Gripenet: an internet-based system to monitor influenza-like illness uniformly across Europe

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Gripenet has been monitoring the activity of influenza-like-illness (ILI) with the aid of volunteers via the internet in the Netherlands and Belgium since 2003 and in Portugal since 2005. In contrast with the traditional system of sentinel networks of mainly primary care physicians coordinated by the European Influenza Surveillance Scheme (EISS), Gripenet obtains its data directly from the population. Any resident of the three countries can participate in Gripenet by completing an application form on the appropriate websites (http://www.griepmeting.nl for the Netherlands and Belgium, http://www.gripenet.pt for Portugal), which contains various medical, geographic and behavioural questions. Participants report weekly on the website any symptoms they have experienced since their last visit. ILI incidence is determined on the basis of a uniform case definition. In the 2006/2007 season, 19,623 persons participated in Gripenet in the Netherlands, 7,025 in Belgium and 3,118 in Portugal. The rise, peak and decline of ILI activity occurred at similar times according to Gripenet and EISS. However, ILI attack rates in the Netherlands (6.6%), Belgium (6.1%) and Portugal (5.6%) were remarkably more similar in Gripenet than in EISS (0.8%, 3.9%, and 0.6% respectively). Monitoring ILI activity with the direct participation of volunteers provides similar incidence curves compared to the traditional system coordinated by EISS. Whereas EISS provides an established system whose data is validated by virology tests, Gripenet is a fast and flexible monitoring system whose uniformity allows for direct comparison of ILI rates between countries. A current objective of Gripenet is to engage more European countries.

Introduction

During the winter 2003/2004 season, the Netherlands and Belgium launched a system to monitor the activity of influenza-like-illness (ILI) with the help of volunteers via the Internet [1]. The success of this initiative, which attracted over 30,000 participants in the first year, inspired the establishment of a similar system in Portugal in 2005/2006 [2]. Throughout this paper, the system is referred to as "Gripenet".

Traditionally, influenza surveillance in Europe is monitored by the European Influenza Surveillance Scheme (EISS), a collaborative programme of mainly primary care physicians, epidemiologists and virologists who actively collect clinical and virological data on influenza [3]. In this paper, we argue that the Gripenet monitoring system in which the data is gathered directly from the population offers some advantages over the established surveillance system based on the network of general practitioners (GPs). It has previously been shown that the participants of Gripenet in 2003/2004 in the Netherlands were representative for the Dutch population [4]. Here, we compare Gripenet results in the three countries with the EISS results from the same countries during the 2006/2007 season.

Methods

Gripenet

Gripenet is a fully internet-based system, currently hosted on two websites: http://www.griepmeting.nl for the Netherlands and Belgium (Flanders), and http://www.gripenet.pt for Portugal. Any resident of these countries can register for Gripenet by completing an online application form containing various medical, geographic, and behavioural questions (Table 1). Participants are mainly recruited via mass-media, which present information on the system and give regular updates of the latest results. Participation is further stimulated by email newsletters, online educational materials, competitions and presentations, and other activities. Once registered, participants receive a weekly email newsletter reminding them to complete their symptoms questionnaire. In this questionnaire participants are asked to select from a list of symptoms the ones they have experienced since their previous visit to the Gripenet website (Table 2). If symptoms are reported, participants are asked to provide the date of onset, and whether these led to change of behaviour and/or a GP consultation, and if so, the outcome of the consultation.

Table 1

Intake questions. List of questions the participants are requested to answer each year upon registration for Gripenet

- Postal code
- Month and year of birth
- Sex
- Daily occupation (school / work / home / other)
- Means of transportation (car / public / bike / foot)
- Number of common colds per year (<2, 2-5, >5)
- Vaccinated against flu this season (yes / no)
- Any of the following diseases (asthma / diabetes / none)
- How often do you smoke? (never / sometimes / daily)
- Do you eat 2 pieces of fruit and 200g of vegetables per day? (no / sometimes / always)
- Do you use supplements like vitamins? (no / sometimes / daily)
- How many hours of exercise per week (<1, 1-4, >4)
- Household situation (alone / only adults / with adults and children)
- Where do the children go? (nursery / school / stay at home)
- Do you have pets? (no / cat(s) / dog(s) / bird(s) / other)

The incidence of ILI is determined based on the symptoms reported, using a uniform case definition. ILI is defined as acute onset of fever of >=38ºC, plus muscle pain, plus one of the following: cough, sore throat, and/or chest pain. The day of fever onset determines the onset of ILI. A participant is considered to be active between the day of registration and the day of the last completed symptoms questionnaire. Only participants who have completed at least three symptoms' questionnaires are included in the analyses. The daily incidence is determined by the number of participants with an onset of ILI on a given day, divided by the number of active participants on that day. The weekly incidence for each day is determined by the total number of participants with an onset of ILI in the previous seven days, divided by the average number of active participants during those seven days. The ILI attack rate for both Gripenet and EISS is defined as the cumulative incidence rate over the total surveillance period, i.e. the fraction of the population under observation that had a reported onset of ILI.

EISS

During the 2005/2006 influenza season, 39 countries were members of EISS, and the sentinel surveillance was carried out by 21,162 GPs, paediatricians and other physicians. The population under clinical surveillance by the sentinel networks represents at least a median number of 24.8 million inhabitants of Europe. The population under surveillance in the Netherlands accounts for 0.7% of the total population, in Belgium 0.4%, and in Portugal 0.7%. Although there are differences in the general characteristics of the sentinel systems in each of the countries, the majority collect weekly incidences of ILI cases per 100,000 inhabitants, as is the case in the Netherlands, Belgium and Portugal [5]. The different case definitions used in these countries are shown in Table 3. Using historical data, several countries within EISS introduced an influenza activity baseline. The intensity of influenza activity is determined by measuring the influenza activity against the baseline and its geographical spread. A proportion of the sentinel physicians additionally collect nose and/or throat swabs for virological surveillance according to a uniform swabbing protocol. The weekly incidence covering the period from Monday to Sunday is published on the EISS website the following Wednesday or Thursday. This number is usually updated one week later to include the latest available information.

Results

We compared the Gripenet and EISS data from 15 December 2006 to 1 May 2007. Gripenet data showed that in the Netherlands, 17,056 out of 19,623 participants (87%) completed at least three symptoms questionnaires, in Belgium 6,062 out of 7,025 (86%) and in Portugal 2,167 out of 3,118 (69%). The national participation rate was 0.1% in the Netherlands (total population - 16.3 million,), 0.1% in Flanders (6.2 million), and 0.02% in Portugal (10.5 million). In all three countries, the younger and older age groups are underrepresented (Figure 1). The geographical distribution of participants follows the patterns of population density, with higher concentration in the larger cities.

In the Netherlands, 25% participants matching the ILI case definition visited a GP (225 out of 907), in Belgium 67% (215 out of 322) and in Portugal 45% (45 out of 99). Influenza activity in Europe was, in 2006/2007, mainly due to influenza A (H3N2) [7]. In all three countries, the incidence curves provided by Gripenet show the same trends as the incidence curves of EISS (Figure 2). For each country the shapes of the curves are similar, with peak incidence occurring in the same week and approximately equal onset and decline of ILI activity. However, incidences calculated from Gripenet data are higher than those reported by EISS. According to Gripenet data, the ILI attack rate in the Netherlands was 6.6%, in Belgium 6.1%, and in Portugal 5.6%, while according to EISS data, it was 0.8%, 3.9%, and 0.6% respectively.

Table 2

List of symptoms from which participants of Gripenet can choose in the symptoms questionnaire

- Cough
- Running nose
- Headache
- Sore throat
- Chest pain
- Muscle pain
- Diarrhea
- Abdominal pain
- Cold shivers
- Sick irritated eyes
- Temperature (not measured, <37º, 37º – 40º in steps of 0.5º, >40º Celsius)
- Sudden onset of fever

Table 3

Influenza-like-illness case definitions. The case definitions for ILI as used by Gripenet and by the sentinel GPs reporting to EISS in The Netherlands, Belgium and Portugal[3]. The Gripenet definition is the same in all three countries

	ILI case definition
Gripenet	All of the following characteristics: 1. a temperature of at least 38º Celsius, and 2. acute onset of fever, and 3. cough and/or sore throat and/or chest pain, and 4. muscle pain
EISS: The Netherlands	An acute onset (i.e. at most a prodromal stage of three to four days), accompanied by a rise in rectal temperature of >38ºC, and at least 1 of the following symptoms: cough, coryza, sore throat, frontal headache, retrosternal pain, myalgia. (Pel criteria)
EISS: Belgium	Sudden onset with fever, myalgia and respiratory symptoms (cough or thoracic pain)
EISS: Portugal	6 of the following criteria: sudden onset, fever, cough, chills, prostration and weakness, myalgia or general pain, rhinitis and/or pharyngitis, contact with a case.

Discussion

Although there is an approximately simultaneous rise, peak and decline of ILI activity in the Gripenet and EISS epidemic curves, quantitatively the incidences obtained by Gripenet are much higher than those provided by EISS. This could be partially explained by the use of different denominators in the incidence calculations. Gripenet participants are requested to fill in the questionnaire each week irrespective of whether they have experienced any symptoms, and the incidence of ILI is determined, considering only those participants who have filled in their symptoms' questionnaire.

Gripenet is therefore independent of the rate at which people seek advice from a health professional. In contrast, the incidence determined by EISS depends on the GP visiting rates which differ across countries (as can be seen also in the Gripenet data), reflecting differences in the health care systems.

Other population-based surveillance systems for ILI have been tested [4], but they often depend on the proportion of the people which seeks advice from a health professional when experiencing ILI symptoms. An interesting real-time monitoring system used data on symptoms reported through the NHS Direct service in the UK, a nurse-led telephone helpline for medical advice [8,9]. Although such systems may perform very well within one country, applying them in other countries can bring very different results. Social and cultural differences between countries may affect the tendency for people to seek advice when experiencing ILI symptoms, leading to differences in reported incidence rates.

The ILI attack rates measured by Gripenet in winter 2006/2007 were very similar in the three countries (5.6% - 6.6%), while according to EISS, the ILI attack rate in Belgium (3.9%) was five times higher than in the Netherlands (0.8%) and seven times higher than in Portugal (0.6%). This is reflected in Figure 3 by comparing the incidence curves of the three countries according to Gripenet and EISS. The reasons for this discrepancy could be the different case definitions used by Dutch, Belgian and Portuguese sentinel GPs (Table 3), the different GP visiting rates per country and the extent to which the population under observation is representative for the general population. EISS is in the process of standardizing the case definitions for ILI used by the GPs in the different countries [10]. The GP visiting rates, however, are not realistically controllable.

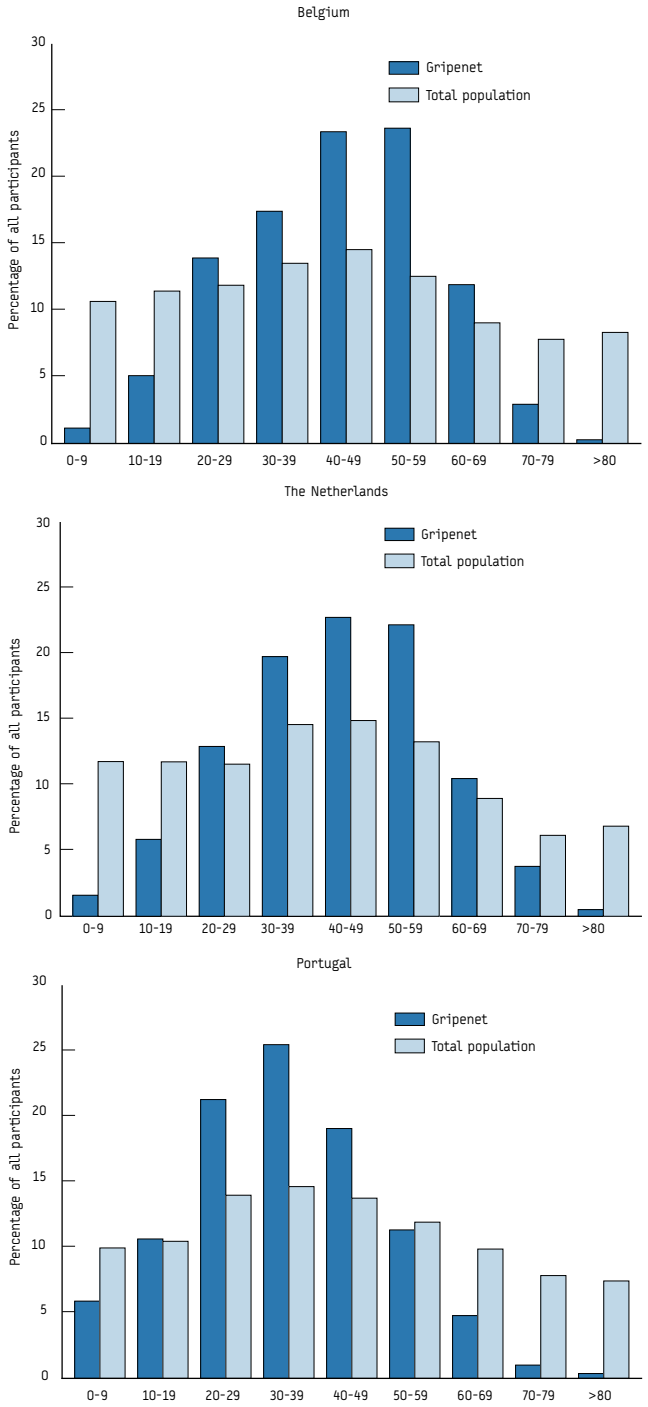
More data and analysis are needed to establish a baseline for Gripenet. According to the Gripenet data collected in 2006/2007 (Figure 2), the ILI incidence outside the epidemic peak in the Netherlands (~200 per 100,000) is different from the rates in Portugal and Belgium (~50-100 per 100,000). However, outside the influenza seasons, virology tests only rarely confirm influenza cases, rendering a system based on symptoms to low specificity. Hence the reported differences are not necessarily related to differences in influenza attack rates.

Although Gripenet aims to attract a representative sample of the population, people who do not experience any ILI symptoms may not consider themselves suitable for participation. To remove the selection bias related to the new participants who have already been experiencing ILI symptoms at the moment of registration, participants are only active from the day of registration onwards, and the first symptoms questionnaire concerning the week before registration is not included in the analyses.

The non-representative nature of the Internet-using population results in a selection bias that is generally a major concern in web-based surveys [4]. Based on the data supplied by all participants upon application, the representativeness of the Gripenet sample can be determined. Marquet et al. showed that the demographic and health characteristics of the Gripenet participants in 2003/2004 in the Netherlands were remarkably similar to those in the general Dutch population. Similar studies for the Portuguese and the Belgian populations have not been performed yet. There is evidence, however, that the younger and older age groups are similarly underrepresented in all three countries (Figure 1).

Figure 1 a, b, c.

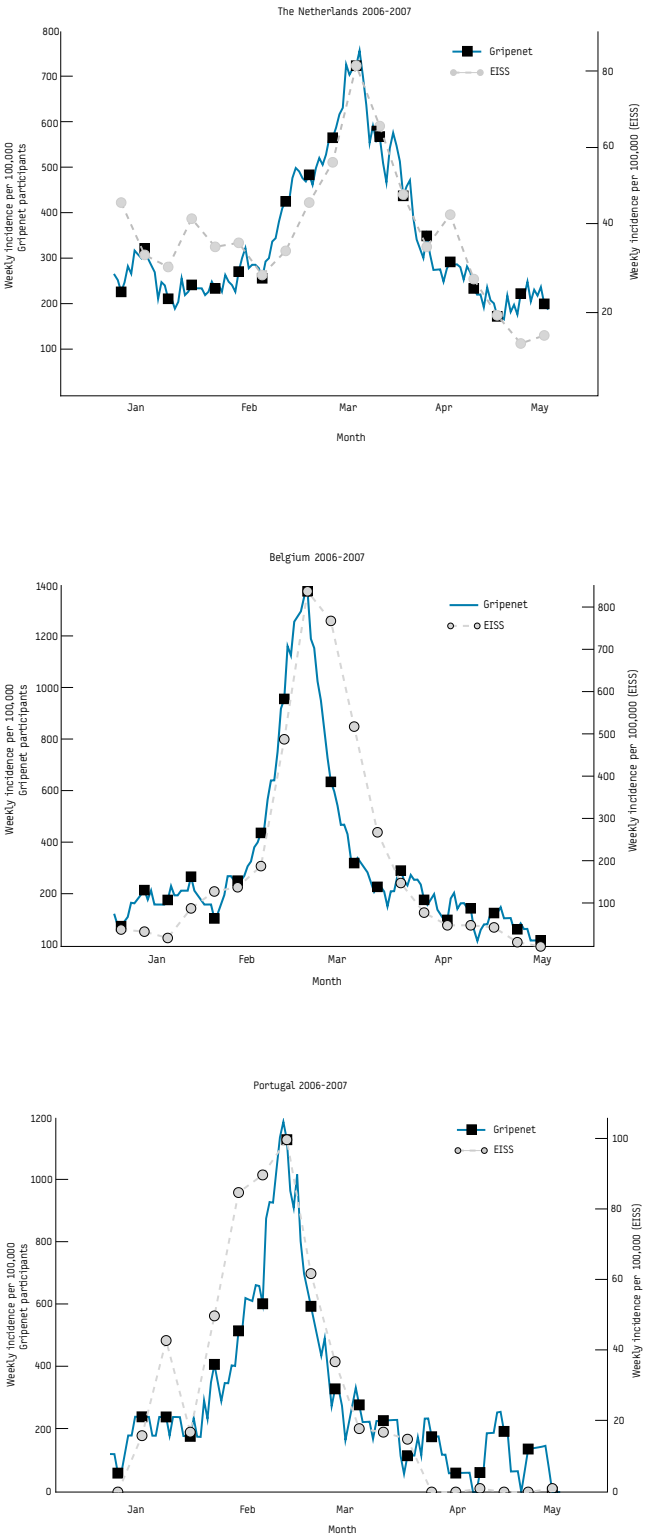
Age distributions of the Gripenet populations and the national population in (a) The Netherlands (b) Belgium (c) Portugal



Note to Figure 1 a,b,c. In the Netherlands and Belgium the age-groups <20 and >=70 years are under-represented, with a very clear under-representation in the age groups <10 and >=80 years. In Portugal the age-groups <10 and >=60 years are under-represented, with a very clear under-representations in the age group >=70 years. [6].

Figure 2 A, B, C.

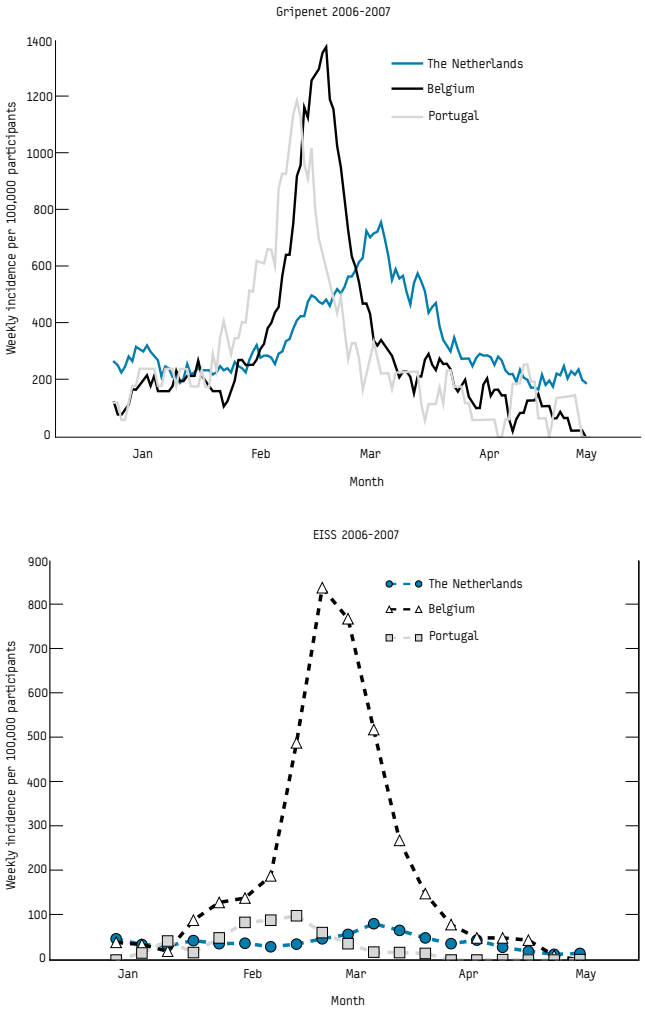
Comparison of incidence curves between Gripenet and EISS: (a) The Netherlands (b) Belgium; (c) Portugal



Note to Figure 2 a,b,c. The three plots represent weekly ILI incidences. EISS provides for each week (Monday - Sunday) the number of patients diagnosed with ILI, per 100,000 of the population under observation by the sentinel network. Gripenet provides for each day the number of ILI onsets per 100,000 active participants (those who filled in their symptoms questionnaire for that period) in the preceding 7 days. The data points in the incidence curve of Gripenet which monitor the same time period (Monday – Sunday) as EISS are marked with squares. Note that Gripenet only monitors the Northern Dutch-speaking part of Belgium (Flanders), whereas EISS monitors the whole of Belgium.

Figure 3 A, B.

Comparison of incidence curves between the Netherlands, Belgium and Portugal: (a) Gripenet; (b) EISS



Note to Figure 3 a,b. Both plots represent weekly ILI incidences. The peak of the ILI activity was first reached in Portugal, closely followed by Belgium and then in the Netherlands. According to Gripenet data the height of the peak in ILI incidence in the Netherlands is lower than in Belgium and Portugal, but the activity lasted longer. Therefore, ILI attack rates in the three countries are similar according to Gripenet data (a). However, according to EISS data there is great variation (b).

Gripenet seeks to monitor the representativeness of the participants in all three countries, and direct recruitment aims at targeting the underrepresented sections of the population. The number of participants is critical for Gripenet's success. A survey performed among 4,500 Dutch participants of Gripenet at the end of the first season showed that most of them were recruited via radio or television (47%), via newspaper (21%) and via internet sites (16%)

Since the Gripenet data are collected and analysed in one place, results can be published in real time, whereas EISS reporting each Thursday the ILI incidence for the previous Monday – Sunday period is four days behind. Gripenet also has the capability to publish a daily incidence rate, although it has been noted that participants with ILI tend to fill in their symptoms questionnaire earlier than participants without symptoms. This leads to an overestimation of ILI incidence rates for the most recent days, but the continuous updating ensures that they become increasingly more reliable as time passes. The advantage of Gripenet, however, lies not only in its potential for an earlier assessment of weekly ILI incidences, but also in the possibility of observing the daily fluctuations in real time, thus allowing to detect early warning signals. These time advantages could be reproduced by EISS as well, if all GPs reported electronically in real time, as has been demonstrated by pilot projects in France and Germany [11, 12].

The Gripenet system gathers a variety of valuable data on ILI activity, however, only a fraction of these have been analysed so far. For example, Gripenet has the potential of monitoring the geographical spread of ILI, using the postal codes of the participants. Demographic data can also be used to monitor ILI activity in different subgroups of the population. Comparing participants with different behaviours could give indications on risk factors. Detecting an earlier rise of ILI activity in certain subgroups could make Gripenet an even faster early-warning system.

The uniformity of this monitoring system makes it possible to compare ILI activity between countries without further data standardization. This has important practical implications for studies concerning the global spread of ILI activity. Current efforts are directed at recruiting more European countries to join the Gripenet. The strength of Gripenet lies in the unique central control of every element of the monitoring system: the recruitment of participants, the questionnaires, the case definitions, the analyses of the data and the presentation of results. This makes the system not only efficient but also very flexible. If desired, any specific component can be altered without disturbing the overall system functionality. For example, the case definition can at any moment, even retrospectively, be adapted to include demographical variables. Further advantages and disadvantages of Gripenet and EISS are listed in Table 4. The two systems can complement each other to provide a better understanding of ILI activity in Europe.

Conclusion

Based solely on voluntary online reports from participants in the Netherlands, Belgium and Portugal, Gripenet detected an approximately simultaneous rise, peak and decline of the ILI activity as compared to EISS during the 2006/2007 influenza season. In contrast to EISS, however, Gripenet uses a uniform monitoring system, allowing the direct comparison of ILI activity between countries, potentially offering a platform to monitor the geographical spread of ILI throughout Europe. We believe that the established system of EISS, which is validated by laboratory results, could be complemented by the fast and flexible system of Gripenet. Furthermore, Gripenet could provide an important channel for influenza awareness and education in Europe. Our current strategy is to extend Gripenet to include more European countries, thus increasing the value of its results and its impact. Those interested in implementing Gripenet are encouraged to contact the corresponding author.

Table 4

Gripenet and EISS compared. The advantages and disadvantages of the monitoring system as used by Gripenet and EISS

	Advantages	Disadvantages
EISS	• Established system • Combine clinical and virological data in the same population	• Participating countries using different case definitions • Dependent on the GP visiting rate
Gripenet	• Uniform method, allows for direct comparison of ILI rates across countries. • Flexible • Real-time monitoring • Channel to participants for influenza-related information	• Self-selection bias of participants • Dependent on continuous participation of volunteers

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