monitoring such as an application is, to our knowledge, the first of its kind anywhre.

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報告

学校欠席者情報収集システムの構築と評価

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Development and Evaluation of a School Absenteeism Reporting System

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【Object】Since pandemic A/H1N1 2009 emerged in May 2009, as the Ministry of Labour, Health and Welfare reinforced the surveillance at school and especially first outbreak in Japan had occurred at high school, we developd the web-based system for reporting and summarize, and practically applied it at some prefectures.

【Result】All schools in 10 prefectures used this system. In total, 9000 schools joined the system, which accounted for about 20% of all elementary, junior, and senior high schools in Japan. Moreover, 682 organizations such as educational board, public health center, local government or medical associations, also joined the system so as to reduce their burden. Data input at school required only about 7–8 minutes. Willingness to pay at all current participated school amounted 12.29 million yen, and 61.43 million yen at the all school in Japan. Benefit-cost ratio was estimated as 1.76 in 2009, as 4.55 in 2010 for current participated schools, as 4.84 for all schools in Japan.

【Discussion】We saved cost for 65.7 million yen in the ten prefectures. Moreover we can prove its cost-effectiveness.

Key words：school absenteeism, class/school closure, suspension, pandemic influenza, automatic information sharing
学校欠席，臨時休業，出席停止，新型インフルエンザ，自動的な情報共有

Ⅰ．研究目的

日本では世界的にも珍しくインフルエンザによる学級閉鎖が例年実施されているが，2009年の新型インフルエンザにおいてはより積極的な学級閉鎖などの対応，そのためにはより早い情報共有が学校，教育委員会，県庁の間に強く求められた．一方で2007年度から，学校における感染症の早期探知，情報共有のシステム（学校欠席者情報収集システム）が厚生労働科学研究費補助金健康安全・危機管理対策総合研究事業「健康危機事象の早期探知システムの実用化に関する研究」によって地道に開発されてきており，2007年度は3校，2008年度は30校で基礎的な検証が行われていた[1]．

この「学校欠席者情報収集システム」はASP（Application Service Provider）方式，つまりすべてのプログラム，データベースは安全なインターネット越しのサーバで稼働，保管し，学校や行政といった関係者からは入力や参照を行うだけで，追加的なソフトのインストールやあるいはハード的な拡張を行う必要がなく，拡張性に富んだシステム構成となっている．学校での入力が行われたその瞬間に教育委員会，保健所，県庁，校医，医師会あるいは他校との情報共有が行われるために，地域での感染症の発生状況を最も迅速に把握することができる．感染症の予防および感染症の患者に対する医療に関する法律に基づく感染症発生動向調査では，インフルエンザ等の一般的な疾患について，一部の医療機関のみからおおむね7－10日間遅れて状況が把握，公表されることを考えると本システムは，対象が学齢期に限定されるという欠点があるものの，学校あるいは地域での感染症の発生状況をより早く，より漏れなく把握する手段として非常に優れている．

2009年5月の新型インフルエンザの国内発生後，特に高校をはじめ学校での流行が本格化するにつれ，本システムの需要が急激に伸びた．また厚生労働省が学校でのサーベイランスを強化したことから，2007年度からの情報共有システムの経験をベースに，本システムにおいて