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INTERNET SURVEILLANCE SYSTEMS FOR EARLY ALERTING OF HEALTH THREATS

J P Linge¹, R Steinberger¹, T P Weber¹, R Yangarber², E van der Goot¹, D H Al Khudhairy¹, N I Stilianakis (Nikolaos. Stilianakis@irc.it)¹

1. Joint Research Centre (JRC), European Commission, Ispra (VA), Italy

2. Department of Computer Science, University of Helsinki, Helsinki, Finland

In order to gather a comprehensive picture of potential epidemic threats, public health authorities increasingly rely on systems that perform epidemic intelligence (EI). EI makes use of information that originates from official sources such as national public health surveillance systems as well as from informal sources such as electronic media and web-based information tools. All these sources are employed to enhance risk monitoring with the purpose of early alerting and initial risk assessment. In this context *Paquet et al.* [1] distinguish between *indicator-based* risk monitoring and *event-based* risk monitoring. As indicator-based monitoring relies on classical routine surveillance, many systems will use methods and data sources familiar to most epidemiologists and public health officials. The event-based component of EI is in contrast rather new; its methods, strengths and limitations are generally not widely known in the public health community. The purpose of this editorial is thus to provide an overview of the methods used in pro-active event-based monitoring and to put them into context with regard to the structured indicator-based monitoring such as that described in the article on the Lithuanian electronic surveillance system published in this issue of *Eurosurveillance* [2].

More and more national and international public health agencies employ systematic event detection systems using informal sources (news wires, media sources or websites) on the internet to monitor the potential threat of emerging and re-emerging infectious diseases. Such web-based event detection is the first step in EI systems designed to provide early warning signals to public health institutions. A number of different systems have been developed for this purpose. There is, however, still the need to emphasise some fundamental differences between the available systems and to identify the challenges that lie ahead. Existing event detection systems can be classified into three categories.

First, *news aggregators* collect articles from several sources, usually filtered by language or country. Users gain easy access to many sources through a common portal, but still need to examine each individual article.

Second, *automatic systems* such as the Medical Information System (MedISys) (<http://medusa.jrc.it/>) [3], Pattern-based Understanding and Learning System (PULS) (<http://puls.cs.helsinki.fi/medical/>) [3], HealthMap (<http://www.healthmap.org/>) [4], and BioCaster Global Health Monitor (<http://biocaster.nii.ac.jp/>) [5] go

beyond the mere gathering task by adding a series of analysis steps. Automatic systems differ in their levels of analysis, in the range of information sources, their language coverage, the speed of delivering information and visualisation methods. HealthMap currently covers five languages, BioCaster seven languages, and MedISys more than 40 languages. While HealthMap mainly relies on Google News, World Health Organization (WHO) news feeds, ProMED-Mail (<http://www.promedmail.org/>) [6], and Eurosurveillance as sources, MedISys monitors ProMED-Mail, web sites of national public health authorities, specialist web sites (including Eurosurveillance), news from about twenty news wires, plus a balanced list of approximately 2,200 news sources from around the world, hand-selected with a view of ensuring a geographic balance.

Analysis steps may include: recognition of relevant terms (names of diseases, symptoms and organisations), recognition and disambiguation of geographical locations mentioned in the articles, grouping related articles into clusters, and extraction of full events from the news, providing the users with aggregated information about the disease, the number of cases, as well as time and place of an outbreak. Ideally, news items should be clustered across languages and national borders. Most systems focus on recognising communicable diseases and visualise the location of the extracted events on geographical maps. As a domain-specific application of the Europe Media Monitor (EMM) system, MedISys covers not only the whole range of chemical, biological, radiological and nuclear threats (CBRN), but also allows using a filter to only show outbreak-related information. MedISys additionally monitors trends and calculates alert levels per disease and per country, by comparing the number of recent news items with averages. PULS, which is integrated with MedISys, extracts event data from the English MedISys articles and produces searchable outbreak data in table format.

All automatic systems will clearly benefit from better machine-translation software so that a more diverse range of sources can be tapped. Ideally, a summary of each article should be shown in the original language together with its translation.

Third, *moderated systems* such as ProMED-Mail [6], GPHIN (Global Public Health Intelligence Network) [7] and ARGUS [8] rely on a group of analysts to scan available news sources. The analysts take into account information from individual web sites, aggregator sites, automatic systems, and other sources such as reports from

medical practitioners and health authorities. In combination with its Rapid News Service (RNS) tool, MedISys also allows for manual moderation.

There are fundamental differences in these approaches. Non-moderated systems are able to search the web and display new articles without time delay in an unbiased manner. Moderated systems show fewer irrelevant news items (fewer false positives). However, moderator bias represents a risk (false negatives); users might have a different focus than the moderators.

For users who need to react to threats quickly and possess the man-power to entertain their own monitoring effort, automatic systems are appealing because of the detection speed. Other users might prefer to wait for human-moderated feeds.

Technical implementation of aggregators is straight-forward, but for both automatic and moderated systems, many challenges lie ahead. Redundancy is a major issue. Naturally, news agencies, online and printed news sources, national and international authorities or blogs may report the same event in different ways at various time points. This often leads to misclassification of events and overestimation of impact. Furthermore, feedback loops are created when automatic systems accept input from moderated systems (or vice versa). In any moderated approach, long-term funding or volunteer participation is necessary to maintain the analyst base.

Automatic approaches are the only option to sieve relevant information out of the abundant pool of multilingual media sources in real time. However, human moderation is needed eventually.

A further challenge for the future will be to improve the transition from risk monitoring to risk assessment. Recent approaches on extracting patterns of influenza-related search terms from queries stored by Google and Yahoo [9, 10] showed that patterns of searches matched with official influenza surveillance data, thus indicating that search-term analysis could be a useful complementary tool to surveillance. However, although search-term analysis and event-based monitoring can provide an important signal of a potential outbreak, the data gathered is usually not detailed or reliable enough to estimate relevant epidemiological parameters of incipient outbreaks and the methods are prone to false alarms.

Lithuania's electronic reporting system described in this issue of *Eurosurveillance* [2] is an example of an indicator-based component of EI which allows the collection of structured data at country level. Such national information is typically fed into the European Surveillance System (TESSy) [11] of the European Centre for Disease Prevention and Control (ECDC) which collects surveillance data on infectious diseases at the European Union (EU) level to support outbreak detection, risk assessment, outbreak investigation and control measures. This is complemented by the Early Warning and Response System (EWRS) which establishes permanent communication between public health authorities in the EU member states [12].

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Rapid communications

FIRST IDENTIFICATION OF CLASS A CARBAPENEMASE-PRODUCING *KLEBSIELLA PNEUMONIAE* IN THE REPUBLIC OF IRELAND

C Roche¹, M Cotter², N O'Connell³, B Crowley (bcrowley@stjames.ie)^{1,2}

1. Department of Clinical Microbiology, Trinity College Dublin, Ireland

2. Department of Microbiology, St James's Hospital, Dublin, Ireland

3. Department of Microbiology, Limerick Regional Hospital, Limerick, Ireland

The *Klebsiella pneumoniae* carbapenemase (KPC) was detected in a carbapenem-resistant respiratory isolate of *Klebsiella pneumoniae* in an Irish hospital. This is the first report of a KPC-producing isolate in the Republic of Ireland. The isolate was resistant to all β -lactams. Furthermore, it had reduced susceptibility to three other classes of non- β -lactam antibiotics. The isolate was not associated with travel abroad. Detection of KPC-producing bacteria has important infection control and public health implications.

In February 2009, a tertiary care centre in Limerick, Ireland identified by Etest a *Klebsiella pneumoniae* isolate resistant to meropenem (MIC \geq 32 mg/L). The isolate was recovered from a sputum sample collected 48 hours after hospital admission from a 60-year-old male with exacerbation of chronic obstructive pulmonary disease (COPD). A sputum sample collected on admission to hospital did not yield any bacterial growth, which suggested that the carbapenem-resistant isolate had been acquired nosocomially. Furthermore, the patient had never been treated with a carbapenem antibiotic and no discernible linkage could be established to the United States, Greece, Israel, China or South America where carbapenem-resistant *Enterobacteriaceae* are commonly encountered [1–5]. Interestingly, the patient was treated successfully with piperacillin/tazobactam and discharged from hospital three days after admission.

The isolate was sent to St James's Hospital, Dublin for further analysis. Antimicrobial susceptibility testing showed a high level of resistance to β -lactam and carbapenem, including piperacillin/tazobactam, ertapenem, imipenem and meropenem, as well as to fluoroquinolones, amikacin and reduced susceptibility to tigecycline (4 mg/L). The isolate remained susceptible to colistin and gentamicin (2 mg/L). The rapid clinical response to piperacillin/tazobactam suggests that the exacerbation of COPD was likely due to another bacterial or viral infection, not identified, whereas the results of sputum testing indicated colonisation with carbapenem-resistant *K. pneumoniae*.

In order to identify the molecular mechanism of carbapenem resistance, the isolate was screened for production of a carbapenemase with the modified Hodge plate test [6]. The latter was positive. The MBL test for metallo- β -lactamase production

was performed but it was negative. However, the presence of *K. pneumoniae* carbapenemase (KPC) was indicated on phenotypic testing by determining meropenem MIC values in agar, with and without boronic acid (200 mg/L) [2]. Further confirmation by PCR amplification using specific blaKPC primers and sequencing showed the isolate carried the KPC-2 gene (GenBank accession number FJ853623).

This is the first documented appearance of a class A carbapenemase-producing isolate of *K. pneumoniae* in the Republic of Ireland and it was not associated with travel abroad. KPC β -lactamases (KPC 1–7) confer decreased susceptibility or resistance to all β -lactams [7]. As presented in this case, the isolate showed reduced susceptibility and resistance to four different classes of antibiotic, limiting the therapeutic options only to polymixin, colistin and gentamicin. Most isolates of KPC-producing *K. pneumoniae* remain susceptible to tigecycline. In this report the isolate had reduced susceptibility. It is important to note that treatment failure with tigecycline has been reported with MIC value of 2 mg/L, which may be related to low serum concentrations of the antibiotic so that caution is warranted when using it for treatment of severe bacteraemic infections [8]. Furthermore, the clinical efficacy of colistin in treatment of cases of infection with KPC-producing *K. pneumoniae* is very limited [9]. Of more concern is the observation of colistin resistance in KPC-producing *K. pneumoniae* [10]. Fortunately, in the case reported here the patient was only colonised with carbapenem-resistant *K. pneumoniae*.

Patients with unrecognised colonisation with carbapenemase-producing *Enterobacteriaceae* have been shown to transmit these bacteria in the hospital setting [11]. Following the identification of this case, microbiology records for the preceding six months were reviewed to ascertain if other isolates had been cultured from clinical specimens. No other isolates with reduced susceptibility to carbapenems were identified. Furthermore, no subsequent samples from patients on the same ward as the case reported here grew *K. pneumoniae* with reduced susceptibility to carbapenems.

The emergence of KPC-producing *K. pneumoniae* in Ireland is worrying from a public health point of view, particularly since KPC β -lactamases are plasmid-borne and, like extended spectrum

beta lactamases (ESBLs), can accumulate and transfer resistance determinants to other classes of antibiotics. Therefore, infection control guidelines on early identification and control of the spread of organisms carrying these resistant determinants are needed.

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IS THERE A NEED FOR ANTI-RABIES VACCINE AND IMMUNOGLOBULINS RATIONING IN EUROPE?

H Bourhy (hbourhy@pasteur.fr)¹, M Goudal¹, A Mailles², M Sadkowska-Todys³, L Dacheux¹, H Zeller⁴

1. WHO Collaborative Center for Reference and Research on Rabies, National Reference Centre for Rabies, Institut Pasteur, Paris, France

2. Institut de veille sanitaire, Saint-Maurice, France

3. National Institute of Public Health, Warsaw, Poland

4. Preparedness and Response Unit, European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

Rabies is a lethal encephalitis caused by a lyssavirus and transmitted from animals to humans via bite wound, scratch wound, or licking of mucous membranes. It is preventable by timely administration of post-exposure prophylaxis (PEP) consisting of four or five doses of rabies vaccine combined, in the most severe cases of exposures, with anti-rabies immunoglobulin (RIG). Although the rabies incidence in humans remains low, rabies is still present in some European countries. Moreover, rabid animals imported from enzootic areas are reported every year in rabies-free areas. These importations threaten the rabies-free status of terrestrial animals in western European countries and challenge the public health surveillance system and the health structures responsible for rabies prophylaxis and control. The importations frequently result in the prescription of a large number of PEP including RIG, especially in western European countries. The situation is inverted in some central and eastern European countries where RIG is underprescribed. Only a limited number of rabies vaccines and particularly of RIG are licensed for use in Europe. Their availability is also limited, a situation that may become worse in the future. It therefore seems important to study the possibility of comparing and unifying national PEP guidelines in Europe, if needed, and to generate effective solutions in the event of a shortage of anti-rabies biological products and RIG in particular, such as rationing these products.

Introduction

Rabies is a lethal encephalitis caused by a lyssavirus which is transmitted from animals to humans via bite wound, scratch wound, or licking of mucous membranes [1]. Human-to-human transmission has not been proven. However, some cases of rabies transmission through organ transplantation have been described [2,3]. Since Louis Pasteur's discovery of the rabies vaccine, rabies has been a disease that can be prevented through the timely administration of post-exposure prophylaxis (PEP). Today, PEP consists of four or five doses of rabies vaccine administered on three to five visits. Anti-rabies immunoglobulin (RIG) is given in addition, if the exposure fulfils the criteria of Category III as defined by the recommendations given by the World Health Organization (WHO) [4,5].

Rabies is still present on the European continent, although some countries have rabies-free status according to the criteria of the World Organisation for Animal Health (OIE). Its incidence in humans remains low (fewer than five human cases per year) owing to the strict application of PEP and to veterinary rabies control measures in domesticated and wild animal populations.

The main indigenous animal reservoirs are dogs in eastern European countries and on the borders with the Middle East, foxes in central and eastern Europe, racoon dogs in north-eastern Europe and insectivorous bats throughout the entire territory [6]. In addition, cases of rabid animals imported from enzootic areas outside Europe are reported every year, which shows the permeability of borders and travellers' lack of awareness of the rabies risk [7]. These importations constantly threaten the rabies-free status of terrestrial animals in western European countries. The associated risk also complicates the decision concerning human PEP when the biting animal is not accessible for rabies assessment (clinical examination and/or laboratory examination) [6,8]. In view of the complexity of rabies epidemiology in the European Union (EU), it is important to keep health professionals, particularly physicians and veterinarians, updated in order to maintain vigilance. Recommendations to improve rabies control in animals and prevention of human transmission have recently been published in the WHO Expert Consultation on Rabies [4].

The objective of this paper is to review the current situation in the EU countries regarding the needs for rabies vaccine and anti-rabies immunoglobulins as well as the risk of a potential shortage, using as examples the current practice in France and in Poland.

Different usage of rabies biological products in Europe

Data on the use of rabies vaccine and anti-rabies immunoglobulin and on the number of PEP in Europe are scarce. Therefore, we will mainly focus our report on two countries, France and Poland, that have implemented centralised surveillance.

In France, data from 2007 showed that 3,631 people (47% of all people who sought medical care in anti-rabies centres) received PEP treatment with 11% of them receiving RIG. In February 2008, two cases of autochthonous rabid dogs lead to the prescription of

241 PEP in people who had been bitten, 34 of whom also received RIG, in accordance with the French and WHO recommendations. The index case was a dog illegally imported from Morocco [9]. Following this event, France lost its rabies-free status according to the OIE criteria. Since then, no other case of canine or feline rabies have been diagnosed in non-travelling animals, which makes us confident that the veterinary control measures taken after the incident have been effective in controlling further spread of the virus. In November 2008, a rabid dog imported to France from Spain was identified. The three month-old animal was found to be infected by a strain phylogenetically very close to those circulating in Morocco, indicating a potential recent importation from Morocco (unpublished results). Of 32 people who were in contact with this dog, seven received PET including vaccine and RIG, 18 received vaccine only and the remaining seven people were not considered at risk and therefore did not receive any PET. Unfortunately, such episodic importations of rabies-infected dogs are not rare. Between 2000 and 2008, seven rabid dogs had been illegally imported into France from Africa. For each imported rabid dog, between two and 187 people with direct contact had received post-exposure vaccination, and nearly 15% of them had also received anti-rabies immunoglobulin.

Several other rabies-free countries in Europe have also reported importation of rabid animals in the past (e.g. Belgium, Switzerland, and the United Kingdom). These episodes further supported the recommendation of prescribing PEP for patients bitten by a dog of unknown origin or suspected to come from an enzootic country. The recent re-emergence of fox rabies in Italy has stressed further that rabies in non-flying wildlife is not completely under control in Europe and that it can re-infect areas from which it was eliminated years before [10]. Consequently, the periodical re-introduction of rabies in any of the EU countries has an immediate impact on the number of PEP interventions, i.e. the number of rabies vaccine and immunoglobulin doses used in EU.

The number of reported human exposures to bats in Europe has also increased in recent years. In these cases, patients received RIG together with the vaccine in accordance with national and WHO guidelines [4]. In France alone, an average of 100 people receive PEP including RIG after exposure to bats every year.

On the other hand, RIG may be underprescribed in some countries in central and eastern Europe. In Poland, for example, PEP is administered to about 7,000 people every year (54,767 patients in total during the period from 2001 to 2007), and only 0.8% of these patients also receive RIG. In the same time period, 644 individuals received PEP after a contact with bats and only 4.7% of them received RIG. In these countries, a strict application of WHO guidelines would therefore immediately lead to an increase in the use of RIG in particular.

Risk of vaccine shortage

According to the number of rabies vaccine sold every year and in the absence of more precise data, we can estimate that worldwide, at least 15 million PEP are administered annually. The EU, the United States (US) and Canada only represent 1% of the global consumption. European producers have implemented high quality control standards for the production of rabies vaccines and immunoglobulin. The two European producers supply about 25% of the rabies vaccine doses used annually worldwide.

An official health advisory report published in June 2008 by the US Centers for Disease Control and Prevention (CDC) indicated a temporary decrease in human rabies vaccine supplies in the US [11,12]. The two European producers (Sanofi Pasteur and Novartis) are the only suppliers of rabies vaccine for the use in humans in the US. Supplies of rabies vaccine went down in the US after Sanofi Pasteur started renovations in the French production facility for the IMOVAX rabies vaccine (produced on human diploid cells) in June 2007, and after Novartis had to suspend its supply to the US and the EU in September 2007 following an inspection conducted by the US Food and Drug Administration (FDA) (http://www.fda.gov/foi/warning_letters/archive/s6644c.pdf). The renovations conducted by Sanofi Pasteur are expected to be completed by mid-2009 and the registration of IMOVAX (the rabies vaccine produced in this facility) by the end of 2009. Novartis started building a new rabies vaccine production facility in Germany in May 2008. It is expected to be fully operational in 2011 [11,13].

As a consequence, the US CDC strongly recommend that healthcare providers, public health authorities at state and local level, animal control officials, as well as the public take immediate steps to ensure appropriate use of human rabies biological products. The US CDC stressed that the judicious and appropriate use of rabies vaccine is crucial in order to avert a situation that puts individuals exposed to rabies at increased risk due to depleted vaccine supplies [13]. Therefore the use of rabies vaccine is restricted to situations meeting the criteria indicated in the recommendations [13]. Regarding pre-exposure prophylaxis in the US, priority is given to those at greatest risk of rabies exposure (e.g. people working in rabies laboratories, animal control officers, veterinary staff or wildlife workers), taking into consideration the available rabies vaccine supplies. For groups at lower risks of exposure (e.g. travellers and veterinary students), the US CDC proposes to suspend pre-exposure prophylaxis until the vaccine supply levels are restored.

The availability of rabies vaccines in Europe differs from that in North America where only vaccines produced in chicken embryo cell culture or human diploid cells are licensed. In Europe, vaccine is produced in Vero cells in large amounts and widely used in Europe, particularly in France, as well as in Asia and Africa. It represents a possible alternative in the event of a shortage of the two other products.

Risk of RIG shortage

The stock of specific human RIG is more limited and it has been known for some time that there is a world-wide shortage [14]. Only three to five million doses of anti-rabies immunoglobulin are produced and sold every year. Considering that the number of doses used in one protocol of PEP varies according to the patient's weight in kg, no more than an estimated 2-5% of patients seeking PEP can have received anti-rabies immunoglobulin. The current level of production does not cover the needs. According to WHO estimates, about 60% of the people seeking care for PEP do not receive an injection of anti-rabies immunoglobulin, although they fall into the category of exposure that would require it [4,15,16]. This is mainly due to difficulties with access to this biological product, but also to limited production compared to the world-wide demand. In Europe, two types of purified anti-rabies immunoglobulin are produced, human (HRIGs) and equine (ERIGs). The entire production of HRIGs, which is limited due to the lack of plasma donors, is almost exclusively sold in the US and Europe. Therefore any increase

in demand may cause problems. However, ERIGs are now highly purified, well tolerated and have been demonstrated to be efficient in post-exposure treatment [17]. They are produced in large amounts and may be a suitable alternative in case of a shortage of HRIG, although they have not yet been licensed in Europe. Other products of good efficacy and safety manufactured outside Europe could also be used as a complementary source of supply. Cocktails of monoclonal antibodies have also been recently developed for this purpose [18]. Although promising, the first licence of this type of product cannot be expected before 2012 or 2013.

Discussion

In France and Poland, recommendations for rabies PEP (both vaccine and immunoglobulin) followed national guidelines and/or WHO guidelines which recommend that people should receive PEP when bitten by an animal suspected to be infected by rabies. Clinicians make an individual risk assessment for each patient bitten or scratched, and decide to administer rabies vaccine with or without immunoglobulins according to the general recommendations, epidemiological data and the category of the bite. The veterinary situation is taken into account in this assessment, namely the species of the biting animal and the possibility of carrying out examination of the animal if it can be identified. Although no study has investigated the actual prescription practices, it is suspected that some PEP prescriptions are not based on the guidelines [19]. In Europe, practices vary, relying either on special anti-rabies centres (such as in France) or on private general practices (such as in Germany). Furthermore, there seems to be large variations in the use of PEP and especially RIG between European countries, with some countries overreacting (for example France) and others underprescribing (like Poland). Therefore, it would be important to review and analyse practices in the EU, as has been done in North American countries [20].

The risk of a potential shortage of rabies vaccine seems limited in Europe. However, it is important to note that the risk of a potential shortage of RIG in the event of an unplanned increase in demand or a limitation in supply is shared by many countries in Europe and other continents [8,21-23]. The availability of other RIG that have proved their efficacy and safety and that are presently not widely licensed in this area constitutes a possible alternative.

Note added in proof

Since the time of submission of this paper, an European consultation was conducted at the European Centre for Disease Prevention and Control (ECDC) in Stockholm on 15 January 2009. The group of experts gathered at this occasion further emphasised the need to review the rabies epidemiological situation in Europe. It also recommended to map practices and usage of anti-rabies biological products in Europe in order to be able to propose effective options for optimisation, as has been done for other vaccines [24]. The conclusions of this meeting will be available from ECDC.

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IMPLEMENTATION OF A NATIONAL ELECTRONIC REPORTING SYSTEM IN LITHUANIA

M Domeika (marius.domeika@medsci.uu.se)^{1,2}, G Kligys³, O Ivanauskiene³, J Mereckiene⁴, V Bakasenas⁵, B Morkunas⁶, D Berescianskis⁷, T Wahl⁸, K Stenqvist^{9,10}

1. Department of Medical Sciences, Uppsala University, Uppsala, Sweden
2. East Europe Committee of the Swedish Health Community, Stockholm, Sweden
3. Kaunas Public Health Center, Kaunas, Lithuania
4. Vilnius Public Health Center, Lithuania
5. The State Public Health Service (SPHS) under the Ministry of Health, Lithuania
6. Lithuanian Center for Communicable Diseases Prevention and Control, Lithuania
7. Computer technology company "Compidea", Vilnius, Lithuania
8. Department of Communicable Disease Control and Prevention, Stockholm County, Sweden
9. Hivprevention i Västra Götaland, Region Västra Götaland, Sweden
10. Department of Social Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden

Electronic reporting systems improve the quality and timeliness of the surveillance of communicable diseases. The aim of this paper is to present the process of the implementation and introduction of an electronic reporting system for the surveillance of communicable diseases in Lithuania. The project which started in 2002 was performed in collaboration between Lithuania and Sweden and was facilitated by the parallel process of adapting the surveillance system to European Union (EU) standards. The Lotus-based software, SmittAdm, was acquired from the Department of Communicable Diseases Control and Prevention of Stockholm County in Sweden and adopted for Lithuania, resulting in the Lithuanian software, ULISAS. A major advantage of this program for Lithuania was the possibility to work offline. The project was initiated in the two largest counties in Lithuania where ULISAS had been installed and put in use by January 2005. The introduction was gradual, the national level was connected to the system during late 2005, and all remaining counties were included during 2006 and 2007. The reporting system remains to be evaluated concerning timeliness and completeness of the surveillance. Further development is needed, for example the inclusion of all physicians and laboratories and an alert system for outbreaks. The introduction of this case-based, timely electronic reporting system in Lithuania allows better reporting of data to the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) compared to the former reporting system with paper-based, aggregated data.

Introduction

Well-functioning surveillance systems for communicable diseases are fundamental in providing information needed to take appropriate and timely measures. Studies from countries with electronic reporting systems show that such systems improve the quality and timeliness of the surveillance [1-4]. In addition, there is need for an integrated European surveillance system so that the epidemiology of communicable diseases can be compared between

countries and early warning systems can function in an international perspective. The present project was initiated in order to improve the Lithuanian system for the surveillance of communicable diseases which hitherto had been time consuming to administer and only paper-based, aggregated data had been reported to the national level. Duplication of data was also a problem since aggregated data was sent in parallel from both local and county level to the national centre. During the project period, Lithuania joined the European Union (EU). Consequently, the Lithuanian law on communicable diseases was adapted to the EU standards [5]. The main goal of this paper is to present the introduction process of the electronic surveillance system for communicable diseases ULISAS in Lithuania, a project that was performed with financial support and expertise from Sweden.

Materials and methods

Organisation of the surveillance of communicable diseases in Lithuania

Lithuania has 3.4 million inhabitants and is organised in ten counties, each with one Public Health Centre (PHC). Each county has one or more Territorial Public Health Centers (TPHC), altogether 36 in the country. The PHC has an overall responsibility for the surveillance of communicable disease within the county [6]. Notifiable diseases are reported from the PHC to the Lithuanian Centre for Communicable Diseases Prevention and Control (CCDPC) as shown in Figure 1.

Physicians from a total of 1,257 primary care centres, hospitals and polyclinics and 21 laboratories report notifiable diseases by post, fax or e-mail to the TPHC and the PHC within 72 hours according to the rules and regulations. In unusual situations, for example the occurrence of plague and yellow fever, notifications should be sent by post, fax or e-mail, within 12 hours. The clinical notifications contain full patient identity and a unique personal identification number which is issued to all Lithuanian residents.

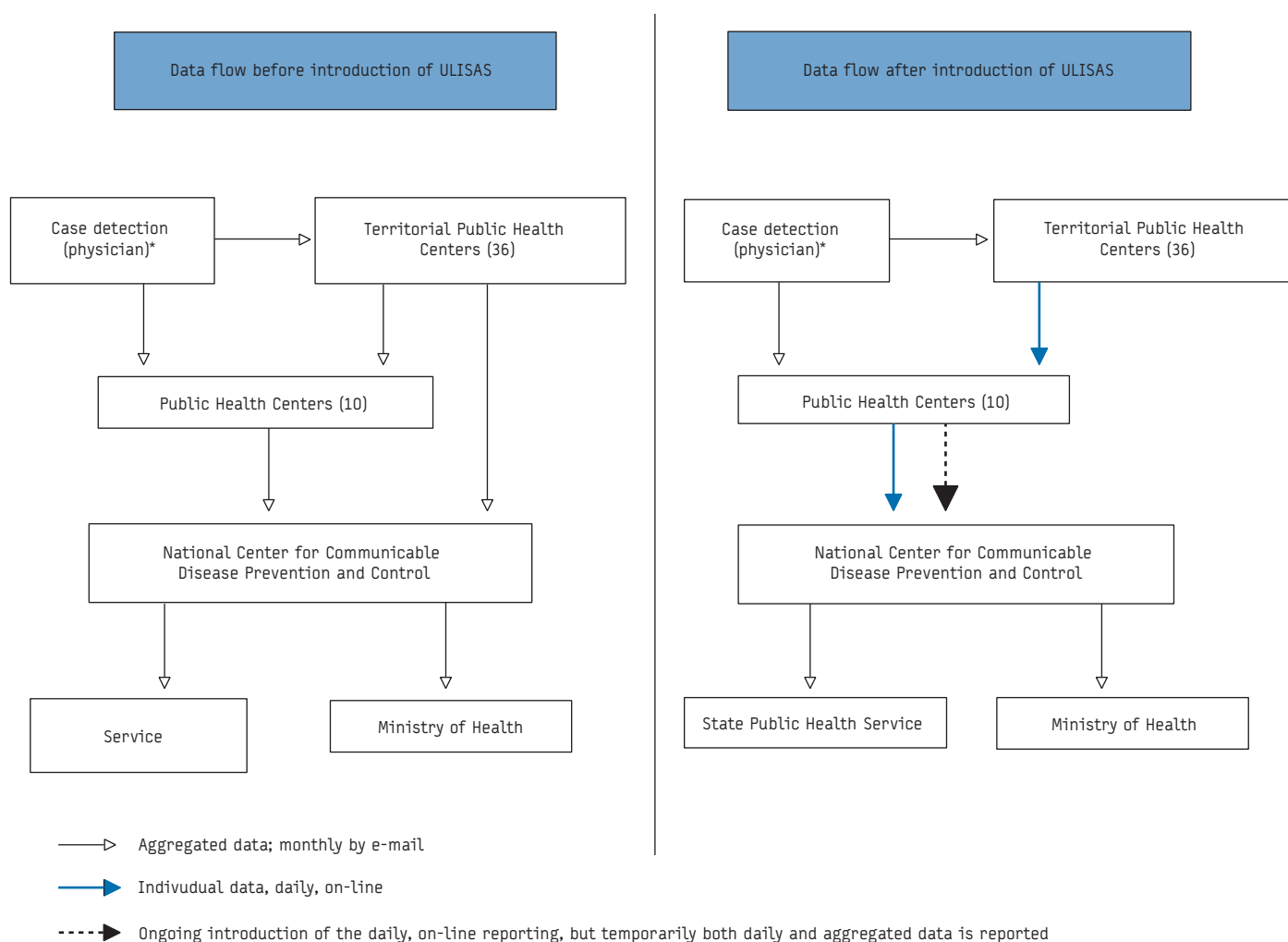
Exceptions are the sexually transmitted infections (STI) and cases of human immunodeficiency virus (HIV), which are reported with a specially designed code, so that the personal identity is not revealed. The number of clinical notifications amounts to about 55,000 per year in the whole country. The epidemiologic investigations of individual cases and outbreaks are performed by epidemiologists at the TPHC and the PHC and reported on standardised paper forms to the CCDPC. For STI and HIV, physicians perform the epidemiological investigation and report weekly to the TPHC and PHC. Prior to the development of the electronic reporting system, aggregated data on 82 notifiable diseases collected at the TPHC and the PHC had been summarised using a standard statistical form at the end of every month and sent to the CCDPC in paper format. In addition, aggregated data had been reported yearly to the CCDPC using 17 different statistical forms.

Organisation of the surveillance of communicable diseases in Sweden

Notifiable diseases are reported by physicians to the County Medical Officer (CMO) at the county level and to the Swedish Institute for Infectious Disease Control (Smittskyddsinstitutet, SMI) at the national level. The CMO has an overall responsibility for the surveillance in his or her county. A national electronic surveillance system, SmiNet-1, had been operational from 1997 and in use by 16 of 21 counties since the beginning of the 2000s [3]. With this system, notifications were mainly sent in paper format to the CMO and manually entered at the county level, with the exception of the infectious diseases clinics and laboratories which were connected to the electronic reporting system. After a technical revision of SmiNet-1 in 2001, a new web-based system, SmiNet-2, was developed and implemented in 2004 [1]. Parallel to this, the Department of Communicable Diseases Control and Prevention at the county of Stockholm developed a program for electronic reporting, SmittAdm, which has been in use from 1998. This

FIGURE 1

Data flow in the Lithuanian national reporting system of communicable diseases before and after the introduction of ULISAS electronic system



*Case data – notification by phone, fax, mail and e-mail according to the legal requirements

program supplemented SmiNet-1 with functions for administrative and judicial tasks which according to the Swedish Communicable Diseases Act are performed at the county level. SmittAdm and SmiNet-1, both being built in Lotus Notes, were easily connected. The staff at the county level used SmiNet-1 only for submitting notifications to the national level; data was then replicated to SmittAdm for further regional work and analysis. SmittAdm was also used by the second largest region, Västra Götaland, and three other counties.

Project organisation

The project was initiated in 2002 by the Swedish Institute for Infectious Disease Control (SMI) and the PHC in Kaunas with financial support from the East Europe Committee of the Swedish Health Care Community (SEEC).

The project manager (of Lithuanian origin, which facilitated communication) was based at SMI and a coordinating study group was formed in Lithuania consisting of epidemiologists from the national level and the counties of Kaunas and Vilnius, and an external IT specialist. This group defined the requirements for an electronic reporting system in Lithuania. Such a system should enable timely reporting of individual data to the county and national level, ascertain a uniform quality of notifications for the whole

country, and support the integration of laboratory and clinical notifications. Due to limited access to the internet the system had to allow working offline at the TPHC and the PHC. Since the project was not fully financed from the beginning, extra costs for staff were to be avoided. The study group was responsible for: 1) revising the surveillance procedures and the list of notifiable diseases according to the EU requirements, 2) creating adequate epidemiological forms for notifiable diseases, 3) studying the present Swedish electronic surveillance systems and participating in the process of developing and adapting the software for Lithuania, 4) establishing an action plan for the implementation of the system in the Lithuanian organisation, 5) assuring the provision of hardware and software for participating units, and 6) organising training for users at all levels.

Project sites

The overall goal was to include all counties and the national level in the project. The plan was to start the project at the PHC of Kaunas and Vilnius, counties with the largest populations in Lithuania. The authorities in Kaunas and Vilnius were motivated to introduce an electronic surveillance system; they identified its potential to reduce their work load and to improve not only the surveillance at the national, but also at the county level. The next target would be the national level, the CCDPC, followed by the remaining eight counties in Lithuania. The reason why this step by step approach had to be taken was that the resources were limited at the national level, not allowing the CCDPC to be involved from the start, and that the project at this point lacked financing for the whole country.

Results

Revision of notifiable diseases and notification forms

The number of diseases notifiable in Lithuania was revised and reduced from 82 to 76. The revisions were made in accordance with the Commission Decision No 2003/542/EC [7]. The lists of notifiable diseases and microorganisms were regulated by law by the Ministry of Health of the Republic of Lithuania in May 2004 and January 2005 respectively. New epidemiological forms were elaborated for nine groups of diseases and defined by the Director of the State Public Health Service under the Ministry of Health in June 2004 [9].

Selection of electronic reporting system and development of the software

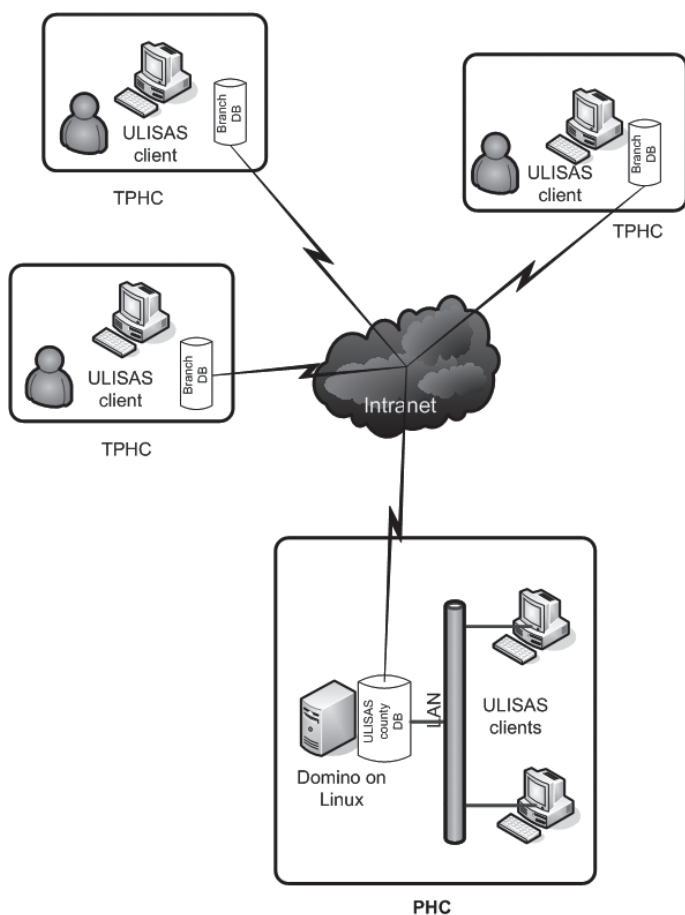
Since the Lithuanian authorities wanted to see the result at county level before a central server was to be established, it was important to focus on the needs at the PHC level. SmiNet-1 and SmittAdm were both suitable in the respect that they allowed working offline, which was necessary since the internet was not sufficiently available for the majority of the PHC and TPHC. An advantage of SmittAdm was that this program, contrary to SmiNet-1, allowed integration of patient records and notes on contact tracing and outbreaks, facilitating work at the county level. Thus SmittAdm was chosen as the model for the Lithuanian software; a contributing factor for the choice was that SmittAdm was easily and quickly accessible to buy from the county of Stockholm. At the time SmiNet-2 had not been implemented in Sweden yet and would not be suitable since it was web-based [1].

Software and hardware

In 2004, SmittAdm was acquired from the county of Stockholm and translated into Lithuanian. Subsequently, a new program, the System for Data Collection and Analysis of Communicable Diseases

FIGURE 2

**Electronic reporting system of communicable diseases
ULISAS in Lithuania, the county level**



(ULISAS), very similar to SmittAdm, was created in collaboration with an IT company, COMPIDEA. ULISAS uses the IBM Lotus Domino and Lotus Script and Java programming languages. The minimal requirement for ULISAS servers was any commercially available server with Pentium 2GHz, 2GB RAM, 2 HDD and 36 GB each, running Notes Domino 6.5 and higher (currently 8.0.2) on Linux or Windows servers and for workstations simple commercially available Windows computers with Lotus Notes 6.5 and higher. At the national level the requirements for the DB2 Lotus Domino server was 3 GHz, 4GB RAM, 300GB HDD.

Databases and architecture of the system

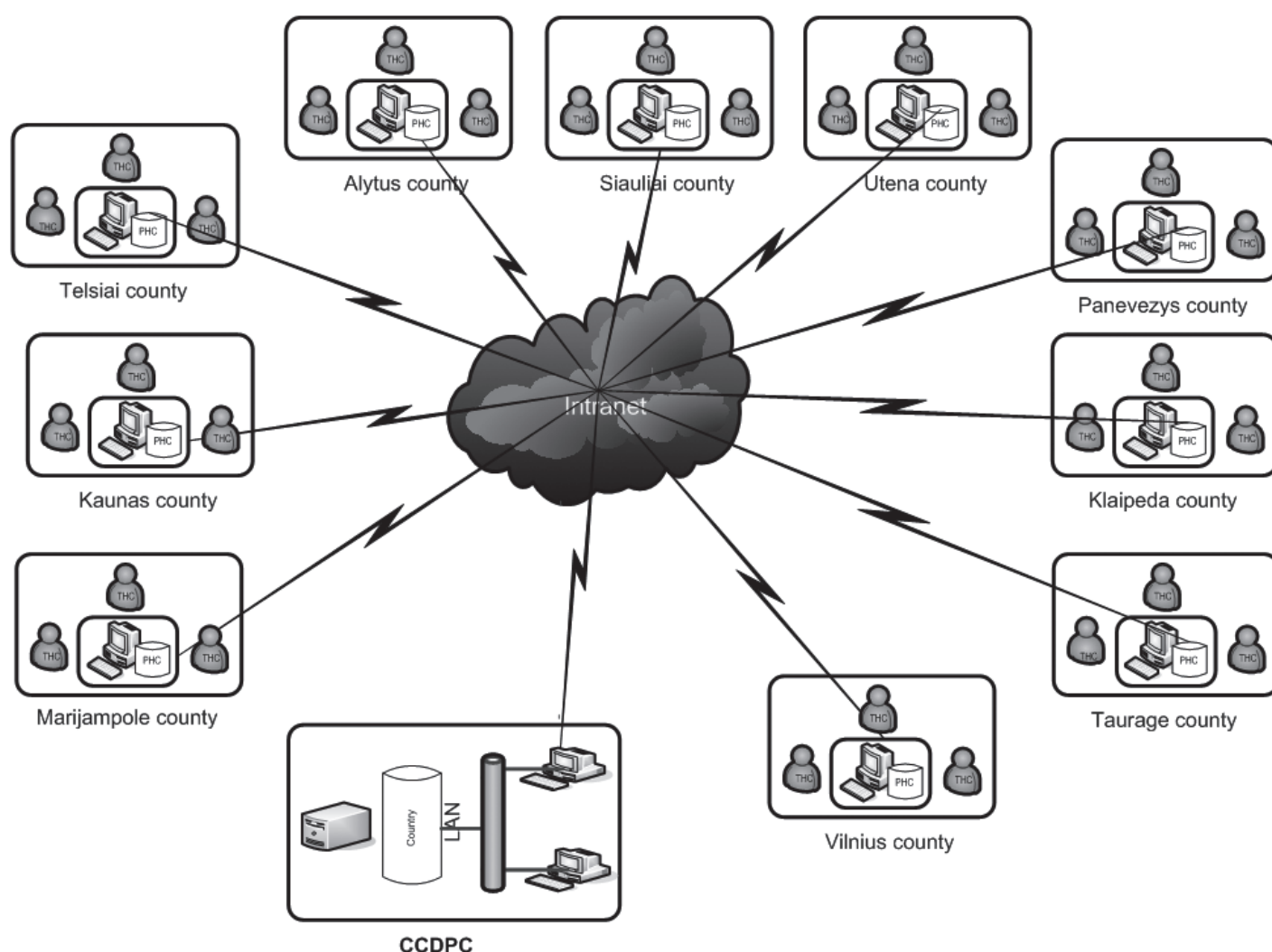
The ULISAS database is built in Lotus Notes. The staff from COMPIDEA monitors all activities and provides continuous support to users at the TPHC and PHC. The dataflow of the electronic reporting system is shown in Figure 1. The electronic reporting system with workstations and servers at the county and the national levels is shown in Figures 2 and 3.

The TPHC: There is usually one Lotus Notes client per TPHC. Data is regularly exchanged between the PHC and the TPHC by replication so that the TPHC client can work offline if necessary. If more data entry places are needed, it is possible to install extra, standalone Lotus Notes clients which also replicate to the PHC database. The main three physical .nfs files contain patient records, notifications and staff activity records. The number of fields with defined entry values varies between 33 and 54 between the different records, seven fields are obligatory. Data quality is assured by validation during data entry against a set of validity rules. Further notes concerning a patient or an investigation can be entered in commentary fields. All case records related to one individual over time can be linked to one another. Data is transferred to the county server automatically every hour or manually by the operator at any time.

The PHC: Several Lotus Notes clients or work units are included in a LAN with one Lotus Domino server. The county server keeps records from all TPHC clients in the county, backup and a

FIGURE 3

Electronic reporting system of communicable diseases ULISAS in Lithuania, the national level



historical archive. Backup data can be transferred to an external USB HDD 300GB, allowing space to be maintained at the server. Data is regularly exchanged between the PHC and the CCDPC by replication, and when the internet is inaccessible or slow, the PHC server repeats replication in the following communication interval.

Laboratories: So far only one laboratory in the county of Kaunas has joined the system. Data is entered manually and the Lotus Notes workstation replicates data to the PHC and then to the CCDPC. It is possible to link a laboratory notification to the corresponding clinical notification.

The CCDPC: Several work units in the LAN at the national level are connected to a Lotus Domino server. Data from the databases in the ten counties is replicated to the central database; the CCDPC has an additional relational database based on DB2 version 8.2 in order to integrate the databases from each county. Defined fields from the records are exported to DB2 for further statistical analysis in SPSS. All data is archived in the central server.

Present organisation of the surveillance of communicable diseases in Lithuania

Case-based data is reported continuously via the electronic reporting system from the TPHC to the PHC and further to the CCDPC as demonstrated in Figure 1. Since the national level has not yet developed a system for analysis of the electronic reports, the old and new reporting systems still work in parallel. However, a change has been made so that the TPHC submits reports to the PHC only, which means that duplicates are avoided.

Implementation process

During the preparatory phase, 2002-2004, the main task of the project leader was to mediate collaboration between specialists from Kaunas PHC, the SMI and the Department of Communicable Diseases Control and Prevention, Stockholm County in Sweden. It was also important to stimulate a dialogue between the pioneering counties and the national Lithuanian authorities concerning the full implementation of ULISAS. By January 2005, ULISAS had been implemented in the counties of Kaunas and Vilnius with two servers and nineteen workstations at the PHC and the TPHC. The IT company trained the senior county epidemiologists who thereafter trained the remaining staff. During 2005, export functions for statistical analysis were developed. Later during 2005, the central server at the national level was installed and connected to the existing servers at the county levels. By 2006, a further six counties with 35 workstations were connected to the reporting system. The last two counties joined the system in 2007 when a total of 70 workstations were functioning. Personnel were trained as soon as their local working stations were installed and all throughout the project. Contracts for long term distance maintenance of the software and the hardware were signed. During 2009, servers are to be installed at the national level allowing all local servers to be connected into one national system.

Further financial and political support

In April 2004, the Director of the State Public Health Care Service under the Ministry of Health issued an order to initiate "The Study for the Implementation of the Computerised Program for Epidemiological Surveillance of Communicable Diseases at Kaunas and Vilnius Public Health Centres" [9]. This resulted in the provision of hardware for the CCDPC and a further six counties. The last two counties were included with financial support from the Swedish- Lithuanian project. The full integration of the reporting

system with the national level will be supported by a Lithuanian-Norwegian project during 2009. The fact that costs for staff at the TPHC and PHC levels was reduced facilitated the financing of the project. This can be exemplified by the county of Kaunas where the implementation of the new system with centralised organisation of the work process resulted in a reduction of costs for statisticians by 75 percent and for IT support by 85 percent. Staff members at the TPHC and the PHC were made redundant. The IT company use remote control in combination with hotline support, server administration and back-ups are managed centrally. The total costs for the development of the electronic reporting system is estimated to 60,000 EURO, the cost for hardware not being included since existing hardware was used. The yearly maintenance and support of the system amount to 12,000-15,000 EURO.

Data output

The national analysis is still based on monthly aggregated data from the ten counties and the reports to the ECDC the WHO have not yet been changed. The PHC of Kaunas developed a website during the project where statistics in the form of tables, graphs and maps were presented [10]. A corresponding website will be accessible at the CCDPC after the full integration of the national level during 2009.

Data security

Each individual user at the TPHC, PHC and CCDPC is given a Lotus Notes ID file protected by a password. Users have varying degree of access rights to the system depending on his or her function. All data in the database is encrypted and all data is transferred through encrypted channels. A governmental agency provides internet access for the system. A control system for further quality assurance is developed by the IT company during 2008-2009.

Discussion

In this paper we outline the structure and implementation of ULISAS, a new comprehensive electronic reporting system for the surveillance of communicable diseases in Lithuania. The process, which started in 2000, has led to a change from paper-based aggregated monthly data at the county and national level to a timely case-based electronic reporting system. Parallel to this, the number of notifiable diseases was standardised according to the EU case definitions. The initiative and establishment of ULISAS was a joint venture between Lithuania and Sweden, the communication between the two counties and Sweden and financing through the SEEC being of vital importance [10]. Political engagement and further financial support was facilitated by the new Lithuanian legislation in 2001 on communicable diseases and the EU directives concerning notifiable communicable diseases [5].

The organisation of the surveillance of communicable diseases in Lithuania and Sweden are similar, the main difference is the existence in Lithuania, but not in Sweden, of local public health centres, TPHC. Epidemiologists at the TPHC perform epidemiological investigations on patients who have been reported with notifiable communicable diseases by the physicians [6,8]. For diseases belonging to the STI group, the same as in Sweden, a physician is responsible for the epidemiological investigation [12]. The main objective of the planned cooperation between the two countries was that Lithuania should take advantage of the Swedish experiences concerning electronic reporting systems. At the start of the project, Sweden had a national electronic reporting system in use, SmiNet-1, built in Lotus Notes. Since SmiNet-1

did not have functions for administrative notes and records on patients and contact tracing a complementary program, SmittAdm, had been developed by the county of Stockholm. The Lithuanian project group chose SmittAdm as the prototype for the Lithuanian reporting system because it met the requirements at both county and national level, most importantly the possibility to work offline. A disadvantage with the choice of a Lotus Notes based program lay in creating export functions for statistical analysis and reporting, i.e. tasks that are not primarily performed with Lotus Notes. The new Swedish electronic reporting system, SmiNet-2, was under development during the study period but was not an alternative for Lithuania since it was web-based.

The implementation of the system in Lithuania started in 2004 and by 2007 the whole country had been covered with a total of 70 workstations and trained staff at the county level. The bottom-up policy with the work process starting at the county level was crucial for the completion of the project. The two counties with the largest populations initiated the project from the Lithuanian side and were able to develop the program from the requirements at the county level. The staff in these counties with the heaviest workload was motivated to change to an electronic reporting system. In addition, they were able to initiate the present project since they had access to hardware through previous state-supported programs. The national level had not been involved until late 2005 after the system had been established in the two pilot counties. This was in accordance with the initial plan and due to the fact that resources were lacking at the national level, and that it had to be proven that the system worked before the national level was connected. Financing was a risk factor in this project, since resources were limited and financial support was granted step by step. This explains why the national level has still not been fully integrated in the project, still lacking instruments for the analysis and data output. For comparison, the Swedish reporting system SmiNet-1, which was in use between 1997 and 2004, was not implemented in all counties [3]. This may be due to the fact that the Swedish organisation is decentralised and that some counties had developed their own tailor-made systems.

ULISAS needs to be further developed. Physician and laboratory notifications from the whole country should join the system in the future and algorithms for the detection of outbreaks should be elaborated. When access to the internet is stable at all levels a web application may be developed so that ULISAS can be extended to private clinics and physicians. The future work and development of ULISAS will be supported by the National Public Health Strategy Implementation Plan in 2006- 2013 [13].

The impact of ULISAS on the surveillance of communicable diseases in Lithuania remains to be evaluated. When the national level has joined to full extent it will be possible to leave the old system and to analyse the data from the new case-based electronic reporting system, to present data on the national website and to adapt better to the European surveillance system administered by ECDC and reporting of data to the WHO. According to the ECDC there is a wide variability in the design and effectiveness of the surveillance systems between countries [14]. With ULISAS, Lithuania has developed an important tool for further adaption to the EU directives.

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