Participatory syndromic surveillance of influenza in Europe

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Abstract

The growth of digital communication technologies for public health is offering an unconventional means to engage the general public in monitoring community health. Here we present Influenzanet, a participatory system for the syndromic surveillance of influenza-like-illness in Europe. Through standardized online surveys, the system collects detailed profile information and self-reported symptoms volunteered by participants resident in the Influenzanet countries. Established in 2009, it now includes ten countries representing more than half of the EU-28 population. The experience of seven influenza seasons illustrates how Influenzanet has become an adjunct to existing ILI surveillance networks, offering coherence across countries, inclusion of non-medically attended ILI, flexibility in case definition, and allowing individual-level epidemiological analyses generally not possible in standard systems. Having the sensitivity to timely detect substantial changes in population health, Influenzanet has the potential to become a viable instrument for a wide variety of applications in public health preparedness and control.

Keywords: influenza, surveillance, crowdsourced data, Internet, cohort, risk factors

Influenza surveillance in Europe

Seasonal influenza is a contagious respiratory disease that annually infects approximately 10 to 30% of Europe's population, causing increased hospitalization rates and excess deaths during winter [1] . Influenza surveillance is conducted by Member States and coordinated by the European Center for Disease Prevention and Control (ECDC) via the European Influenza Surveillance Network (EISN). EISN combines epidemiological and virological data obtained at different layers of surveillance. Nationally organized networks of general practitioners (GPs) constitute the basis of public health surveillance (Figure 1a), reporting the weekly number of patients visited with influenza-like-illness (ILI) or acute respiratory infection (ARI) in selected healthcare facilities (sentinels). Some countries also report virological information from a subset of patients, influenza-confirmed hospitalizations or mortality data. The aim of collating data from different layers of surveillance is to better assess the intensity and spread of influenza, identify trends and risk groups, and inform actions to reduce the influenza-associated burden in Europe.

The increased use of digital communication technologies for public health [2] has recently facilitated adding the *general public* as a key actor for surveillance, enabling individuals to contribute to monitoring the health of their community. The result is a large amount of crowdsourced digital data that can be rapidly analyzed to track disease activity directly in the general population, thus providing health authorities with an additional and potentially scalable layer of surveillance (Figure 1a). Participatory systems generally rely on individuals' self-assessment of their health. ILI has thus offered a straightforward surveillance objective for the early development of these

77 systems [3–7] , given its seasonal occurrence, its large incidence in the population, and
78 the set of easily recognizable clinical symptoms that it may cause [8] .

79 The Influenzanet participatory surveillance system was established in Europe in 2009
80 and included a total of five countries (Figure 1b), four of which (the Netherlands,
81 Belgium, Portugal, Italy) had already prior web-based participatory surveillance
82 experience [4] . The system is based on online survey technology to conduct syndromic
83 surveillance through self-reported symptoms volunteered by participants resident in
84 the Influenzanet countries. It is based on a website describing the system, its objectives
85 and main results (www.influenzanet.eu), and pointing to the national web platforms
86 responsible for data collection for national surveillance. These platforms collect
87 background demographic and risk-factor data from participants upon enrolment and
88 their weekly symptoms, and report analyzed surveillance results.

89 At its start, the Influenzanet platform was not homogeneous across countries because of
90 historical developments leading to the project [4] . It was built on the Dutch and Belgian
91 experience of de Grote Griepmeting (The Great Influenza Survey) launched during the
92 2003-2004 influenza season [3] . The system was next adopted by Portugal (2005) and
93 Italy (2008) with a different technological platform though similar survey. The aim of
94 Influenzanet was to establish a standardized syndromic surveillance system across
95 European countries, from both a technological and epidemiological point of view.
96 Standardized technology is crucial for the seamless introduction of the system in a new
97 country, thus minimizing costs and technological challenges in the implementation and
98 adaptation to a different population (e.g. language, content, server), while ensuring high
99 functionality and usability. A standardized epidemiological survey is needed to
100 maximize coherence across national surveillance networks and thus overcome the

differences in case definitions, population under surveillance and data formats across countries, currently present in sentinel influenza surveillance in Europe [1] .

The first Influenzanet season (2009-2010) was rather unusual as it was characterized by the spread of the 2009 H1N1pdm. Technological development of Influenzanet was halted to give priority to ILI surveillance through intensified recruitment efforts and surveillance during Summer 2009. By the start of the 2011-2012 influenza season, the Influenzanet standardized framework was ready and implemented in all countries.

Since its launch in 2009, Influenzanet has doubled the number of participating countries, now representing 36% of the EU-28 Member States and more than half (58%) of the EU-28 population. Its web approach has the ability to generate data from the general population and not only from medically attended ILI. Its crowdsourced data offer flexibility for the exploration of different ILI or ARI case definitions, provide detailed information to profile the population under surveillance, estimate vaccine coverage or assess ILI-associated behaviors. Its standardized framework and centralized European database allow for country level analyses and rapid extension to the European level, maintaining identical criteria and definitions. Here we review the Influenzanet surveillance system since its launch, summarize main findings and limitations, present a new study on ILI risk factors as an example application, discuss Influenzanet value for public health, and explore its future developments.

Influenzanet system: data collection, management, and analyses

Participation in Influenzanet is voluntary and anonymous, and open to all residents of participating countries. Recruitment occurs through communications of supporting institutions, mainstream and social media, dissemination events (e.g. science fairs or school dissemination activities) and word of mouth (social media or email invitations

through the system). ~~In some countries, weekly reports on Influenzanet results are also published within the national surveillance bulletins.~~

To join the network, individuals register on their national platform and complete an intake survey covering demographic, geographic, socio-economic (household size and composition, occupation, education, transportation), and health indicators (vaccination, diet, pregnancy, smoking, underlying medical conditions). The intake survey can be updated throughout the season to account for changes (e.g. vaccination or pregnancy). Multi-user accounts are also available to facilitate group participation and report for children, or elderly not familiar with the Internet.

Crowdsourced symptoms data are obtained on a weekly basis through a symptom survey. Participants are asked if they experienced any of the following symptoms since their last survey (or 'no symptoms'): fever, chills, runny or blocked nose, sneezing, sore throat, cough, shortness of breath, headache, muscle/joint pain, chest pain, feeling tired or exhausted, loss of appetite, colored sputum, watery/bloodshot eyes, nausea, vomiting, diarrhea, stomach ache, other symptoms. If symptoms are reported, further questions are asked to assess the syndrome (e.g. sudden onset, temperature measure) and participant behavior (e.g. health-seeking behavior, medicines uptake including painkillers or antipyretics, cough medications, antivirals, antibiotics).

The list of symptoms was chosen to include the various ILI definitions adopted by national surveillance systems in Europe. Moreover, following the 2009 H1N1pdm experience, we decided to enlarge the list to include also gastroenterological symptoms. The aim was to get a comprehensive list of symptoms that could be clearly articulated and understood by participants, and that would enable us to distinguish within a range of potentially flu-related illnesses.

Individuals can access and fill the survey at any time, and are reminded weekly by a newsletter also summarizing Influenzanet findings. Additional questions can be implemented by countries for specific studies. Crowdsourced data are analyzed in real time and national and regional results are posted on the system websites. They are also published in the weekly national surveillance bulletins of some participating countries (also increasing the system's visibility for recruitment). Targeted and more local information are accessible to participants only.

Influenzanet is carried out by Universities and Research Institutions (Italy, Spain, Ireland), Public Health Agencies (United Kingdom, Sweden, France, Portugal, Denmark), and private company (Netherlands, Belgium); some countries transitioned in recent years (United Kingdom and Portugal are supported by Public Health Agencies since 2015). Some of the teams are also members of the EISN (France, Portugal, Sweden). Influenzanet is conducted in agreement with national regulations on privacy and data collection and treatment [9] .

Influenzanet surveillance season generally runs from October/November to April/May, allowing for flexibility (e.g. press conference on vaccination campaign to increase dissemination at season launch). ILI syndrome assessment is built on the basis of reported symptoms. Influenzanet uses the ECDC case definition (sudden onset of symptoms; at least one of fever or chills, malaise, headache or muscle pain; at least one of cough, sore throat, or shortness of breath) [8] , in addition to country-specific case definitions to allow for comparison with GP surveillance [10].

Inclusion criteria for participants may vary depending on the aim of the study. Several Influenzanet works [9,11–13] included participants who submitted at least 3 reports per season, whereas a more constrained definition was used to study enrollment

strategies [14] . Here, for the analysis of ILI risk factors we included participants who reported at least once before, during, and after the epidemic period, to ensure a minimum participation level throughout the season. We considered data from United Kingdom, France, Spain, Ireland, Denmark in the 2014-2015 season and use ECDC case definition to complete previous work conducted on the remaining countries [11,13]. Odds ratios (ORs) were calculated for the covariates collected with the intake survey based on a multivariate logistic regression model through a backward stepwise selection. As the ILI outcome is not a rare event, we also corrected ORs to estimate the relative risk (RR) and 95% confidence intervals. Additional details are provided in Table 1.

Influenzanet results and discussion

Since the launch of Influenzanet, a total of 243,109 individuals (considered independently per season) joined the system completing the intake survey and reporting at least once. Participation across seasons saw a general decrease after the pandemic (Figure 1b,c), visible for the UK and statistically significant for the Netherlands and Portugal once compared to their previous results (average number of participants per season before vs. after 2009: 20,597 vs. 15,564 $p < 10^{-3}$, and 3,447 vs. 1,800 $p = 0.003$, respectively, Student t-test). This may be a reaction to the substantial effort required to participants for continued surveillance during pandemic season. We argue that it may also be a resulting effect of the controversies over vaccine safety and pandemic management [15], fueling public dissonance and translating into negative experiences for individuals [15–17] . The effect appears to rapidly wane in the Influenzanet system, with a stabilized number of Dutch participants (the largest contribution to Influenzanet) and the addition of new countries since 2011.

For the 2015-2016 season, Influenzanet registered 36,192 participants with a rate of participation of 13 per 100,000. Participation by country varies considerably [9] , with averages over all seasons ranging from 1.2 per 100,000 (Spain) to almost 100 per 100,000 for the Netherlands, notably the most successful example within Influenzanet [18]. New countries have shown to be able to quickly attract a large enough number of participants to generate reliable surveillance data [10,19], a promising result for further extending the system. The observed heterogeneity across countries may be associated with diffused trust in the media and Internet, larger interest of the general public in health-related topics and larger healthcare expenditure (ongoing work).

Recruitment and retention are the two main challenges for Influenzanet. TV appearances at the early stages of de Grote Griepmeting and dissemination by communication scientists led to a considerable growth of participants, successfully retained across years [11,13]. By comparison, isolated spikes in participation indicating high drop-out rates were instead observed in a similar participatory system in the United States [5]. Continuous reporting throughout the season is essential to ensure data quality. Since the standardized framework is in place, Influenzanet collected a total of 2,694,065 symptom reports (up to April 2016), 543,895 in the last season with a weekly average of 22,768 reports. Participants can join the system at any time during the surveillance season and on average they submit 14 to 16 reports each in a season. 67-91% of them, depending on the country, submitted at least 3 reports in season 2014-2015, with small variations across seasons [9]. These statistics indicate a good compliance for reporting that can be due to various factors: strong interest in being actively engaged in a health project [18], and rather easy access and use of the Influenzanet platform (>93% of French and Portuguese participants declared that surveys' length was good and >97% of them were satisfied or very satisfied with the

website). Individuals with a higher participation were found to be recruited more likely through offline communication than through online media, except for France [14], where a considerable fraction of participants (21%) is referred to Influenzanet from Institutional Public Health websites. Different strategies need therefore to be considered by countries to promote the project and grow in participation.

Statistically significant differences exist when the Influenzanet cohort is compared to national populations [9,10]. Higher female participation occurs in the majority of countries, as in other studies [5,7], possibly due to a more active information-seeking behavior in women [20] . All age classes are represented in the cohort, but younger (<30 years) and older (70+) classes are considerably underrepresented, perhaps for lack of interest or difficulty of access. Specific communication activities and tools (e.g. for schools and senior classes) have been implemented in several countries to target these age groups. Also, a marked increase in participation of the elderly has been observed over the years [11], likely due to a growing Internet usage in that group, suggesting that discrepancies may decrease in time. Vaccination coverage in the 65+ age class is generally higher in the Influenzanet population, suggesting a higher health awareness in the cohort.

Despite these discrepancies, trends of estimated ILI incidence from Influenzanet reports compare well with those of national sentinel systems [4,10,11,19,21] . An anticipation of about 1 week in the peak of Influenzanet incidence is found compared to sentinel estimations, suggesting that the time needed to consult a doctor and collate sentinel data may be absorbed once data is collected directly from the general population and timely analyzed. The Influenzanet cohort has also been used to estimate vaccine effectiveness in real-time [22], vaccine coverage in specific subgroups [23], individual perception

246 towards vaccination [17], and to correct estimations of pandemic burden accounting for
247 changes in social contacts patterns and in health-seeking behavior [24,25].

248 Most importantly, individual data on demographic indicators, lifestyle and health
249 variables, and the monitoring of a wide variety of cases allow us to examine risk factors
250 for specific conditions to a detail that is hardly achievable in sentinel systems. The
251 analysis based on single and multiple influenza seasons (Table 1) suggests that
252 belonging to a younger age group, being female, living with or having contacts with
253 children, having an underlying chronic health conditions, respiratory allergies, daily
254 smoking and having pets are factors associated with an increased risk of having an ILI
255 episode during influenza season. Vaccination provided a reduction in the risk, though it
256 was found to depend on the season [13]. ~~Some discrepancies are found across countries~~
257 ~~that may be due to the small sample sizes.~~ These results are generally consistent with
258 previous findings [26–28]. Children are known to have a major role in the dissemination
259 of influenza [26]. Chronic illness was found to be a major driver for influenza
260 complication and hospitalization [27]. Cigarette smoking represents a substantial risk
261 factor for important bacterial and viral infections [28]. In addition, we found that
262 women have an increased risk in all countries and seasons under study, even when
263 adjusting for living or having contacts with children. Though this risk factor was not
264 reported by GP surveillance, it was found in previous cohort studies also in adults
265 without children [26]. It would be interesting to explore whether such gender
266 differential is not observed in routine GP surveillance due to differences in health-
267 seeking behavior between men and women. This is not observed in self-reporting in
268 many Influenzanet countries, thus other factors, such as unmeasured confounders, may
269 be at play. Daily use of public transport was not statistically associated with a higher risk

of contracting ILI, contrary to widespread public concerns. This is in line with previous work for the risk of ARI once frequent use is considered [29].

Influenzanet flexibility allows the integration of additional questions for specific studies or target populations that are usually not considered in routine analyses. A study of French Influenzanet pregnant women showed a higher ILI incidence in 40+ women and during first/second semester [23]. Investigating stress indicators revealed significant trends between stress and self-reported ILI [30].

Conclusions

Influenzanet is a well-established standardized participatory surveillance system for ILI in Europe, covering more than one third of EU-28 Member States. Its strength lies in: (i) the standardized technological and epidemiological framework for a coherent surveillance across countries; (ii) the ability to timely monitor ILI in the general population, including individuals who do not seek medical assistance; (iii) its sensitivity in detecting substantial changes in population health earlier than GP sentinel networks; (iv) its potential scalability to large numbers with rather limited costs; (v) its flexibility in exploring different ILI definitions; (vi) the detailed profile data allowing individual-level epidemiological analyses generally not possible in standard systems; (vii) its potential extension to other diseases. Its limitations are mainly due to the self-selected sample, potential misreporting and lack of validation by a medical doctor or virological testing. However, the agreement found with GP incidence trends suggests that these limitations have little effect once results are adjusted for lack of representativeness.

Immediate steps for Influenzanet include the extension to other European countries and establishing a global collaborative framework for ILI surveillance with other similar

293 participatory systems outside Europe. Virological confirmation has also been tested in
294 pilot studies for future integration.

295 Main challenges remain the baseline maintenance resources to sustain the system in the
296 long run, and the recruitment and retention of participants. While the identification of
297 socio-cultural determinants for participation will provide additional insights, the strong
298 willingness for engagement found in most countries' participants confirms the feasibility
299 of the approach. Moreover, the platform represents a crucial channel for communication
300 with the public, to inform and grow awareness, an increasingly important aspect after
301 the 2009 pandemic.

302 Launched as a research project, Influenzanet is currently considered as an adjunct to
303 existing ILI surveillance systems and has been adopted in some cases by Public Health
304 Agencies. Its flexibility in system configuration potentially allows for a wide variety of
305 applications in public health preparedness and control. Sweden for example has tested a
306 different method, based on invitation only, in the last two seasons to track the health
307 situation of the country.

308 Influenzanet may therefore represent a viable complement to existing monitoring
309 approaches to provide additional information that standard methods cannot rapidly
310 achieve. Italy is now extending the surveillance effort to monitor Zika cases with the
311 approaching of the Summer. In France, a food consumption survey submitted to
312 Influenzanet participants for an outbreak investigation during a Salmonella epidemic in
313 early 2016 provided public health authorities with timely findings to identify the source
314 of the outbreak. With the large majority of participants willing to contribute to
315 additional studies beyond ILI, Influenzanet may become in the near future a powerful
316 system that, once adjusted for sample biases, can offer a timely 'thermometer'

measuring the epidemiological status, opinion or behavior of the general population along different indicators and diseases.

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Conflict of interest.

Authors declare no conflict of interest.

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Table 1. Adjusted risk factors for ILI across Influenzanet countries obtained from multivariate regression analyses. The analysis for Denmark (981 participants) and Spain (368 participants) for the 2014-2015 season showed similar results for the age classes (both countries) and for the female gender (Denmark). The analysis for Ireland (210 participants) for the same season did not show significant results.

Countries		NL + BE + PT + IT [13]	UK	FR
Study period		2003-2013[a]	2014-2015	2014-2015
# of participants included in the study		Average # per season[b]: NL: 16,481 BE: 5,072 PT: 1,894 IT: 1,219	2,629	4,475
Variable		**RR (95% CI)[c]**	**RR (95% I)[d]**	**RR (95% CI)[d]**
Female gender		1.22 (1.17-1.28)	1.25 (1.14-1.36)	1.12 (1.02-1.23)
Vaccinated		0.80 (0.71-0.91)	–	0.87 (0.78-0.97)
Age		**<18** 1.59 (1.46-1.74) **18-49** * **50-64** 0.82 (0.78-0.86) **65+** 0.46 (0.41-0.51)	**0-14** 1.27 (1.03-1.50) **15-44** * **45-64** 0.99 (0.89-1.11) **65+** 0.82 (0.71-0.94)	**0-14** 0.95 (0.76-1.16) **15-44** * **45-64** 0.87 (0.76-0.98) **65+** 0.68 (0.58-0.79)
Household	Living w. children	1.31 (1.22-1.40) (vs. living alone)	–	–
Contacts w. groups[e]		X	1.11 (1.01-1.21)	1.12 (1.01-1.23)
Smoker		1.16 (1.10-1.22)	–	–
Underlying health conditions	Asthma[f] Diabetes Heart Kidney Immune	1.58 (1.47-1.69) 1.27 (1.15-1.41) 1.29 (1.13-1.47) 1.23 (0.80-1.90) 1.23 (1.02-1.49)	–	Any: 1.17 (1.05-1.30)
Having respiratory allergies		X	1.14 (1.05-1.24)	1.19 (1.07-1.29)
Declaring often having ILI		X	X	1.31 (1.17-1.45)
Sports >1h per week		0.95 (0.90-1.00)	X	X
Having pets	Dogs Cats	1.15 (1.09-1.22) 1.07 (1.02-1.12)	X	Any: 1.17 (1.08-1.28)
Daily transport	Bike/Foot Car Public	0.95 (0.90-1.00) * 0.97 (0.89-1.05)	* * 0.91 (0.78-1.05)	–

[a] Except vaccination results here shown for 2012-2013 season

[b] Inclusion criteria in this study were slightly different: at least 3 symptoms survey, considering ILI episodes during the weeks when influenza strain were circulating in the population.

[c] All covariates considered as potential risk factors were included and remained in the final multivariate model. All participants were considered independent between seasons. Only vaccination was considered as a season-dependent covariate, and country of residence and season were added in the model as extra covariates.

[d] All covariates collected in the intake survey were considered and included in the final multivariate analyses if they had univariate p-value <0.2. Backward stepwise selection was considered. A Hosmer-

Lemeshow test was computed to estimate the final models quality. All models had a p-value above 0.05 suggesting that they were correctly specified.

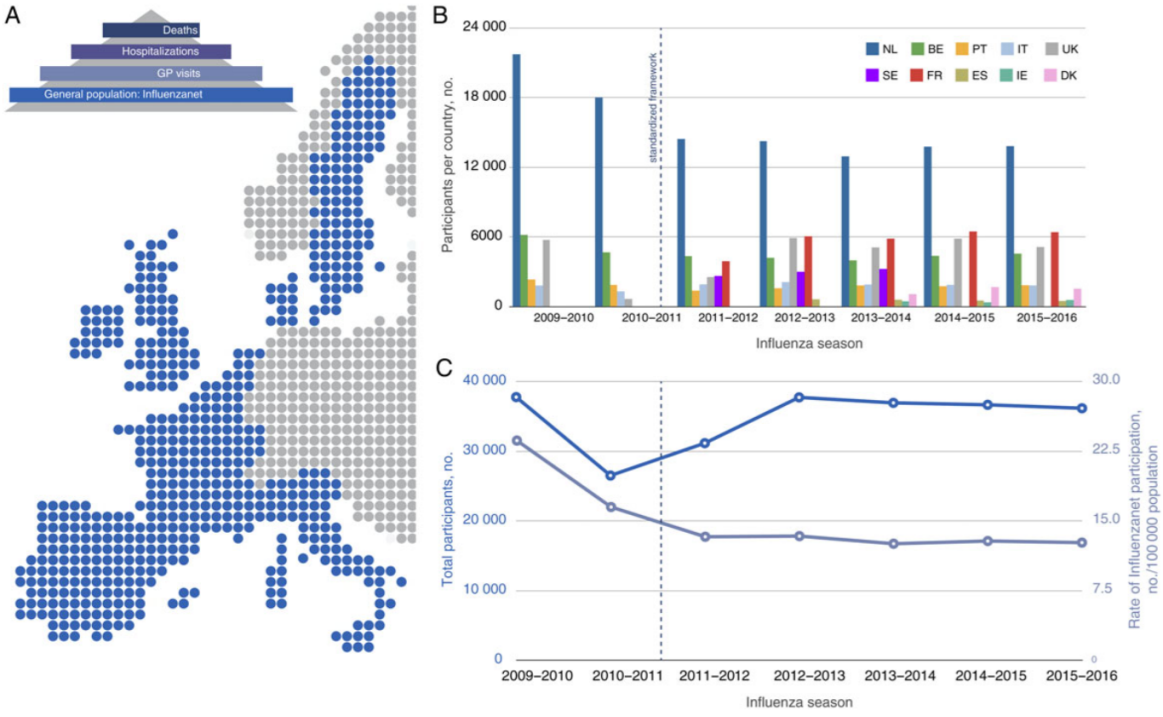
[e] Contacts with any groups of children, elderly, patients or crowds during the course of a typical day

[f] Asthma or other lung diseases

* Reference category

– Significant covariates in the univariate analyses, but not selected by the multivariate logistic regression (p>0.05). Blank cells indicate non-significant variables in the univariate logistic regression analyses.

X not available data



436 **Figure legends**

437

438 **Figure 1. Influenzanet participatory surveillance system for ILI.** (a) ILI monitoring
439 scheme illustrating different layers of surveillance used by public health authorities,
440 including (depending on the country) sentinel GP networks counting ILI visits, ILI-
441 associated hospitalization data, ILI-associated mortality data. Influenzanet represents an
442 additional layer for ILI monitoring, through syndromic surveillance in the general
443 population by means of a web-based participatory system. It includes 10 countries
444 schematically represented in the map: NL (www.degrotegriepmeting.nl), BE
445 (www.degrotegriepmeting.be), PT (www.gripenet.pt), IT (www.influweb.it), UK
446 (flusurvey.org.uk), SE (www.halsorapport.se), FR (www.grippenet.fr), ES
447 (www.gripenet.es), IE (flusurvey.ie), DK (influmeter.dk). (b) Number of Influenzanet
448 participants per country per season since its launch in 2009-2010 influenza season. The
449 dashed vertical line indicates the standardized framework introduced from the 2011-
450 2012 season. (c) Total number of Influenzanet participants per season (left vertical axis)
451 and Influenzanet rate of participation per season (right vertical axis) expressed as
452 number of participants per 100,000 individuals of the total population of Influenzanet
453 countries.