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The European Centre for Disease Prevention and Control: 10 years of protecting health in Europe

Ten articles, representing a year each, mark the organisation's evolution and show its leadership and influence in the areas of its mandate.

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From SARS to Ebola – 10 years of disease prevention and control at ECDC

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A decade ago, the European Centre for Disease Prevention and Control (ECDC) appeared as a new player among international health organisations, with the mandate 'to identify, assess and communicate current and emerging threats to human health from communicable diseases' in the European Union (EU) [1]. As part of the ECDC 10-year anniversary celebrations, *Eurosurveillance* compiled a print issue with a selection of articles published over this period in the journal. The 10 articles, representing a year each, mark the organisation's evolution and show its leadership and influence in the areas of its mandate.

The first five years

During 2005 to 2010, the focus was on developing the Centre's core functions. ECDC officially started its operations on 20 May 2005 and in the autumn of that year, wild birds were found positive for influenza A(H5N1) virus in Croatia, Romania, and Turkey. The then newly established ECDC was asked to answer questions from public health experts and policymakers in EU Member States and the European Commission. Without having the current systems and processes, ECDC experts had to 'build the plane while flying'. An editorial by Nicoll in the first year shows that ECDC was, from the very start, able to strategically shape the activities needed to improve the level of preparedness – for influenza and in general – in Europe [2]. Even retrospectively and in the light of the 2009 influenza pandemic, the answers given to the questions posed in the editorial published in 2005 still hold. Some of the issues raised have been addressed in the meantime by the Commission Decision 1082/2013 [3].

One of ECDC's key tasks is to identify threats from current or emerging infectious diseases. In its second year of operations, ECDC presented a proposal to complement the traditional indicator-based surveillance, using epidemic intelligence as an early detection and warning system [4]. Such epidemic intelligence would take into account changes in the information sector, and pick up relevant information from sources such as traditional and social media and others, and analyse it. The proposed framework became the basis for rapid risk assessments, one of the cornerstones of the Centre's work today and one of its most appreciated outputs.

Another ECDC core function is capacity building. The European Programme for Intervention Epidemiology Training (EPIET) was transferred to ECDC in 2007 and the article by Varela and Coulombier describes the efforts to define and agree on standards for core competencies required for epidemiologists, which still serve as foundation for this important ongoing task [5]. A short-term vision for surveillance of infectious diseases in the EU was presented in October 2005 to ECDC's governing bodies and in 2008, the single EU surveillance database, The European Surveillance System (TESSy), was successfully established. EU-wide supranational surveillance is at the core of ECDC's mandate and the start of TESSy was accompanied by a long-term strategy with challenging goals, with the aim of adding value, on top of national surveillance systems [6]. Even if not all goals have been achieved today, it is of note that TESSy data are increasingly used, also by non-ECDC scientists as basis for their analyses indicated by the increasing numbers of request to access TESSy data. This demonstrates the added value and that TESSy has become a point of reference for EU data on infectious diseases.

The emergence of a new disease in 2003, severe acute respiratory syndrome (SARS), together with a perceived pandemic threat, sparked the establishment of ECDC. The 2009 influenza pandemic could thus be considered its first 'real' test. In June 2009, early in the pandemic, an article was published with contributions from a large group of collaborators from all EU countries, demonstrating the capability of ECDC to rapidly collate and disseminate information necessary for public health action during a public health event [7]. The article specifically pointed out two important features of the pandemic that were confirmed in several publications thereafter: the relatively mild clinical course and children and adolescents as the main groups affected by and involved in indigenous transmission.

After the pandemic: 2010–14

A new era began in 2010, with a focus on further developing disease-specific functions. Antimicrobial resistance (AMR) is one of the most important infectious disease threats today and most likely also in the future. It has increasingly become a crucial aspect of ECDC's work. The article by the ECDC Antimicrobial Resistance and Healthcare-Associated Infections Programme (ARHAI) provides an overview of the initiatives that ECDC undertook from an early stage to improve the understanding of the risks associated with AMR and to support the response [8]. It also demonstrates the priority given to raising awareness about the relevant health threats.

Another example of how ECDC fulfils its mandate to strengthen prevention and control of cross-border threats in Europe is the guidance described in an article by Leitmeyer [9]. Since its finalisation, the European risk assessment guidance for infectious diseases transmitted on aircraft (RAGIDA) has become a de facto reference for many public health authorities in Europe.

Aside from AMR, healthcare-associated infections are a health threat posing a major burden on individual patients and health systems alike. Prior to a pilot point prevalence survey (PPS) of healthcare-associated infections and antimicrobial use survey, ECDC and a large group of experts from all EU countries developed a standardised methodology, training materials, a train-the-trainer course for national PPS coordinating staff, free-of-charge hospital software for data collection and a validation methodology. The article by Zarb et al. describes one of the most complex epidemiological activities ECDC has coordinated: the pilot survey included nearly 20,000 patients from 66 hospitals in 23 European countries [10]. National PPS coordinating staff trained an estimated 2,800 healthcare workers from 1,200 hospitals across Europe to implement the standardised PPS methodology. Besides being impressive on a technical level, it also provided the first (relatively) comparable picture of prevalence of a fast-growing public health concern. The initiative is another important marker of ECDC's role in identifying and communicating serious threats to health.

Evidence-based approaches aim at improving the quality of scientific findings as a basis for decision-making. The article selected for 2013 reflects the growing demand for evidence-based methods (EBM) in some of the Centre's core functions, where the currently available tools do not provide good-enough answers. Rapid risk assessments are usually developed under time constraints and yet need to form the basis of public health decisions. ECDC and an interdisciplinary group of experts developed a conceptual framework of how to address the current gaps [11] and support public health experts in the future to produce rapid assessments using the best available evidence, even when the evidence may still be limited.

Launched as an ECDC initiative in 2008, the European Antibiotic Awareness Day, marked on 18 November each year, is another example of ECDC activities in the area of communication. It has grown to become a European-wide coordinated health campaign, joined by many countries beyond the EU. Several public health organisations (in the United States and Canada, and the World Health Organization) have aligned their respective campaigns on the same day [12].

In addition to the disease programmes on influenza and the ARHAI, programmes on other disease groups such as emerging and vector-borne diseases, food- and waterborne diseases, HIV, sexually transmitted infections and viral hepatitis, tuberculosis, vaccine-preventable diseases and the microbiology team were established; some of them took up their work already in the early days of ECDC. A list with scientific peer-reviewed publications from 2005 onwards is available on the ECDC website and illustrates the work done by the programmes and ECDC experts and expert groups [13].

The future

The selected articles show that ECDC tackled from its very first year cross-border health threats in close collaboration with a network of experts across the EU and beyond. The expertise of these networks is one pillar of ECDC as most, if not all, of ECDC's work is based on the collaboration of numerous colleagues in the countries' national public health institutes, research and other institutions. I would like to express, on behalf of ECDC, my sincere gratitude for their dedication and constructive input during all these years, which have contributed to shaping ECDC.

As the emergence of the Middle East respiratory syndrome coronavirus (MERS-CoV) and the Ebola outbreak in West Africa have recently demonstrated, some of the issues described in the articles are still relevant today, others might emerge in the future, indicating both the complexity and dynamics of infectious diseases. ECDC will continue to deliver independent outputs of high scientific quality and will endeavour to further increase their usefulness and value for decision makers. In this and in line with the recently published recommendations from the second external ECDC evaluation, ECDC will work closely with the countries and the European Commission to support them in facing threats to human health from current or emerging infectious diseases.

Conflict of interest

None declared.

Authors' contributions

Andrea Ammon wrote the editorial and approved the final version before publication.

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Avian and pandemic influenza–Five questions for 2006

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In January this year it was observed that 2005 was going to be the Year of the Rooster in the Chinese calendar, and that perhaps was an ill omen for bird (avian) and pandemic influenza. Certainly, influenza was the infection that then dominated the popular press in 2005, and so in a certain way this was a very 'good' year for influenza and those who study it. The infection has been getting the attention it deserves as a human threat.

In this edition of Eurosurveillance there is an important report of one highly pathogenic avian influenza virus (HPAI type A/H7N7) that affected humans during the 2003 poultry epidemic in the Netherlands and Belgium [1]. The human infections were mostly among those working to control the infection, and their families. In response, ECDC, together with an expert group, has produced interim occupational guidance for Europe that will reduce the risk [2]. However, this experience also emphasises the variability in the influenza virus families. While H7N7 was quite infectious for humans and showed measurable person to person transmission, another better known avian influenza, A/H5N1, is quite different, as it currently seems to infect humans only rarely and human-to-human transmission seems to be even rarer [3].

The year's end is traditionally a time for reflection, and I would like to propose five fundamental questions about pandemic risk for the start of 2006.

Has the risk from avian and pandemic influenza been exaggerated?

The answer to this question must be both 'Yes' and 'No'. In the autumn of 2005, when H5N1 appeared on the borders of Europe in Romania, Turkey and Croatia, there was suddenly massive public interest and gross confusion of three separate, although related, influenza types: Seasonal Influenza, Avian Influenza and Pandemic Influenza. [see ECDC website http://www.ecdc.europa.eu/influenza/factsheet_influenza.php for definitions] Even the serious media's presentations of the situation gave the strong impression that a human influenza pandemic was about to start, and that the pandemic virus would probably be brought to Europe by migrating birds. If there is no pandemic in 2006, members of the lay public may reasonably feel that some authorities have been 'crying wolf'. Although official statements have been mostly measured and accurate, the reporting of those statements tended to exaggerate the current threat from H5N1. The reality is thus far in its evolution, the family of H5N1 viruses available for study are avian viruses that are poorly adapted to humans, for whom they are not very infectious, but highly pathogenic in those few humans that they do infect [4,5]. That low risk (of becoming infected) - high risk (of severe disease if you are infected) message is a difficult one for risk communicators to convey. Occasionally, H5N1 transmits on from one human to another, but none of the viruses at present seem to represent a pandemic strain, as their reproductive rate in humans (Ro) is far below unity [3,6].

That is not to say that the H5N1 viruses are without social impact. In Thailand they have prejudiced that country's economically important export trade in poultry products to Europe and Japan. For societies like China and Vietnam where poultry are key to food security, the threat to the rural communities is considerably greater [7]. It is not surprising that both China and Vietnam are turning to the potentially risky measure of poultry immunisation as a measure to protect their huge flocks. This is a massive task. It is estimated that at any moment China's human population of 1.3 billion keeps around four billion domestic birds (point prevalence) and that each year they require fourteen billion domestic birds (period prevalence).

The main threat, however, is of a human pandemic. Any pandemic would represent a major risk to human health and a threat to social functioning worldwide. The two lesser pandemics of the 20th century (1957 and 1968) are each estimated to have killed between one and four million people worldwide. A pandemic on the scale of 1918-1919 (at least 20 million deaths) would be catastrophic [8]. Arguably, the interconnected industrialised world of today is more vulnerable to a pandemic than it was even forty years ago. Not only is there much more international travel to

spread infection, but societies are more dependent for daily existence on goods and services that are produced elsewhere. Efficient 'just in time' stockkeeping systems, e.g. for food, will be vulnerable to the sudden mass illness in production and distribution staff that would take place in a pandemic. It is estimated that for short periods at the height of a pandemic up to 20% of working adults might be unavailable for work, because they are ill with influenza, or caring for others who are ill, or simply out of fear of infection. Fortunately, these periods of intense illness will not occur everywhere at the same time, but the disruption could nevertheless be considerable.

Will the next pandemic be due to H5N1?

We do not know. Pandemics occur through the emergence of a new strain of influenza virus which can infect and is pathogenic to humans, to which there is little pre-existing immunity and which can transmit readily from person to person. This is thought to happen by one of two mechanisms. Either through two pre-existing influenza virus types exchanging genetic material (recombination) or spontaneous genetic shift (mutation) from a single pre-existing influenza strain. Could H5N1 do either? It is certainly a candidate for a pandemic strain, as it can infect humans and is highly pathogenic. Some have argued that it only needs to make the final step of efficient person to person transmission, and WHO has set its global scale at Pandemic Alert Phase 3, the last phase before efficient human-to-human transmission. Others, however, consider that the next pandemic is equally if not more likely to come from a low pathogenicity avian influenza, such as H9N2 [5]. None of the three pandemics of the 20th century were based on a H5 strain, and H5N1 has been around at least since 1996 without a pandemic having resulted. It is also relatively uninfectious for humans, unlike the H7N7 strain observed by De Ry et al [1]. At the same time, H5N1 has spread massively, with the result that there are outbreaks in poultry in many East and South East Asian countries, including the huge bird populations of China. Although recombination involving H5N1 has not yet been detected, the possibility of it happening must have increased. H5N1 is not a uniform strain, but rather a large and complex family of viruses, and one of these may eventually mix and exchange genetic material with a transmissible human influenza [9]. However further risk assessments to determine whether or not H5N1 will cause a pandemic are of less value than making preparations for a pandemic due to H5N1 or any other influenza virus.

How bad will the pandemic be and what will be its characteristics?

Again, we do not know. Pandemics are not standard. The three 20th century pandemics varied not only in their driving viruses and scale, but also in their characteristics. For example, the 1918-1919 pandemics affected young adults in particular, while the later epidemics more often affected the elderly. We cannot assume that the next pandemic will be driven by transmission in particular groups, and data that can only be derived during the actual pandemic must guide interventions. It could be that workplace transmission will be crucial or that transmission among school-age or younger children will predominate. When a pandemic happens, the two most important investigations will be isolating the virus (to develop tests and the pandemic vaccine) and carrying out early quick, focused epidemiological studies at the sites of first outbreaks, both in Europe and beyond (to determine basic parameters such as mode of transmission, age-specific attack rates, and case-fatality rates, to guide countermeasures) The analogy with the evidence-based approach to controlling SARS is clear [10].

What role will antivirals play during a pandemic and how big a stockpile should countries have?

There is a danger that the availability of antivirals (especially oseltamivir) dominates thinking and preparations for a pandemic [11]. A detailed and rational approach to the use of antivirals in a pandemic has yet to be determined. Hospital doctors will, quite reasonably, expect to have available antivirals to treat those requiring hospitalisation, although it will be impossible to know ahead of time whether they will be effective at later stages in a patient's illness. Some countries are planning to have national stockpiles. However, simply having a stockpile is not enough, and if one European country has a stockpile ten times larger than its neighbour, it cannot be therefore judged to be ten times better prepared. Since in order to be effective in treatment of influenza, antivirals must be delivered within 48 if not 12 hours of symptom onset, it can be seen that mass delivery to populations will be a major issue. A stockpile without a rapid delivery system will provide little protection. Some have proposed that there be a European Union stockpile of antivirals. A modest European stockpile could for example assist in protecting workers during poultry outbreaks close to Europe[1,2]. It would also be an asset in the unlikely event that the next pandemic started in or near Europe, so that WHO's stamping out tactic could at least be attempted, supposing the existence of a practical plan to do so [12]. However, rapid development and production of a pandemic vaccine will probably be more important for the second wave, with the more distant hope of more cross-protective vaccines that would protect against pandemic first waves (so-called universal vaccines) [13]. Equally important and more immediately accessible will be the simple public health measures (early self-isolation of those with symptoms, handwashing, respiratory hygiene, etc.) that are already available, and will save lives [14].

Is Europe prepared for a pandemic?

Not as prepared as it could or should be. Six national assessments have been undertaken by countries using a standard assessment tool and working with teams from ECDC, the European Commission and WHO European Region. These assessments (which will

continue in 2006) found that while all six countries were preparing rapidly, all also had considerable way yet to go. Major issues remain to be addressed, notably the need for preparations to extend outside the health sector alone and for plans to be made more operational [15].

In conclusion, the threat from a pandemic has not been exaggerated. It could happen in 2006 from H5N1, or, more likely, in the future, and with another strain. However, in 2005 most European authorities and politicians started to give the risks the serious attention they deserve, and to invest the necessary resources to develop countermeasures. It is to be hoped that as the media interest inevitably declines, those in authority will sustain the investment and the levels of preparatory activity. Certainly, the pandemic risk will not decline.

* Angus Nicoll was a Seconded National Expert at ECDC where he coordinated its influenza activity.

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Epidemic intelligence: a new framework for strengthening disease surveillance in Europe

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In a rapidly changing environment, national institutions in charge of health security can no longer rely only on traditional disease reporting mechanisms that are not designed to recognise emergence of new hazards. Epidemic intelligence provides a conceptual framework within which countries may adapt their public health surveillance system to meet new challenges.

Epidemic intelligence (EI) encompasses all activities related to early identification of potential health hazards, their verification, assessment and investigation in order to recommend public health control measures. EI integrates both an indicator-based and an event-based component. 'Indicator-based component' refers to structured data collected through routine surveillance systems. 'Event-based component' refers to unstructured data gathered from sources of intelligence of any nature.

All EU member states have long-established disease surveillance systems that provide proper indicator-based surveillance. For most countries, the challenge lies now in developing and structuring the event-based component of EI within national institution in charge of public health surveillance.

In May 2006, the European Union member states committed to comply with provisions of the revised International Health Regulations (IHR(2005)) considered relevant to the risk posed by avian and potential human pandemic influenza. This provides for the European Centre for Disease Prevention and Control (ECDC) with an opportunity to guide member states in developing and/or strengthening their national EI , in addition to the ECDC's task of developing an EI system for the EU.

Justification

Population movements, behavioural changes, food production and many other factors linked to globalisation and economic development are responsible for the continuous emergence of infectious hazards [1]. Diseases such as SARS or avian influenza, not to mention deliberate release of biological agents, represent new challenges for outbreak alert and response in Europe and elsewhere.

Modern technologies, mainly related to development of the internet, are rapidly changing the way we access health information. Online media, scientific forums and direct electronic communication now allow us to shortcut traditional reporting mechanisms that travel through the various levels of public health administration [2]. Health authorities are no longer in full control of an environment that puts journalists, politicians and the general public in direct contact with raw data.

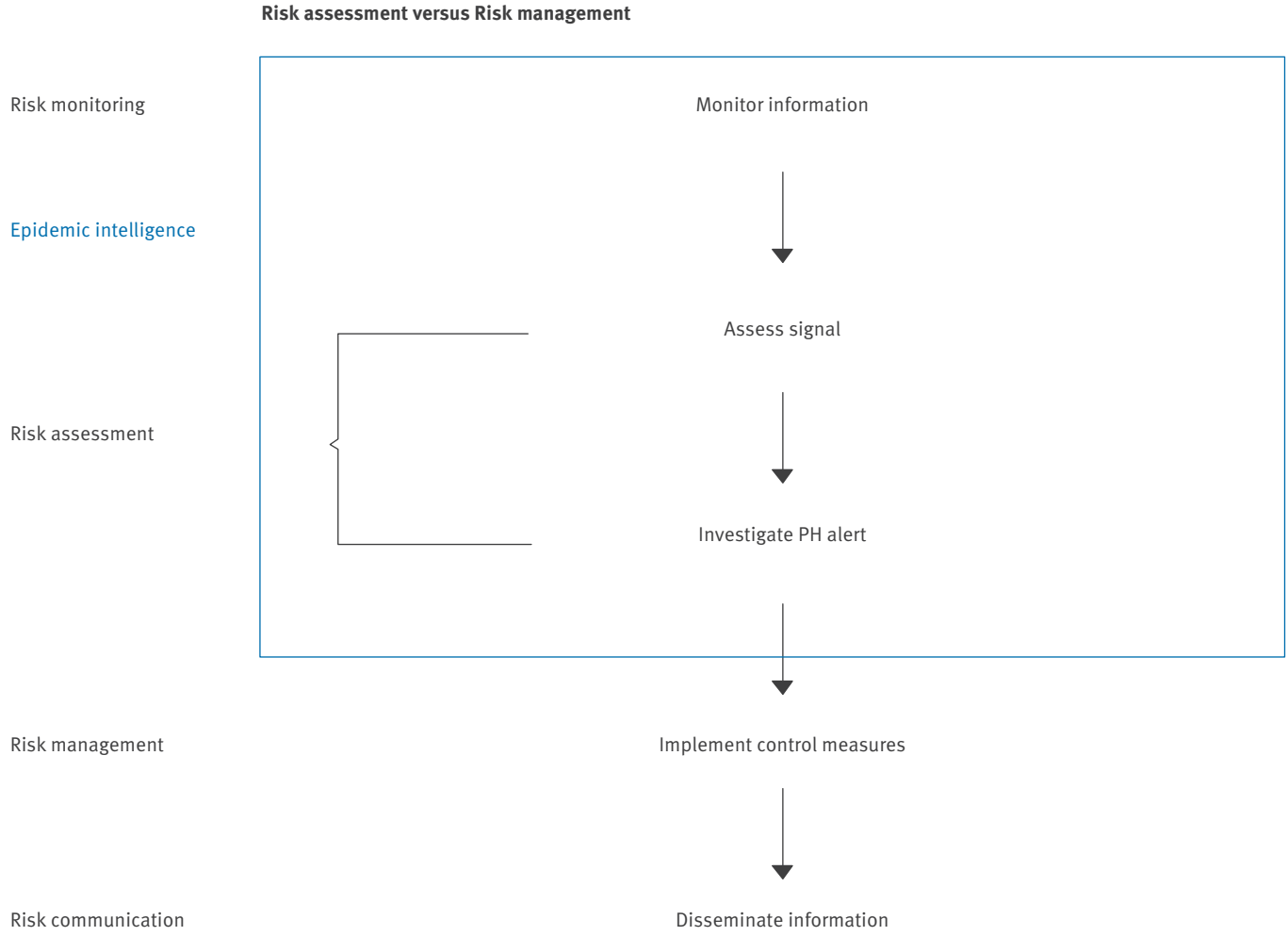
These phenomena contributed to the revision of the International Health Regulations (IHR(2005)) approved during the 2005 World Health Assembly [3]. Member states of the World Health Organization (WHO) will soon be legally bound to notify both case on a preset list of diseases and all 'public health events of international concern'.

In such a new and rapidly changing environment, national institutions in charge of health security can no longer rely only on traditional disease reporting mechanisms such as mandatory notification of diseases. While these systems can ensure appropriate public health response to identified risks, they cannot recognise the emergence of new threats such as SARS, human cases of avian influenza or potential bioterrorist-initiated outbreaks. In order to overcome the limitations of traditional surveillance for the detection of previously unknown threats, new approaches have been developed, including the monitoring of syndromes, death rates, health services admissions or drug prescriptions [4]. These new approaches represent an attempt to enhance the performance of traditional surveillance system.

At the same time, the media and other informal sources of information are increasingly recognised as valuable

Figure 1

Functions of early warning and response related to epidemic intelligence



sources of public health alerts. Epidemic intelligence provides a conceptual framework into which countries may complete their public health surveillance system to meet new challenges [5]. This approach represents a new paradigm aiming at complementing traditional surveillance systems.

In January 2006, the European Centre for Disease Prevention and Control (ECDC) convened a meeting in Stockholm with representatives from the 25 EU member states to agree on the role of EI in Europe [6]. Basic terminology and methods framework were agreed upon and further developed within a smaller working group. We present here the state of this project as of October 2006.

Definition and principles

Epidemic intelligence (EI) encompasses all activities related to the early identification of potential health hazards that may represent a risk to health, and their verification, assessment and investigation so that appropriate public health control measures can be recommended. The scope of EI includes risk monitoring and risk assessment and does not include risk management [Figure 1]

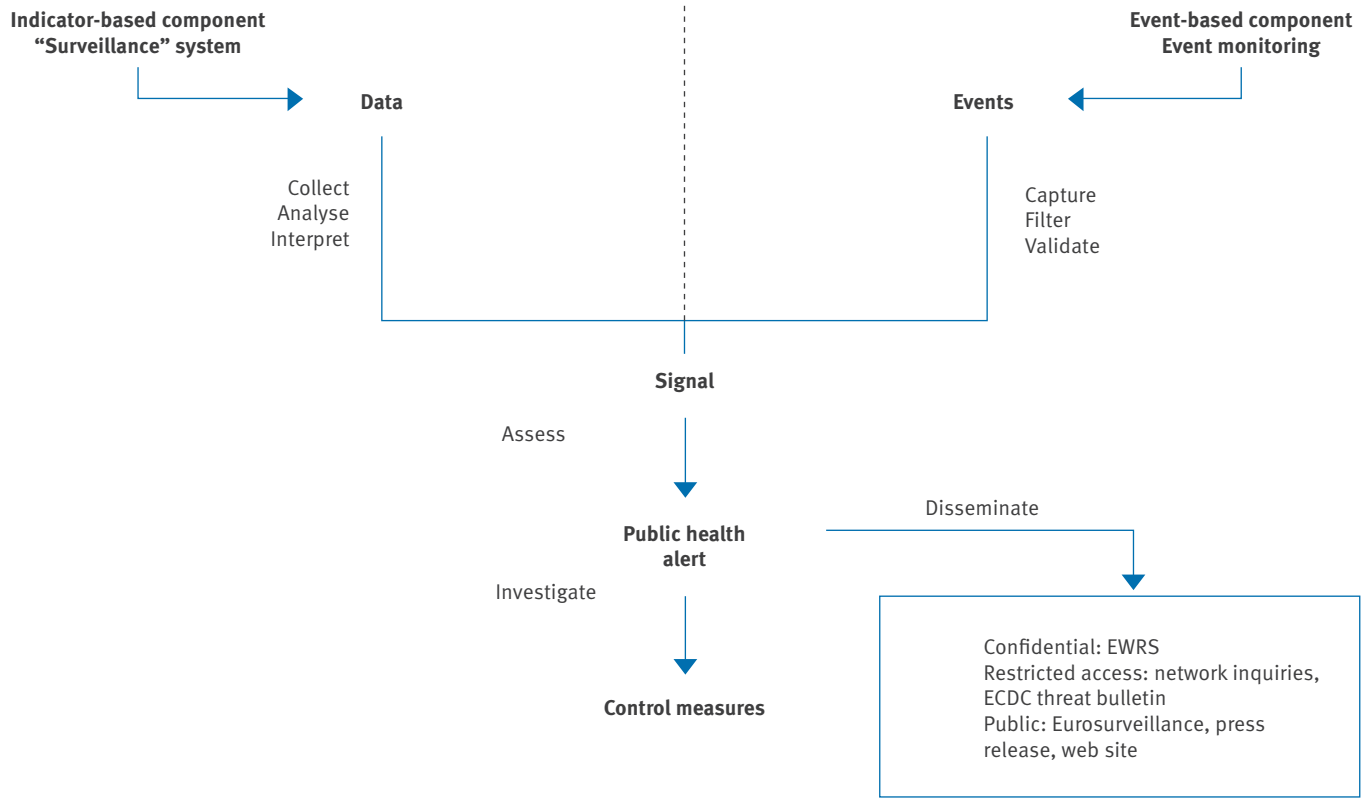
EI integrates indicator-based and event-based components. 'Indicator-based component' refers to structured data collected through routine surveillance systems. 'Event-based component' refers to unstructured data gathered from sources of intelligence of any nature. As a basic principle of EI, both components are given equal attention and processed in the same way, since a signal leading to a public health alert can originate from either one [Figure 2].

Epidemic intelligence framework

The EI framework is made up of five standard steps. It applies to any situation considered from any level of the public health system. Within a single situation (for example, an outbreak), these different steps may be covered several times as an iterative process allowing new developments to be integrated, and progressively improving the decision making process. There are two ways of entering the framework, corresponding to indicator-based and event-based components of EI, respectively.

Figure 2

Epidemic intelligence framework



EWRS: Early warning response system

The first step is data collection (indicator-based component) and the detection/capture of events (event-based component). Data collection refers to quantitative indicators (number of cases, rates, etc.) routinely obtained from established surveillance systems [Table 1]. Capture of events potentially encompasses a much broader scope, as shown in Table 2.

As a consequence of gathering large amount of information from a variety of different sources, EI requires strong filter and validation capacities to avoid an overflow of information. Indicator-based data must be checked for relevance in order to rule out surveillance biases, artefacts or reporting errors (step 2). The significance of the data should then be established (step 3), usually through statistical comparison with baseline rates or thresholds. As far as events are concerned, these steps correspond to evaluating their relevance (step 2: 'is the event within the scope of public health?'), which is usually straightforward; and their reality (step 3: did the event really happen?), which may require a few phone calls to verify.

Indicators and events that have gone through steps 2 and 3 of the framework without being discarded are considered to be signals. A signal is a verified health-related issue. Whatever its origin (indicator or event), a signal has the same value for EI purposes and is processed in the same way.

Many signals have few or no public health consequences and only a few represent genuine public health alerts. Initial signal assessment is thus a key component of EI framework (step 4). Depending on the nature of the signal, the scope of the problem, the type(s) of disease(s) potentially involved and the population of concern, initial assessment may require different methods, of varying degrees of sophistication. It is very often necessary to go back to the source of the signal at this stage, and field investigation is sometimes required (step 5).

Once ascertained, the alert is classified according to its scope; that is, the level of the health system which will have to deal with it. As a simplified scheme, local, national and international levels can be considered. The IHR (2005) contain a decision instrument to help assess whether or not an alert is of international concern [3].

Implementing epidemic intelligence at country level

All EU member states have long-established disease surveillance systems that provide proper indicator-based surveillance to meet early warning objectives. The detection of non-specific events or health events of unknown origin could, in some cases, be improved by building up the sources of indicators with some of the one listed in table 1.

Table 1

Indicator-based component–Example of EI sources

EI Source	Rationale	Method
Mandatory notification	Some rare but serious diseases need prompt and targeted action	Legal framework
Surveillance on a sample of sources (sentinel)	Trends of some diseases can be obtained from a representative network of health professionals	Sentinel network
Syndromic surveillance	Emerging diseases may not fit into disease-specific definitions. Early detection of cluster of syndromes may trigger an alert before cases appear in traditional surveillance systems	Lists of syndromes
Mortality	Serious emerging threats may initially be recognised by an increase of deaths	Real time death reporting
Health services activities	Serious emerging situation may initially present with increased admissions to health services such as emergency rooms	Real time activity reporting
Drug consumption	Increase in specific drug consumption may indicate emerging disease	Pharmacy networks

EI: Epidemic intelligence

However, for most countries, the challenge lies in developing and structuring the event-based component of EI. Paying the same degree of attention to a local newspaper article as to a statistical analysis may represent a paradigm shift for most national institutions in charge of surveillance. Examples presented in Table 2 provide suggestions based on which each country can progressively develop systems based on its own objectives: a country with overseas territories and large numbers of people travelling in and out of the country on a regular basis may decide to concentrate on watching international factors, and develop sophisticated methods, using tools such as the Global Public Health Intelligence Network (GPHIN) [7], while another country with fewer overseas interactions may decide to rely on WHO postings in this regard [8].

EI must be seen as a consistent system and there is mutual benefit from implementing each of its two components: clinicians engaged in notifying disease under traditional surveillance will be keen to notify abnormal events while clinicians approached for notification of abnormal events will better understand the need for traditional surveillance. Good scientific principles of surveillance represent a perfect incentive for facilitating notification of events that may not be covered by a surveillance scheme.

Signal processing must be organised in an integrated way, allowing intelligence from different sources to be cross-checked and assessed together: a journal article reporting sewage problems along with an increase in admissions to the local hospital emergency department may lead to the recognition of an outbreak.

For the reasons given above, EI must be developed within the national institution in charge of public health surveillance as an extension of their current scope. Furthermore, all processes related to signal management should be carried out from a transversal structure within the institution, allowing experts from the various surveillance systems, as well as media officers, international health specialists and "epidemic intelligence managers" to jointly perform the risk assessment related to threats being detected.

EU perspectives

The founding regulation of ECDC specifies its mandate regarding risk identification and risk assessment. The Centre's tasks under this regulation include identifying and assessing emerging threats to human health from

Table 2

Event-based component – Example of EI sources

EI Source	Rationale	Method
Scientific watch	Scientific findings related to new organisms, drug resistance, etc. may trigger public health action	Literature review
Direct notifications	Clinicians or public health personnel may come across abnormal health events	On-call numbers
Media watch	Outbreaks and other unusual health events are often picked up early by local media	Media review Web scanning
International watch	A country may be affected secondarily by a health event emerging abroad	WHO reports ProMED, GPHIN
Intersectoral events	Agriculture, environment, industry and other sectors collect information on health related risks and exposure	Communication channels

EI: Epidemic intelligence; GPHIN: Global public health intelligence network; ProMED: The program for monitoring emerging diseases; WHO: World Health Organization

communicable diseases, and establishing, in cooperation with the Member States' (MS) procedures for systematically searching for, collecting, collating and analysing information and data with a view to the identification of emerging health threats which may have mental as well as physical health consequences and which could affect the European Community.

In order to fulfil its mandate, ECDC has begun to monitor potential public health threats from a European perspective [9], under the principle of subsidiarity and building on the experience acquired by the health threat unit of the European Commission. ECDC has developed a threat tracking tool to facilitate the capture, verification and assessment of public health events of relevance. The main output of the tool is a weekly bulletin, for restricted distribution to MS health authorities and to the European Commission. Another EI source is the weekly release of the journal Eurosurveillance, with which ECDC has collaborated since September 2005 [10]. The Eurosurveillance weekly release includes an 'e-alert' capacity used by MS epidemiologists to widely and rapidly share information about ongoing threats.

While ECDC has a mandate to further develop EI at European level, it remains the prerogative of health authorities to implement these activities in their countries. ECDC added value may include facilitating exchange of information among MS and supporting assessments and standardisation of EI systems in MS. ECDC's activities in filtering, processing and summarising information from international sources may also allow MS to reduce their activities in this area and focus on regional threats, or on countries with which they have heavy travel and trade relations.

ECDC will evaluate its EI activities in 2007, after 18 months of operation. This evaluation will focus on finding evidence of the added value of a structured approach to event-based surveillance in complement to indicator-based surveillance. A similar process is encouraged at MS level.

Further operational research on EI is needed in order to optimise the detection of events using keywords and algorithms, filtering of events and other processes involved. It should be carried out in consistence with WHO's activities in this area in order to promote global EI tools.

In May 2006, Members States of the European Community voluntarily committed to complying with provisions of the IHR (2005) considered relevant to the risk posed by avian and potential human pandemic influenza. This provides an opportunity for ECDC to guide MS in developing and/or strengthening their national EI, in addition to the ECDC's task to develop an EI system for the EU. A guideline on EI implementation is currently being prepared.

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Defining core competencies for epidemiologists working in communicable disease surveillance and response in the public health administrations of the European Union

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Strengthening the capacity to combat infectious diseases in the European Union (EU) is a core function of the European Centre for Disease Prevention and Control (ECDC), clearly expressed in its mandate [1].

Two main elements are critical for building and strengthening epidemiological capacity:
(1) Infrastructure - resources in terms of budget, facilities, equipment, etc. of national public health administrations.
(2) Human resources - sufficient numbers of trained and/or experienced professionals.

To fill the gaps in professional performance, it is necessary to define the tasks and skills required of field epidemiologists. The development of such a list of core competencies was highlighted as a priority among the conclusions of the first ECDC consultation with EU Member States on training in field epidemiology, in December 2005 [2].

The ECDC, along with a group of experts, has developed a list of suggested core competencies for field epidemiologists working in public health institutions in the European Union, at all levels, from sub-national (provinces, districts, regions) to national and supra-national (European and international). An agreed definition of the term "field epidemiologist" is not available, but the group of experts has proposed one for the purpose of this activity (Table 1) [3].

Core competencies

A competency is a *combination of knowledge, skills and abilities that a professional must demonstrate and that are critical to perform work effectively.*

Core competencies are defined first for middle-level professionals, as opposed to junior or senior epidemiologists. Despite the risk of creating artificial categories in the career development ladder, this approach has been taken to facilitate the process. At a later phase, the competencies can be developed for other career stages.

The term "core" indicates that the competencies should be a minimum pre-requisite for any field epidemiologist, regardless of the level he/she occupies in the public health administration. They should be common to all professionals in this field.

Use of the list of core competencies

We believe that the list may have several users:
- Employers, such as public health institutes and administrative bodies at all levels in the EU, who may use the list to assess their epidemiological capacities and needs.
- Epidemiologists themselves who may use the list for planning and evaluating their own career development (Table 2).

In addition, teachers and facilitators can use the list to design strategies and programmes to train future generations of epidemiologists in order to meet the needs of public health agencies.

Among the competencies, one can distinguish "workforce" competencies, as opposed to "instructional" ones, depending on the perspective taken for their development: i.e. employers or trainers views, respectively.

According to the MACH model (the acronym is made up of the initials of the authors' surnames [4]), both approaches are complementary and can be part of a more complex cycle, where the primary outcome is organizational performance. In this model, the contribution of employees is defined by the workforce competencies or tasks; from these, the instructional

Table 1

Glossary of terms

Field epidemiologist
"An epidemiologist who applies the science of epidemiology to the prevention and control of public health problems and works in intervention and response activities"
Competency
"The combination of knowledge, skills and abilities that a professional must demonstrate and that are critical to perform work effectively"
Any competency statement should consist of the following elements: • Action verb (observable or measurable performance of a worker) • Content (subject matter, type of performance, specific task) • Context (limitations or conditions of work environment)
Domain
Groups of competencies, organised according to a specific area of knowledge or skills involved
Skills
Ability, proficiency, facility, or dexterity that is acquired or developed through training or experience
Knowledge
Familiarity, awareness, or understanding gained through experience or study
Curriculum
Set of courses and their contents offered by an institution, such as a school or university as part of a training programme

competencies are developed in order to conduct needs assessments and planning of relevant training. The training and the personal skills influence the individual performance, which in turn affect the organisational performance thus closing the cycle [4].

Furthermore, we hope that publishing and promoting this list of core competencies in the EU's public health system can help to:

• agree on a definition of "field epidemiologist" and achieve the recognition of the profession;

• allow Member States to assess their resources and define their needs;
• set priorities by teachers and curriculum developers; and

• increase the comparability of field epidemiology training programmes, which could facilitate mobility in the EU through accreditation initiatives.

Table 2

Use of the list of "workforce" core competencies

Employers
Develop job descriptions
Competency
Plan career development cycle of the professionals in the organisation
Assess the epidemiologic capacity of the organisation in order to shape it according to needs
Evaluate individual performance
Plan training for employees
Epidemiologists
Self-assessment
Plan career development
Plan learning activities according to individual needs

Table 3

Suggested ECDC classification of areas and domains in public health epidemiology

Category	Area	Domain
Specific for the profession	Public health	1. Public health science
		2. Public health policy
	Applied epidemiology	3. Risk assessment
		4. Public health surveillance
		5. Outbreak investigation
		6. Epidemiological studies
		7. Laboratory issues
		8. Public health guidance
Common to other professions	Biostatistics	9. Probability
		10. Inferential statistics
		11. Sampling
		12. Mathematical modelling
	Applied informatics	13. Internet
		14. Statistical and other data analysis
		15. Editing and presentations
	Communication	16. Risk communication
		17. Written communication
		18. Oral communication
		19. Use of new technologies
	Management	20. Planning and use of resources
		21. Team building and negotiation
	Capacity development	22. Mentorship
		23. Training
	Ethics	24. Protection of individuals
		25. Confidentiality
		26. Conflicts of interests

Further development

We want to encourage a discussion of this list of core competencies by experts in the field. We also plan to review and update the list at regular intervals, as public health practice and knowledge evolves.

In July 2007, an online survey was launched on the ECDC website (http://www.ecdc.europa.eu). It seeks to score a list of 85 competencies that belong to 26 domains in eight areas (Table 3), through a Likert scale (1 to 5). The aim is to see whether there is a general agreement as to the core competencies and to collect, comments about the domains and areas included. The survey is anonymous but the participation of epidemiologists from different public health administrations of all EU Member States is especially welcome. To take part, please visit: http://www.ecdc.europa.eu/online_survey.html. The survey is open until 31 August 2007.

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The surveillance of communicable diseases in the European Union – a long-term strategy (2008-2013)

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This article presents the steps and considerations that led to the development of the European Centre for Disease Prevention and Control's (ECDC) long-term strategy for the surveillance of communicable diseases in the European Union (EU) for the years 2008 to 2013 [1]. Furthermore, it outlines the key features of the strategy that was approved by the ECDC's Management Board in December 2007.

Why is it necessary to carry out surveillance at the European level?

National surveillance systems and methods are very diverse and the quality of data collated varies across the EU and the three participating countries of the European Economic Association/European Free Trade Association (EEA/EFTA). This diversity is not limited to different data collection and validation systems and different reporting systems but even to basic issues such as different interpretations of the same standard case definitions. There are also country- specific variations in the organisation of health-care systems and in the availability of facilities and equipment for diagnostics and case confirmation, all of which also contribute to this diversity. As a result, the data produced are often not comparable, as was recently demonstrated in the ECDC's first Annual Epidemiological Report on Communicable Diseases in Europe [2,3].

This diversity also applies to the 17 EU-wide Dedicated Surveillance Networks (DSNs) [4], some of which were established as early as the 1980s. They differ in scope and coverage, objectives, structure of organisation, and development phase. They have developed separate reporting rules and procedures, variable data validity checks and all have their own separate report layouts. Therefore, a more coordinated approach towards surveillance at the European regional level should lead to a better harmonisation of structures and improve the comparability of the data and hence provide an added value for all EU Member States (MS) and EEA/EFTA countries (Table 1).

Types of surveillance

Several definitions of surveillance of health and disease have been published by a number of authors [5,6,7], with only slight variation between them. All these definitions incorporate the main elements of ongoing data collection, analysis to convert this data into statistics, interpretation of this analysis to produce information and then dissemination of this information to those who can take appropriate action.

In the context of the ECDC's work, surveillance is defined as the ongoing collection, validation, analysis and interpretation of that health and disease data that is needed to inform key stakeholders (in MS and elsewhere) to permit them to take action by planning and implementing more effective, evidence-based public health policies and strategies relevant to the prevention and control of disease or disease outbreaks. The prompt dissemination of the information to those who need to know is as essential as ensuring the quality, validity and comparability of the data.

Indicator-based surveillance

The traditional approach to the surveillance of communicable disease consists of routinely collecting data about the occurrence of predefined diseases, specific pathogens, syndromes or conditions from health-care providers. This notification process relies on standard case definitions for surveillance to ensure a uniform approach to reporting by all clinicians and laboratories and to improve the comparability of the data and reports across health-care services. The notifications are then routinely compiled and analysed to produce indicators that could suggest the existence of a threat or a problem that needs addressing. In some cases, a public health intervention would be required from the notification of a single case of the disease while in other situations, a threshold may be applied to an indicator to show up an unusual incidence rate of the disease in a given community. This "indicator-based" approach has proved to be very effective in monitoring threats related to known risks and then in ensuring the prompt implementation of public health measures.

Table 1

The main European Union added value of a more coordinated approach to surveillance

1. Improve inter-country comparability of data through a number of initiatives including by promoting the correct application of standard case definition;
2. Reduce complexity in surveillance systems across Europe;
3. Avoid duplication of work through double reporting with various European organisations;
4. Provide more relevant and reliable data to produce higher quality public health evidence;
5. Strengthen the national surveillance systems by contributing to capacity building and standards setting in the countries;
6. Enhance the detection and monitoring of international outbreaks;
7. Be economically more efficient and sustainable in the long term than the disease-specific projects based system;
8. Allow easier access to and use of data by all who may need it;
9. Better facilitate the inclusion of diseases into the surveillance and general research agenda according to the European priorities.

While this traditional approach remains the backbone of public health surveillance for communicable diseases, it has proven to be less effective in ensuring prompt recognition of emerging problems. Several further approaches seek to complement traditional surveillance in order to enhance its ability to detect pubic health threats. Some of these, such as syndromic surveillance or activity monitoring, remain heavily reliant on the routine collection of structured data, again compiled as indicators. Inclusion of these approaches would only be done after discussion and agreement with MS.

Event-based surveillance

A novel approach takes advantage of the availability of advanced information technology by scanning such sources as the Internet and media continuously to detect information that may lead to the recognition of emerging threats. This "event-based" surveillance [8] approach has been introduced to complement effectively the indicator-based surveillance approach. It uses unstructured data, that then needs to be studied and verified and cannot be summarised as an indicator. Together, both these approaches can conveniently be referred to as gathering strategic information on disease.

Steps towards a coordinated approach to surveillance in the EU

In 2005, a strategy for infectious disease surveillance in Europe was finalised to outline the transition phase from the existing project-based approach of the DSNs, mainly led by the Commission, to a more coordinated and sustainable one coordinated by the ECDC. Following this, the ECDC planned to develop a longer-term vision of the future surveillance of communicable diseases in the EU, to better ensure a common understanding of the direction and the decisions needed for the further development of the European wide surveillance systems. The drafting of this document took into account the ECDC's emergent strategy on how it will be developing the future work with laboratories, to ensure synergy across the organisation.

Goals of the ECDC's long-term surveillance strategy

The strategy defines the terms and scope of surveillance, broad goals and objectives, the organisational requirements, support needs for the MS and outlines a roadmap to implement the strategy. The overall goal of these surveillance activities is to contribute to reducing the incidence and prevalence of communicable diseases in Europe by providing relevant and accurate public health data, information and reports to decision makers and health-care professionals in an effort to promote actions that will result in the timely prevention and control of communicable diseases in Europe. Good comparability of surveillance data between MS and a high validity of communicable disease data is a key component dictating the success of this goal.

In order to achieve these goals, both the ECDC and MS have to work in close partnership to build up a strong surveillance system on the European level. MS need to strengthen, maintain or set up the structures which are required to provide the relevant data – in certain cases this may require support from the ECDC. At the same time, the ECDC will continue to develop the infrastructure and common framework, including quality assurance systems and training support, required at the EU level.

There are a number of areas where further work will be essential. These include revising the case definitions for surveillance on the EU level [9] and having a mechanism for occasional review; introducing clear principles of collaboration on data exchange, access and publication acceptable to all MS and the ECDC; ensuring a regular review of disease-specific surveillance objectives and priorities following wide consultation; developing links to other existing international databases; developing systems to critically review the diseases under EU-wide indicator based surveillance; planning for the greater integration of data from laboratories and developing ways of improving collaboration with them, in particular with the national reference level laboratories (NRL); developing more advanced data analysis methods and studying how best to communicate the results to ensure that this is information used for action.

Apart from these activities, several initiatives and systems will be essential to the success of this strategy.

The European Surveillance System

The ECDC has developed an information system for infectious disease indicator-based surveillance at the European level, The European Surveillance System (TESSy). TESSy will be a valuable tool to improve the collection, validation, storage and dissemination of surveillance data of the EU MS and EEA/EFTA countries. MS are already using it with the collection of a reduced set of common variables important for the routine surveillance of cases of all infectious diseases. TESSy will enable:

- Standardising data collection on infectious diseases surveillance;
- Providing a 'one-stop shop' for reporting and retrieving data for the MS;
- Standardising the basic reports based on surveillance data;
- Providing a consistent and easily available overview of the current situation in the EU.

Epidemic intelligence

Another system being developed focuses on developing event-based surveillance to better provide epidemic intelligence information [10]. The ECDC is working to ensure that all countries have standard procedures and tools in place to monitor and assess threats detected early. Similarly all countries will be able to use the ECDC developed 'Threat Tracking Tool' to perform joint risk assessments in the event of a threat potentially affecting more than one country. Finally the epidemic intelligence system will enable MS to continue to routinely report communicable disease threats through the Early Warning and Response System (EWRS) [11] once their assessment has confirmed the existence of a threat affecting the EU (as defined in the EWRS regulations).

Partnerships

Various collaborative agreements will be finalised with the other regional organisations also involved in the surveillance of disease, such as the World Health Organization (WHO) Regional Office for Europe and their global office in Geneva, the European Food Safety Authority (EFSA) and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), in order to minimise duplication and ensure that activities are complementary. Agreements on the principles of collaboration on data exchange between the ECDC and MS will be developed to define clearly the role of data providers and data users both in MS and the ECDC (and other parties, e.g. WHO) and the procedures for publishing the results of the analysis of data.

Collaboration with the Member States

The future collaboration with disease-specific experts in MS nominated by the ECDC's Competent Bodies, will be structured by a division of the diseases/pathogens into six main groups, namely respiratory tract infections; sexually transmitted infections, including HIV and blood-borne viruses; food- and water-borne diseases and zoonoses; emerging and vector-borne diseases; vaccine-preventable diseases; and antimicrobial-resistant pathogens and healthcare-associated infections. Where necessary, more focussed (disease-specific) subgroups can be established within any of these six groups. Annual meetings will be held for each of these six main groups to discuss issues pertinent to the surveillance of the whole disease group. If needed, specific 'parallel session' symposia can be held at the same time. For each of these six groups, a small Coordinating Group will be established and take over many of the functions carried out by the former DSN steering groups.

The ECDC plans to support the capacity development of MS to strengthen their surveillance by providing training, country visits to deal with MS-specific issues (including needs assessments and exploring ways to strengthen national systems), quality assurance (and EQA) and control processes, protocols, SOPs, guidelines, etc. Furthermore, the ECDC will work to strengthen the laboratory capacity in the EU and EEA/EFTA countries and the candidate countries in collaboration with the Commission, the ECDC Competent Bodies, and nominated National Microbiology Focal points, to ensure that every country should have the capacity of, or at least have the access to, Reference Level Laboratory (NRL) services enabling them to confirm the diagnosis, isolation of and further characterisation of all the important pathogens.

Implementation

The strategy will be implemented in two phases: a transition period until 2010, when the main focus will be on the integration of the coordination of the current DSNs to the ECDC while consolidating its own technical capacity; and the period between 2010 and 2013 when the ECDC will have taken over the full responsibility of surveillance and can then focus on developing and consolidating the highest quality and effective system possible for Europe. In order to keep this strategy and its objectives relevant, it will be revisited from time to time, with the Commission, MS and key stakeholders, so that it may be adjusted to incorporate emerging strategies or new evidence as required.

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Preliminary analysis of influenza A(H1N1)v individual and aggregated case reports from EU and EFTA countries

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Since the first importation of influenza A(H1N1)v virus to Europe in late April of this year, surveillance data have been collected in the Member States of the European Union and European Free Trade Association. This is the first preliminary analysis of aggregated and individual data available as of 8 June 2009 at European level.

Introduction

On 21 April 2009, the United States Centers for Disease Control and Prevention (US CDC) reported two cases of influenza due to a new virus strain of mixed swine, avian and human origin, the so-called new influenza A(H1N1) virus (hereafter named A(H1N1)v virus) [1]. On 25 April, the European Centre for Disease Prevention and Control (ECDC) published a risk assessment, started developing tools to monitor the situation and support the countries of the European Union (EU) and European Free Trade Association (EFTA), and initiated its first situation report distributed daily to more than 700 stakeholders since then. After the World Health Organisation (WHO) raised its pandemic alert level to phase 4 on 27 April and up-scaled again to phase 5 on 29 April, ECDC was monitoring the situation around the clock and provided epidemiological updates on global case numbers three times a day. Subsequently, the European Commission published a case definition for surveillance of the new disease [2], ECDC published information for travellers, updated its risk assessment on 8 May, published several documents on case and contact management, and coordinated the surveillance of influenza A(H1N1)v at EU level.

The objective of this paper is to present the epidemiological situation in the 27 EU and the three countries in the European Economic Area (EEA) and EFTA, Iceland, Liechtenstein and Norway, hereafter called the EU+3 countries, on the basis of the surveillance data provided by the EU+3 countries through individual and aggregated case reports.

Methods

Data used in this analysis of the epidemiological situation in the EU+3 countries, as of Monday 8 June 2009, 08:00 CEST, include individual case reports posted by countries in the Early Warning and Response System (EWRS) and aggregated case reports provided daily through the EWRS or through other official communication channels.

Confirmed cases are defined as persons in whom the infection has been confirmed by RT-PCR, or by viral culture or by a four-fold rise in influenza A(H1N1)v-specific neutralising antibodies. The latter implies, according to the EU case definition, the need for paired sera from the acute phase of illness and from the convalescent stage 10-14 days later [2].

While countries with fewer cases are uploading data on their cases directly into the surveillance database at ECDC, Spain and the United Kingdom (UK), who both have high number of cases, and Belgium are providing extracts from their own national databases, which are then entered into the ECDC database. Re-coding of some of the variables was necessary for Spain and the UK, and data were subsequently validated by the countries. The data from Belgium were imported manually after re-coding the variables.

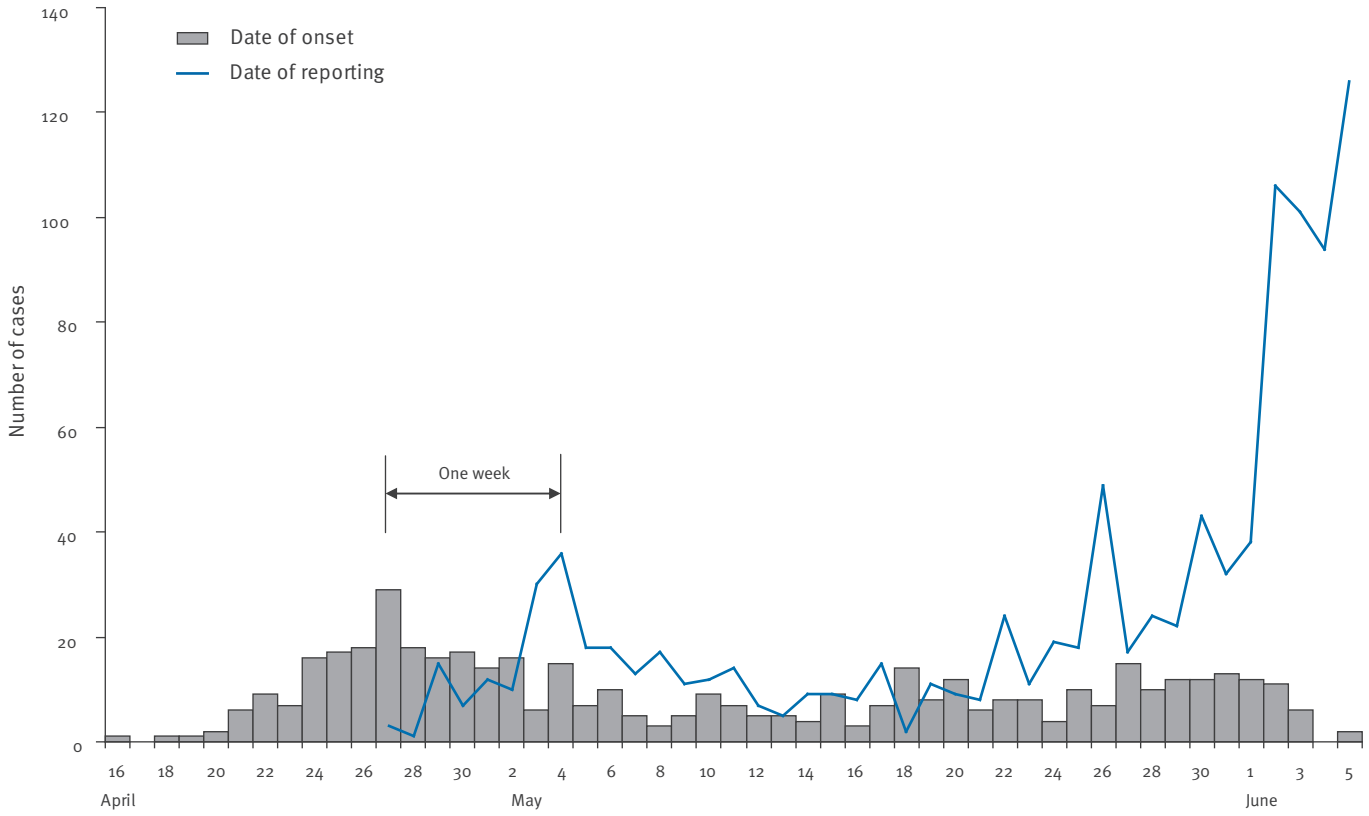
Cases which are not explicitly reported as having been exposed during travel in an affected country (imported cases) are considered to have been infected in their own country.

Results

As of 8 June, 1,128 laboratory-confirmed cases of influenza A(H1N1)v have been reported from 25 of the EU+3 countries through aggregated case reports. Spain (26%) and the UK (49%) together account for 75% of confirmed cases. Of those 1,128 cases, 498 (44%) were also reported through individual case reports (Table 1).

Figure 1

Distribution of confirmed cases of A(H1N1)v infections by date of onset (n=498) and date of reporting (n=1,024), as of 5 June 2009, EU+3 countries



Latvia, Liechtenstein, Lithuania , Malta and Slovenia have not reported confirmed cases so far.

Epidemic curves

The first confirmed case in EU+3 countries was a traveller returning from Mexico to the UK. He was identified on 27 April 2009 and reported onset of symptoms on 16 April. Figure 1 compares the distribution of cases by date of onset from the individual case reports (n=498) with the distribution of cases by reporting date from the aggregated case reports (n=1,024). It shows a delay of one week between date of onset and date of reporting in the first weeks of the outbreak, up to 20 May, followed by an increasing discrepancy in the number of cases reported by the two systems.

Figure 2 shows the distribution of imported and domestic cases in EU+3 countries by date of onset. The first case reported as in-country transmission had onset of symptoms five days after the first imported case. During the first two-week period, 65% of cases were reported to have been imported, compared to 40% during the second and 73% during the third two-week

period. The majority of imported cases in the first two-week period were imported from Mexico and in the third two-week period from the United States (US).

Demographic characteristics of cases

The male to female ratio was 1.1. The median age was 23 years (range: eight months to 73 years). Seven cases were younger than two years. Of 494 cases with known age, 168 (34%) were undee the age of 20 years. The most affected age group was the group of 20-29 year-olds and accounted for 37% of cases.

The proportion of imported cases older than 20 years (78%) was significantly higher than the proportion of over 20 year-old cases who were infected in their own country (27%, p<0.0001). The median age of imported cases was 25 years compared to 13 years for non-imported cases (Figure 3).

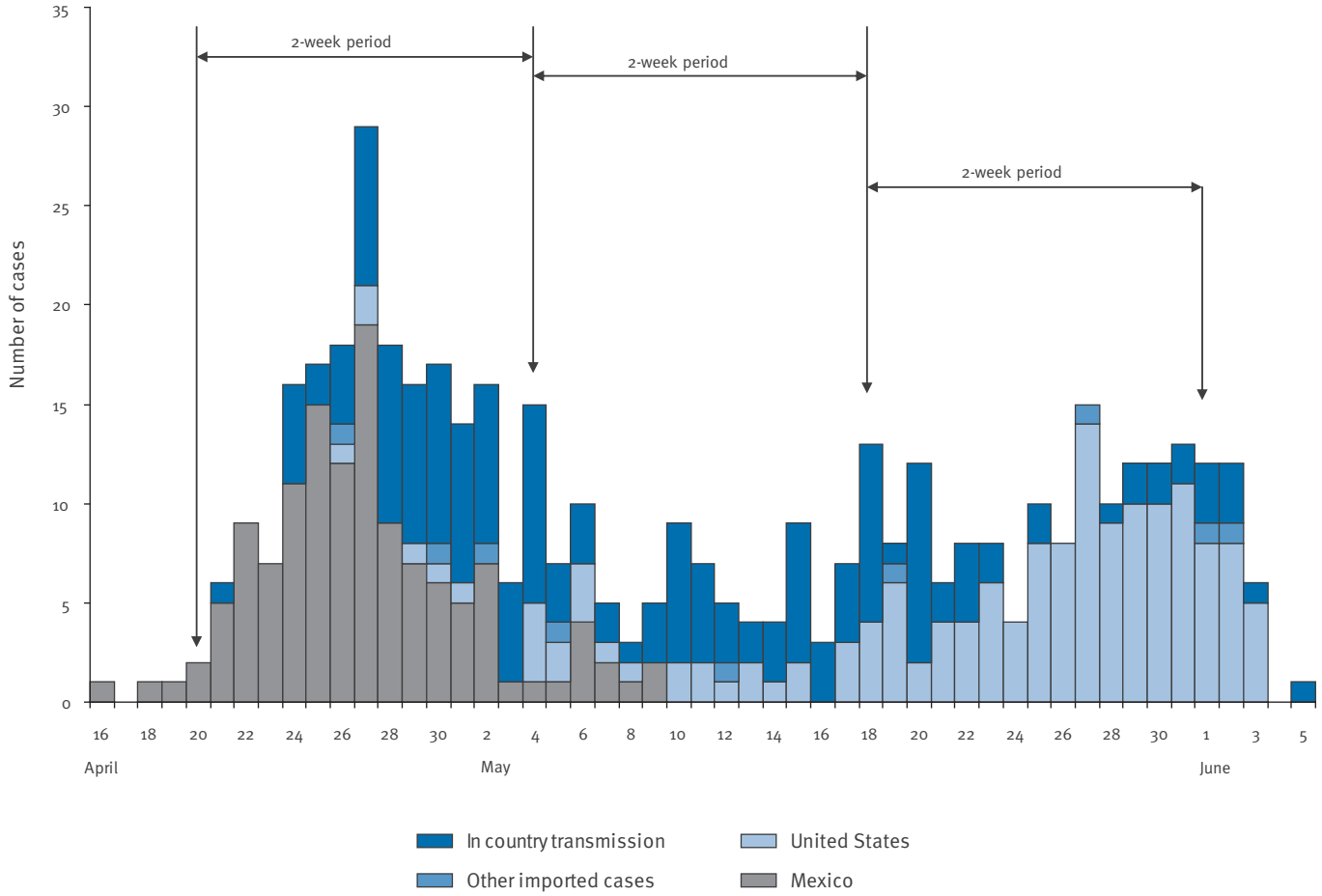
Symptoms

In the analysis of symptoms, the data from Spain and Belgium were excluded due to recoding issues, leaving 371 cases for analysis. Asymptomatic cases constituted 8% of reported cases (28/371), and were more common among cases under the age of 20 years (11%) when compared with older cases (5%, p=0.02).

The most commonly reported symptoms were respiratory symptoms (79%), followed by fever or history of fever (78%). Gastro-intestinal symptoms were reported from 86 cases (23%). Presence of gastro-intestinal symptoms was not significantly associated with travel exposure but was significantly more common among cases under the age of 20 years (32%) than among

Figure 2

Distribution of confirmed cases of influenza A(H1N1)v infections by date of onset and type of transmission, as of 31 May 2009*, EU+3 countries (n=457)



* Individual case reports from Spain were last updated on 14 May, from the UK and France on 29 May, from Italy on 4 June and from Germany on 6 June

older cases (18%, p=0.001). Table 2 shows the distribution of symptoms by category of symptom.

Pre-existing conditions

Underlying disease was reported for 24 cases: lung disease for 12, heart disease for four, renal disease from three, human immunodeficiency virus (HIV) infection from three, and seizures from two cases (one of these two also had a not further specified cancers). One 14 months-old child was reported with combined heart, lung and renal disease. None of the cases was reported to be pregnant. Several cases with other underlying conditions such as hypertension, iodine sensitivity, allergic rhinitis or facial paralysis were reported, which are not considered classical risk groups for seasonal influenza [3].

Treatment and prophylaxis

Of 292 cases for whom information is available, 258 (88%) received antiviral treatment. Oseltamivir was the most commonly used drug (255), zanamivir was reported to have been used for treatment of three cases. Post-exposure prophylaxis was reported to have been administered to 13 (7%) of 198 cases for whom information was available. Twelve received oseltamivir and one received zanamivir as prophylaxis. Six of the cases who received prophylaxis were imported cases.

Complications

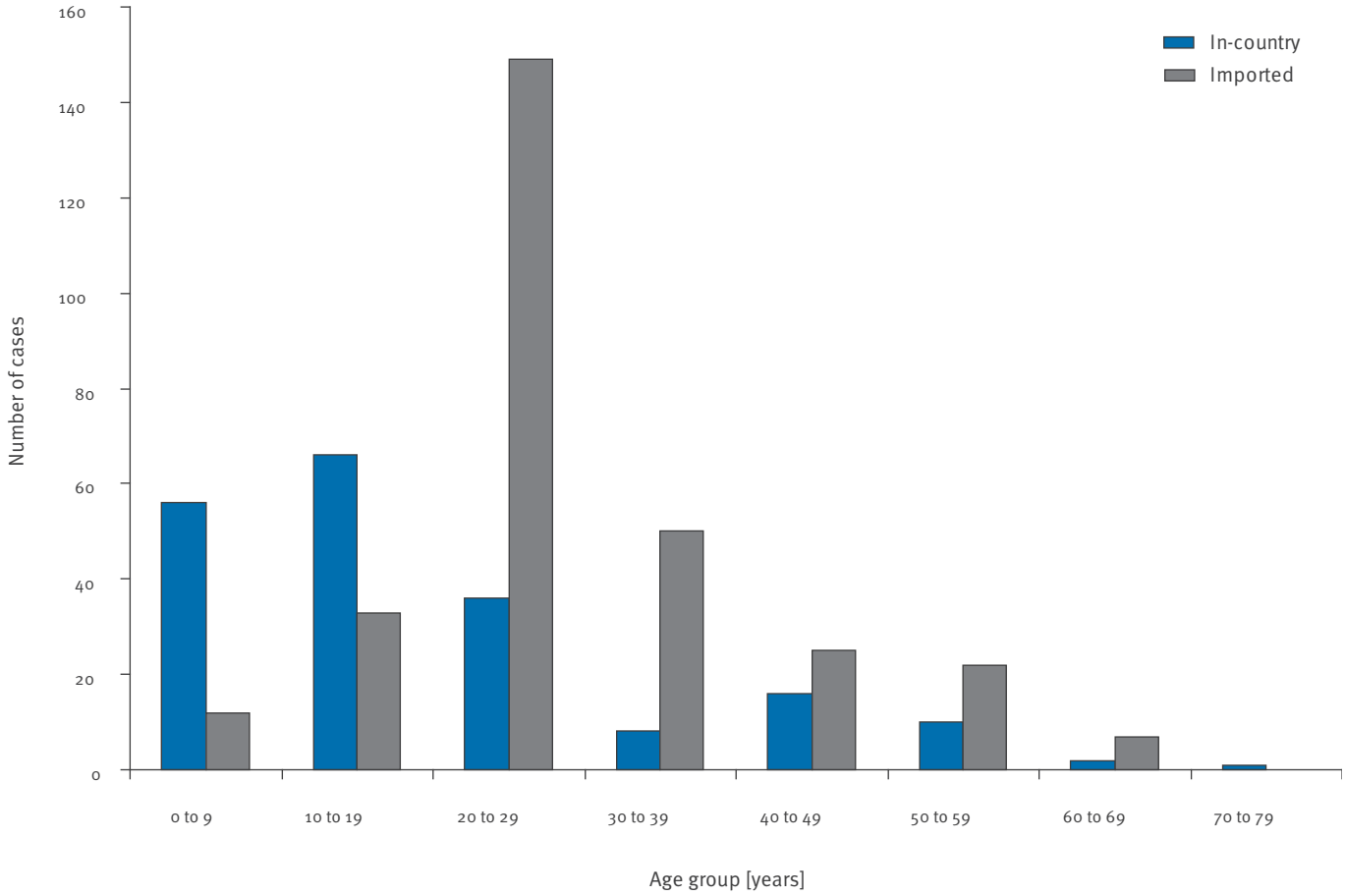
Seven (2%) of the 286 cases for whom information is available were classified as having complications. Four patients were reported with pneumonia, one with otitis, one with elevated liver enzymes and one with the need for steroid treatment. Fifty-three cases reported shortness of breath, one of whom had underlying heart disease.

Previous influenza vaccination

Twenty (8%) of the 260 cases for whom information is available were reported to have received seasonal influenza vaccination in the past season. Vaccinated persons were aged between 8 months and 76 years. Eighty percent of vaccinated persons were returning travellers. Two were reported to have asthma, one with underlying heart disease, one with chronic disease not further specified and one with myalgic encephalopathy.

Figure 3

Distribution of cases of influenza A(H1N1)v infection by age group and type of transmission, as of 8 June 2009, EU+3 countries (n=493)



Hospitalisation

Among 291 cases, 36% (105) were reported to have been hospitalised. The rate of hospitalisation varies by country. In several countries, e.g. France, Austria, Belgium and Romania, cases were hospitalised for isolation purposes.

Discussion

On the basis of the aggregated case reporting, two EU Member States account for 75% of the cases reported in the EU+3 countries. It is unlikely that a difference in the sensitivity of surveillance systems alone could explain such a difference. The one-week delay between date of onset (individual case reports) and reporting date (aggregated case-reports) observed in the first weeks of the epidemic probably reflects the delay in seeking medical care after onset and getting laboratory confirmation (see Figure 1). The discrepancy observed since the third week of May in the numbers reported through aggregated case reports versus individual case reports highlights the increasing difficulties of the Member States in investigating and reporting individual cases as the number of case increases.

This preliminary analysis does not allow an accurate description of the level of in-country transmission, as the data are still incomplete. However, a recent Eurosurveillance article suggests that in the UK, most of the recent cases are due to in-country transmission, although sustained community transmission still has to be confirmed [4].

The age distribution of cases is significantly different among imported and domestic cases. Imported cases tend to be young adults, exposed while travelling abroad, and their demographic characteristics are more representative of travellers than of the population susceptible to A(H1N1)v infection. Domestic cases tend to be younger (median age 13 years) and reflect school children and teenagers among whom transmission is amplified. Therefore, the demographic characteristics of cases documented in the EU so far do not reflect the overall population at risk of infection, but rather the population contributing to seeding events (travellers) and amplification of transmission (school children and teenagers) in the early stage of the spread of a new influenza virus strain.

The relatively high proportion of asymptomatic cases, especially among under 20 year-olds, is probably due to intensive contact tracing during school outbreaks. The difference in the number of cases with gastro-intestinal symptoms observed in under 20 year-olds compared to older cases has been previously described for

Table 1

Distribution of confirmed cases of influenza A(H1N1)v reported until 8 June 2009 by source of information, EU+3 countries (n=1,128)

Member State	Aggregated case reports	Individual case reports	Percentage
Austria	6	6	100
Belgium	14	14	100
Bulgaria	2	0	0
Cyprus	1	1	100
Czech Republic	2	2	100
Denmark	5	4	80
Estonia	3	3	100
Finland	4	4	100
France	57	18	32
Germany	63	63	100
Greece	5	0	0
Hungary	3	3	100
Iceland	1	0	0
Ireland	11	11	100
Italy	50	39	78
Luxembourg	1	1	100
Netherlands	10	6	60
Norway	9	9	100
Poland	5	5	100
Portugal	2	2	100
Romania	9	9	100
Slovakia	3	3	100
Spain	291	113	39
Sweden	14	13	93
United Kingdom	557	169	30
Total	**1128**	**498**	**44**

Table 2

Distribution of symptoms among cases of influenza A(H1N1)v infection, as of 8 June 2009, EU+3 countries (n=371)

	Number	Percentage
At least one symptom	344	93
General	317	85
Fever or history of fever	290	78
Headache	160	43
Muscle pain	145	39
Joint pain	79	21
RESPIRATORY	295	80
Dry cough	188	51
Productive cough	60	16
Sore throat	172	46
Runny nose	120	32
Sneezing	72	19
Shortness of breath	34	9
Gastro intestinal	34	24
Diarrhoea	45	12
Vomiting	49	13
Nausea	57	15
OTHERS	146	39
Conjunctivitis	21	6
Nose bleeding	9	2
Altered consciousness	2	1
Others (various)	117	32

seasonal influenza and is not significantly associated with an exposure abroad [3]. The hospitalisation rate cannot be considered as a factor of severity because many of the cases were reported to be admitted to hospital for isolation. There was great variation among countries in this respect.

Information on the interval between exposure and the start of prophylaxis is not available and therefore no conclusions can be drawn regarding the effectiveness of antiviral prophylaxis.

Individual case reports for less than half of the cases (498/1,128) were available for this analysis, which may bias the results. The bias will particularly affect conclusions drawn on cases from the last three weeks of the dataset, for which information from the most affected Member States were not available. Bias may have been introduced in the age distributions and the frequencies of symptoms and underlying conditions, since the missing data particularly concern in-country transmission. Therefore, the comparisons between cases affected in their won country and travel-associated cases should still be considered preliminary and a change in disease patterns during the period for which data are missing cannot be ruled out. Due to delay in reporting from the Member States to ECDC, the Europe-wide picture presented here may not fully represent the reality of what was known at country level on 8 June.

With the currently available information, conclusions about the severity of the infection are limited. In addition, if cases deteriorate while they are ill, this information would probably not be reported to the ECDC.

Conclusions

The preliminary analysis of the initial few hundred cases reported at European level shows that the epidemiological pattern in the EU+3 countries does not differ from what was documented in the Americas. Currently, the disease seems to be relatively mild and comparable with seasonal influenza. However, it is still too early to define, on the basis of this analysis, the age groups most at risk of infection.

These data are important to guide appropriate policy decisions. In 2008, a working group on surveillance in a pandemic, including ECDC, WHO and experts from the Member States, identified nine strategic parameters which would need to be assessed early in an influenza pandemic [5]. Out of these, six parameters (including disease severity, incidence by age-group and known risk-factors, confirmation/modification of case definition and modes of transmission) can only be properly evaluated using individual case reports.

As the number of cases grows, it will become increasingly difficult for the Member States to investigate and report individual cases. The surveillance currently in place may soon reach its limits. It may well be that targeted outbreak studies will provide better information on risk factors for more severe disease. A switch to sentinel surveillance and/or surveillance of severe cases, as implemented by countries outside the EU, has to be considered. However, the case-based reporting should be continued at least until countries experience community spread or large-scale epidemics. ECDC is currently working with the Member States to automate the upload of data in their own national formats.

In the meantime, aggregated case reporting complementing individual case reports has proven very useful in describing recent trends and anticipating future developments. As recent trends suggest that Europe may be entering the acceleration phase [6], it is important to continue collecting aggregated case reports.

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The final preparation of the report was made by ECDC working group on influenza A(H1N1)v, see below.

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The ECDC working group on influenza

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Antimicrobial resistance 2010: global attention on carbapenemase-producing bacteria

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A year ago in November 2009, a study in this journal highlighted the emergence of infections with totally or almost totally resistant bacteria in European intensive care units [1]. Most of them were Gram-negative bacilli that showed resistance to a class of antibiotics considered last-line therapy: the carbapenems. Already in 2008, Souli *et al*. had reviewed the emergence of extensively drug-resistant (XDR) bacteria in Europe [2] and pointed out the high proportion of isolates that were resistant to carbapenems, through production of a carbapenemase enzyme. Indeed, an increasing number of reports on carbapenemases and infections with carbapenemase-producing bacteria have been published in recent years indicating the rising importance of these bacteria. A PubMed search with the keyword 'carbapenemase' and excluding review articles, yielded 35 articles for the year 2007, 48 articles for 2008, 80 articles for 2009 and 109 articles for 2010 (as of 14 November).

The year 2010 will certainly be remembered as the year when carbapenemase-producing, XDR bacteria attracted global attention. Significant media attention and increasing awareness of these bacteria followed the publication by Kumarasamy *et al*. on 11 August on the spread to the United Kingdom (UK) of a new type of carbapenemase, the New Delhi metallo-beta-lactamase 1 (NDM-1), often associated with travel to India or Pakistan [3]. In this issue of *Eurosurveillance*, Struelens *et al*. review the spread of NDM-1 in the European Union (EU), Iceland and Norway and show that, in addition to the UK, 11 other EU countries plus Norway have identified patients infected or colonised with NDM-1-producing *Enterobacteriaceae* [4]. Similar to the cases described in the UK, the majority of these NDM-1 cases had previously travelled or been admitted to a hospital in India or Pakistan. In addition, a few cases had been hospitalised in the Balkan region [4].

Several other types of carbapenemases have been described since the 1990s such as *Klebsiella pneumoniae* carbapenemase (KPC), Verona integron-encoded metallo-beta-lactamase (VIM) and the oxacillinase-type beta-lactamase OXA-48 [5]. All these have in common that they are able to rapidly hydrolyse most of the beta-lactams including the carbapenems, thus conferring resistance to these antibiotics. In addition, they are in most cases encoded by a gene located on transferable elements which allows transfer of the gene among species of Enterobacteriaceae. This issue of *Eurosurveillance* highlights the challenges represented by carbapenemase-producing, XDR bacteria, but also offers examples from EU countries on how the spread of such bacteria can be contained.

Although NDM-1 has been the focus of media attention concerning antimicrobial resistance during the past months, it is neither the most frequently identified carbapenemase in Europe, nor the only carbapenemase associated with transfer of patients between countries. In this issue of the journal, a group of European experts report on carbapenemase-producing *Enterobacteriaceae* in Europe and show that carbapenemases other than NDM-1 are the dominant types in all European countries except the UK [5]. As an example, Decré *et al*. describe the likely importation from Morocco to France of an OXA-48-producing *K. pneumoniae* strain with subsequent cross-transmission to another patient [6], a pattern similar to that described for previous OXA-48 cases from other countries. As for NDM-1, the spread of KPC- and OXA-48-producing bacteria has been associated with transfer of patients from hospitals in countries where they are frequently found, to hospitals in other countries [7,8].

Accurate laboratory detection, control of patient-to-patient transmission and prudent use of antibiotics are cornerstones of containment

Identification of carbapenemase-producing bacteria remains a challenge. According to the survey by Grundmann *et al*. there is likely underreporting of such isolates in more than one third of European countries [5]. Struelens *et al*. found that less than half of the countries reported having national guidance on surveillance and detection methods for carbapenemase-producing bacteria and, with two exceptions, countries that reported NDM-1 cases also reported having such

national guidance [4]. Availability of guidance and sufficient capacity of laboratories to routinely detect and confirm carbapenemase-producing isolates throughout and beyond Europe, are of paramount importance for their containment. Active surveillance and isolation of patients who are infected or colonised are essential for controlling the spread of these bacteria. Struelens *et al*. indicate that 11 European countries have developed infection control guidelines which in some countries, e.g. France, recommend the pre-emptive isolation and screening of patients transferred from hospitals in other countries [4].

To address the issues above, the United States (US) Centers for Disease Control and Prevention (CDC) developed a guidance document for the detection of metallo-beta-lactamases such as NDM-1 [9] and produced guidance for control of these infections in acute care facilities [10]. In Europe, the European Centre for Disease Prevention and Control (ECDC) is preparing evidence-based guidance on screening and confirmation of carbapenemase-producing bacteria and conducts a systematic review of the published evidence on interventions to control carbapenemase-producing Enterobacteriaceae. A group of European experts convened by the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) reviewed detection and surveillance issues [11]. Another expert group under the auspices of ESCMID, suggested implementation of different control measures for countries with sporadic occurrence of these bacteria and for countries where they are endemic [12].

Early warning and sharing information between countries facilitates prevention and control

In this issue, Kassis-Chikhani *et al*. [13] show that it is possible to contain outbreaks of carbapenemase-producing bacteria if rapid control measures are implemented. National and international early warning and response systems allow for the timely sharing of information that is necessary to investigate possible inter-hospital transmission. The EU Early Warning and Response System (EWRS) is a tool to rapidly share confidential information between countries, with the assistance of the European Commission, to improve prevention and control of communicable diseases. However, the EWRS has rarely been used for communication about resistant bacteria in the past. In addition to rapid exchange of information, discussion between risk assessment entities and experts in EU countries is crucial to prevent the spread of resistant bacteria including the ones discussed in this editorial. To support such discussions, ECDC is developing a specific module of its Epidemic Intelligence Information System (EPIS).

Antimicrobial resistance and consumption in EU Member States

Data on antimicrobial resistance are available from the European Antimicrobial Resistance Surveillance Network (EARS-Net, formerly EARSS) (http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/Pages/index.aspx). They show increasing resistance to third-generation cephalosporins and multidrug resistance in invasive infections due to *K. pneumoniae* and *Escherichia coli* in many EU countries. For this reason, hospital physicians have increasingly used carbapenems, in particular to treat infections in the most severely ill patients, e.g. in intensive care units. In a point prevalence survey on antimicrobial consumption in a sample of 75 European hospitals, the European Surveillance of Antimicrobial Consumption (ESAC) project showed that on average 11%, and up to 50%, of patients in intensive care units were receiving a carbapenem [14]. Since the introduction of antibiotics into medical practice, prescribers have mostly relied on the constant availability of new antibiotics to effectively treat patients infected with resistant bacteria. However, this forward escape strategy now looks like a leap of faith since innovative antibiotics active against these bacteria are unlikely to be developed in the very near future [15], leaving therapeutic options for carbapenemase-producing, XDR bacteria limited. These consist mainly of the polymyxins and tigecycline, but experts agree that neither of them are ideal because of the toxicity of polymyxins and the variable clinical efficacy of tigecycline [8,12]. Avoiding unnecessary use of antibiotics and reserving them for appropriate indications, starting with carbapenems, is therefore essential to preserve options for therapy of infections in hospitalised patients.

Point prevalence surveys have been developed to ascertain the appropriateness of antibiotic prescription practices in hospitals and other healthcare facilities. In the ESAC point prevalence survey, 57% of antibiotic courses for surgical prophylaxis lasted more than one day, thus highlighting short duration of prophylaxis as an obvious target for improvement of antibiotic prescribing practices in hospitals [14]. Even in a country with a history of prudent use of antibiotics such as the Netherlands, Willemsen *et al*. showed that, in their prevalence survey in 19 hospitals, 16% patients were receiving antimicrobial therapy that they judged inappropriate [16]. The Eurobarometer survey on antimicrobial resistance performed in November-December 2009 showed that almost half of Europeans still believed that 'antibiotics are active against colds and flu' and these results point towards a challenge for prudent use of antibiotics outside of hospitals [17].

Meticillin-resistant *Staphylococcus aureus*

Recent data from EARS-Net show that six countries reported decreasing trends in the proportion of meticillin-resistant *Staphylococcus aureus* (MRSA) among *S. aureus* isolates from invasive infections for the period 2006 to 2009. This is likely due to sustained efforts to contain the spread of MRSA in hospitals and other healthcare facilities [18]. MRSA remains a public health threat with a proportion of MRSA above 25% in more than one third of countries participating in EARS-Net. In addition, new strains of MRSA are emerging

from other environments such as human infections in the community, food animals and foods [19]. In this issue, De Jonge *et al.* add to our knowledge about MRSA with a study suggesting that, although present in some meat samples in the Netherlands, the risk to humans of being colonised by MRSA through handling of contaminated meat is low [20].

MRSA emerged in hospitals in the 1960s and, with the exception of the Scandinavian countries and the Netherlands, other European countries did not seriously consider its prevention and control before the 1990s. In countries with a low MRSA prevalence, MRSA control relies heavily on the so-called 'search-and-destroy' strategy which includes the pre-emptive isolation and screening of patients who have been in contact with healthcare facilities in countries with high prevalence of MRSA [18].

International efforts to tackle antimicrobial resistance - joining forces is essential

Europe is reacting much faster to contain the spread of carbapenemase-producing, extensively drug-resistant bacteria when compared with MRSA. It follows the path of a few leading countries which are taking measures similar to those for MRSA prevention and control in low prevalence countries. Contemporary life-style, however, poses an additional challenge with ever increasing international travel and patients seeking healthcare abroad, which means that containment of carbapenemase-producing, XDR bacteria can only be addressed internationally.

The European Commission has reported this year that EU countries have made significant progress toward implementing the Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine. However, there are still several areas where improvement is needed, including education and awareness of healthcare personnel and the general public [21]. On 18 November 2010, 36 European countries will participate in the third European Antibiotic Awareness Day (http://antibiotic.ecdc.europa.eu). The focus of this year's European Antibiotic Awareness Day is to raise awareness about prudent use of antibiotics among hospital prescribers. Key messages have been developed to help hospitals and hospital prescribers in their efforts to reach this goal. Evidence suggests that multifaceted hospital strategies may improve antibiotic prescribing practices and decrease antibiotic resistance. In addition, specific strategies may help prescribers optimise antibiotic therapy and reduce unnecessary use.

Worldwide attention on antimicrobial resistance allows for many stakeholders and countries to be involved. In planning for next year, the World Health Organization has declared antimicrobial resistance and its global spread as the topic for the next World Health Day on 7 April 2011 [22]. Already this year, antibiotic awareness campaigns are taking place at the same time on both sides of the Atlantic. The United States' Get Smart About Antibiotics Week (http://www.cdc.gov/getsmart/) takes place on 15-21 November [23] and Canada's first Antibiotic Awareness Day (http://antibioticawareness.ca/) will take place on the same day as European Antibiotic Awareness Day, 18 November 2010. Joining forces is essential for tackling a global issue such as antimicrobial resistance.

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European Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft – the RAGIDA project

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In order to assist national public health authorities in the European Union to assess the risks associated with the transmission of infectious agents on board aircrafts, the European Centre for Disease Prevention and Control initiated in 2007 the RAGIDA project (Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft). RAGIDA consists of two parts: the production of a systematic review and a series of disease-specific guidance documents. The systematic review covered over 3,700 peer-reviewed articles and grey literature for the following diseases: tuberculosis, influenza, severe acute respiratory syndrome (SARS), invasive meningococcal disease, measles, rubella, diphtheria, Ebola and Marburg haemorrhagic fevers, Lassa fever, smallpox and anthrax. In addition, general guidelines on risk assessment and management from international aviation boards and national and international public health agencies were systematically searched. Experts were interviewed on case-based events by standardised questionnaires. Disease-specific guidance documents on tuberculosis, SARS, meningococcal infections, measles, rubella, Ebola and Marburg haemorrhagic fevers, Lassa fever, smallpox and anthrax were the result of consultations of disease-specific expert panels. Factors that influence the risk assessment of infectious disease transmission on board aircrafts and decision making for contact tracing are outlined.

Background

With increasing numbers of passengers travelling internationally by air the potential risk of introduction and spread of infectious diseases by travellers increases. In 2009, the global airport traffic reported 4.796 x 10^9 passengers arriving and departing from 1,354 airports located in 171 countries worldwide, with passengers on international flights accounting for 42 percent [1]. Almost 800 million passengers are carried on national/international flights annually within the European Union (EU) alone [2].

The outbreak of SARS in 2003 and pandemic influenza A(H1N1) in 2009 illustrated how infectious diseases can suddenly appear, spread, and threaten the health, economy and social lives of citizens even in countries that are not or not yet affected by the epidemic itself. When passengers and/or crew members become exposed to an infectious or potentially infectious person during a flight, early recognition of disease and coordinated risk assessment among the affected countries is needed to initiate appropriate public health response without unnecessarily alarming the public and disrupting air traffic.

There are legal obligations for the member states of the World Health Organization (WHO) to report events of public health concern in accordance with the International Health Regulations (IHR) [3] and for the Member States of the EU to provide information to the Community Network in accordance to the Decision No 2119/98/EC [4]. However, very limited international guidance exists for the public health management of infectious diseases related to air travel, both aboard aircrafts and at airports [5]. Existing international guidance, e.g. the WHO international guidelines for the control of tuberculosis [6], does not necessarily reflect the epidemiologic situation in the individual EU Member States, while the national guidelines, e.g. for meningococcal diseases [7], are frequently inconsistent.

In order to assist national public health authorities in EU Member States in the evaluation of risks related to the transmission of various infectious agents on board aircrafts and to help in the decision on the most appropriate, operationally possible public health measures for containment, e.g. on whether or not to contact-trace air travellers and crew in case of exposure, the European Centre for Disease Prevention and Control (ECDC) initiated in 2007 the project Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft (RAGIDA) [8].

The RAGIDA project consists of two parts: (i) a systematic review of the literature of documented past events of infectious disease transmission on aircrafts, guidance documents and expert interviews assessing case-based information on events (produced by the Robert Koch Institute, Germany in response to an ECDC open call for tender OJ/2007/06/20- PROC/2007/009) [8], and (ii) a series of disease-specific guidance documents

produced by external disease-specific expert panels [9] on which this article will mainly focus. This guidance does not address contacts at the airport or occurring during transit.

Methods

Part I: Systematic review and expert interviews

In the first part of the RAGIDA project a systematic review of over 3,700 peer-reviewed articles and grey literature was performed for the following 12 infectious diseases: tuberculosis, influenza, SARS, invasive meningococcal disease, measles, rubella, diphtheria, Ebola and Marburg haemorrhagic fevers, Lassa fever, smallpox and anthrax. The aim was to evaluate the exact circumstances that led to the transmission of these infectious diseases on board aircrafts. For peer-reviewed publications, PubMed and the database of the German Institute of Medical Documentation and Information (DIMDI) were searched, using the following two combinations of search terms: (aircraft OR airplane OR flight OR flight crew OR air travel OR airline OR air passenger) AND (epidemiology OR microbiology OR transmission), (aircraft OR airplane OR flight OR flight crew OR air travel OR airline OR air passenger) AND (infectious).

Grey literature was searched in ProMed using the search terms 'airline OR air travel OR air passenger'. In addition, general guidelines on risk assessment and management were systematically searched from international aviation boards, the Airport Council International (ACI), International Air Transport Association (IATA) and International Civil Aviation Organisation (ICAO) and several national and international public health agencies such as the WHO, the United States Centers for Disease Control and Prevention, Health Canada, the Health Protection Agency in the United Kingdom and the Robert Koch Institute in Germany. Standardised questionnaires were used to interview an international group of experts to collect case-based information on events.

Contacts were defined as persons with relevant exposure to an infectious or potentially infectious index case. The credibility of an exposure was assessed by referring to event-specific factors such as pathogen, infectiousness of the index case, infectious period, availability of information on on-board exposure, possible alternative exposures, and risk factors for infection. The evidence of on-board transmission was assessed for each event according to a set of established criteria. These criteria took into account the validity and relevance of diagnostic tests (index case(s)/contacts), the validity and relevance of information for exposures or alternative exposures of contacts, and the susceptibility of contacts. Evidence for transmission was graded into four categories: high, probable, possible and none. If no transmission was concluded, the level of evidence for non-transmission was assessed using the proportion of the successfully traced contacts among all susceptible contacts on board the flight. The evidence was assessed as low if the proportion was smaller than 35%; medium if the proportion was between 35% and 75%, and high if the proportion was larger than 75%.

Part II: Disease-specific guidance

Within the second part of the RAGIDA project, the production of a series of operational guidance documents for assisting in the evaluation of risk for transmission of diseases was initiated. In June 2009, ECDC convened the first RAGIDA disease-specific expert meeting that focused on tuberculosis, SARS and invasive meningococcal infections. In 2010 a second meeting followed that concentrated on measles, rubella, Ebola and Marburg haemorrhagic fevers, Lassa fever, smallpox and anthrax.

For both meetings, small, multidisciplinary disease-specific expert panels were established. The participants were selected to include representatives of national public health authorities, particularly those with experience in the investigation and follow-up of incidents involving infectious diseases in travellers, European and international experts for the disease(s) under investigation, experts in microbiology and mathematic modelling, and representatives of the ECDC, the European Commission and the WHO International Health Regulations Coordination Programme. No conflicts of interest were declared by any of the participants.

Evidence obtained included the review of the published literature by disease related to air travel, the review of data on air travellers obtained from national public health authorities (from RAGIDA part I), and expert opinions from the members of the expert panel. Experts discussed basic elements of the Scottish Intercollegiate Guidelines Network (SIGN) approach for developing guidelines [10] and reviewed the evidence base taking into account the available scientific evidence for disease transmission as well as other relevant aspects such as disease severity, the potential for public health intervention, and availability of treatment.

Each disease-specific chapter contains a short literature review, outlines an approach for contact tracing including an algorithm and a template for questions and answers.

Results

Part I: Systematic review and expert interviews

The available information published in peer-reviewed journals was very limited for most of the diseases for which only a few on-board transmission events were described, limiting the power for evidence-based decision making. With the exception of tuberculosis no international guidance for contact tracing was identified [7,11,12]. A detailed report of this first part of the project has been published [8].

Part II: Disease-specific guidance

Overall the expert panels agreed that for each of the diseases contact tracing should be recommended only after careful risk assessment. Contact tracing was considered as reasonable if the probability of an infectious disease causing a secondary infection and/or further spread in the population was high in conjunction with an assessment that the impact on human health in terms of an adverse outcome (the scale of harm caused by the infectious threat in terms of morbidity and mortality) was also high. Several additional factors were identified that influence the decision making regarding contact tracing.

Factors that affect the probability of disease transmission on board aircrafts

The probability that a certain infectious disease is transmitted on board an aircraft depends on characteristics of the causative agent and the host, and on environmental factors. These include:

- infectivity of the index case during the flight in the symptomatic or pre-symptomatic stage, taking into account epidemiological attributes such as Ro, period of shedding, infectiousness period, mode of transmission, as well as signs and symptoms of disease;
- susceptibility of the passengers, considering their level of natural immunity and vaccination status;
- effectiveness of exposure, depending on proximity to the index case, duration of exposure as well as the technical specifications of the airplane and the quality of the cabin air.

Factors that affect the impact on human health

The impact on human health, the scale of harm that a certain infectious disease causes in terms of morbidity and mortality, depends on characteristics of the pathogen and the host, and on the available means for detection and intervention. The relevant factors include:

- pathogen-specific attributes for disease manifestation such as virulence, resistance pattern and case fatality;
- underlying condition associated with severity, considering compromised immune system, comorbidity or pregnancy;
- means for detection and possibilities for diagnosis, taking into account the availability and reliability of diagnostic tests;
- effectiveness of intervention, e.g. availability of prophylaxis and/or treatment.

Factors that influence the decision on contact tracing

In addition to the probability of transmission and the impact on human health, there are several additional factors that influence the decision making regarding contact tracing, such as:

- susceptibility of the passengers for the disease, taking into account the level of natural immunity and the vaccine coverage in the population of the countries of origin and destination;
- the maximum incubation period, i.e. the time period during which it is possible to intervene with public health measures; contact tracing at a later time could be initiated for scientific purposes;
- ethical aspects, e.g. whether treatment is available or whether containment and/or mitigation measures are acceptable for the contacts;
- means for response, i.e. the public health actions taken after identification of infected individuals, the options that can be offered to the infected individuals identified by contact tracing;
- alternative actions instead of contact tracing such as risk communication including leaflets for passengers of the flight and information on airports;
- media coverage and public attention;
- political sensitivities in the involved countries;
- available resources.

Discussion

In a globalised world, the risk for transmission and spread of infectious diseases through travel and trade needs to be addressed. In terms of passenger numbers, Europe has four of the eleven airports receiving the highest passenger numbers worldwide: London, Paris, Frankfurt and Madrid. Each of them receive more than 50 million passengers a year (with the larger proportion of passengers on international flights) [1,2], some of whom are likely to have or incubate infectious diseases. Airline cabins, as confined spaces, may provide an environment for disease transmission. There is some evidence from studies examining microbial contaminants in cabin air, that suggest air quality in an airline cabin is better than in most buildings [13-15] and most other means of public transportation (e.g. buses, trains, subways). Most modern airplanes operate a ventilation system with laminar air flow with exchange rates of 20 air exchanges per hours during cruising. Before re-entering the cabin, the air is filtered through a set of high-efficiency particulate air (HEPA) filters, which remove at least 99.97% of airborne particles between 0.1 and 0.3 µm in diameter and 100% of particles larger than 0.3 µm in diameter. However, when an aircraft is parked at the gate with the engines off for more than 30 minutes with passengers on board, adequate cabin ventilation should be ensured [16].

According to the IHR which legally bind 194 States worldwide, events of disease transmission among passengers on international flights require notification to the WHO [3]. Member States of the EU must further provide information on such cases through the appropriate designated structures and/or authorities in a timely manner to allow an effective joint response of the affected countries [4].

Assessing the risk of transmission of infectious diseases on board an aircraft is not always easy and often has to rely on individual expert opinion. The available

evidence is limited and assessing the publicly available evidence retrieved from the literature/grey literature is challenging. For most of the infectious diseases only a small number of studies are available on a limited number of events. The majority of the studies are observational, lack an appropriate control group and do not control for biases. In most of the reported studies the proportion of passengers (contacts) successfully traced and followed up is small, and for diseases with a long incubation period such as tuberculosis, asymptomatic passengers are often not followed up long enough to document seroconversion. For diseases with a high proportion of asymptomatic or mild cases or with an atypical presentation, cases are less likely to be detected because diagnostic tests are less likely to be performed. In addition, studies not showing transmission or disease outcome are less likely to be published (publication bias).

The decision on public health action and contact tracing has to be made fast and is influenced by several factors that differ between countries, such as the available resources, the purpose of contact tracing, its feasibility and the perception of the risk of the disease when evidence is lacking or when media attention or political pressure is high. Contact tracing requires significant resources in terms of manpower, money, and time. The amount of resources needed further depends on the objective of the tracing, e.g. whether it is done to initiate disease containment measures, disease mitigation measures, to delay the spread of the disease or to eradicate the disease. Only a limited number of studies are available on the cost-effectiveness of contact tracing in this regard. In the case of tuberculosis several studies indicate that the costs are high and the outcome is poor [17,18]. It must also be considered that adequate contact tracing in resource-poor countries may come at the expense of other more effective health measures [18]. Contact tracing is often complicated when passenger information is lacking. Aircraft manifests are not standardised across airlines and passenger lists are rarely kept for more than 48 hours. Legal matters and data protection issues could hamper the exchange of information between countries and organisations. Communication and coordination between the different national authorities can be complex and the proportion of contacts that can be successfully traced is often rather small [19,20].

Finally the perception of a risk plays a crucial role in its assessment and the decision for contact tracing. Assessments are influenced not only by the societal environment in which events occur and decisions are being made, but also by politics and the economic situation in a country. An infectious disease assessed at low risk, for instance, can have a significant economic and political impact in a certain context.

Conclusions

Considering the lack of published data available on evaluating the risk of transmission of most infectious agents on board aircrafts, and taking into account the key factors that influence the decision making, the RAGIDA guidance provides a viable evidence-based tool for public health authorities determining triggers and making decisions on whether to undertake contact tracing in air travellers or crew. These guidance documents may be adapted to the local situation, national and international regulations or preparedness plans. To improve the evidence base for contact tracing and to conclude on the cost-effectiveness of this public health intervention, information on the outcome of disease events during air travel needs to be collected continuously as initiated by this project.

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The European Centre for Disease Prevention and Control (ECDC) pilot point prevalence survey of healthcare-associated infections and antimicrobial use

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A standardised methodology for a combined point prevalence survey (PPS) on healthcare-associated infections (HAIs) and antimicrobial use in European acute care hospitals developed by the European Centre for Disease Prevention and Control was piloted across Europe. Variables were collected at national, hospital and patient level in 66 hospitals from 23 countries. A patient-based and a unit-based protocol were available. Feasibility was assessed via national and hospital questionnaires. Of 19,888 surveyed patients, 7.1% had an HAI and 34.6% were receiving at least one antimicrobial agent. Prevalence results were highest in intensive care units, with 28.1% patients with HAI, and 61.4% patients with antimicrobial use. Pneumonia and other lower respiratory tract infections (2.0% of patients; 95% confidence interval (CI): 1.8–2.2%) represented the most common type (25.7%) of HAI. Surgical prophylaxis was the indication for 17.3% of used antimicrobials and exceeded one day in 60.7% of cases. Risk factors in the patient-based protocol were provided for 98% or more of the included patients and all were independently associated with both presence of HAI and receiving an antimicrobial agent. The patient-based protocol required more work than the unit-based protocol, but allowed collecting detailed data and analysis of risk factors for HAI and antimicrobial use.

Introduction

Healthcare-associated infections (HAIs) and antimicrobial resistance are well known major public health threats. The European Centre for Disease Prevention and Control (ECDC) proposed in 2008 that the total burden of HAIs should be measured regularly and in a standardised manner throughout the European Union (EU) [1]. The initial steps towards standardisation of surveillance of HAIs in Europe had been carried out on surgical site infections and infections in intensive care units by the 'Hospitals in Europe Link for Infection Control through Surveillance (HELICS)' project, from 2000 to 2003 [2-6].

Subsequently, HELICS implemented standardised surveillance of HAIs in 2004 and 2005, and later as part of the 'Improving Patient Safety in Europe (IPSE)' network from 2005 to 2008 [7] which was transferred to ECDC in July 2008. Continuous surveillance, especially prospective active surveillance, is the gold standard [8]. However, repeated point prevalence surveys (PPSs) represent a more feasible alternative for hospital-wide surveillance of all HAIs, while still allowing the estimation of disease burden by HAIs in acute hospitals, and helping to prioritise areas requiring interventions [9]. Based on a review of 30 national or multicentre PPSs in 19 countries that had been carried out between 1996 and 2007 and included a total of 837,450 patients, ECDC estimated in 2008 the prevalence of HAIs in EU acute care hospitals to be on average of 7.1% [1].

However, major methodological differences between these PPSs made comparison between countries impossible [1,10-13]. When coordination of the IPSE network was transferred to ECDC in July 2008, ECDC recommended that surveillance in the EU should include all types of HAIs. Subsequently, the ECDC prepared a protocol for a PPS of HAIs in acute care hospitals, which was finalised in March 2011 [14].

Although most antimicrobials are prescribed in the community [15], the selective pressure they exert is

much higher in hospitals, where the proportion of patients receiving antimicrobial agents is much higher there than in the community [16]. This is considered to be the main reason why microorganisms isolated from hospital infections show more resistant profiles than microorganisms from community infections [17]. Various hospital PPSs on antimicrobial use were carried out in the last three decades [18-22]. Also these PPS varied greatly in aims, protocols and populations surveyed, thus making comparison of their results difficult. The 'European Surveillance of Antimicrobial Consumption (ESAC)' project initiated standardisation of the methodology for measuring antimicrobial consumption across Europe [23-26]. This methodology has proven feasible and reliable [24,25,27]. In view of the transition of the ESAC network to ECDC in July 2011, the ESAC methodology for PPS of antimicrobial use was integrated as part of an ECDC protocol for PPS of HAIs and antimicrobial use in acute care hospitals. Combined PPSs of HAIs and antimicrobial use had also previously been carried out in different populations [28-32], but again with large methodological differences between surveys.

The main aim of this ECDC pilot PPS was to test a common European methodology for PPSs of HAIs and antimicrobial use in acute care hospitals before its implementation across the EU, with the specific objectives to estimate the total burden of HAIs and antimicrobial use and disseminate the results at local, regional, national and EU level. The ECDC pilot PPS protocol met the objectives of the Council Recommendation of 9 June 2009 on patient safety, including the prevention and control of HAIs (2009/C 151/01), and specifically article II.8.c of this recommendation, i.e. "to establish or strengthen active surveillance at institution, regional and national level" [33]. In addition, the ECDC pilot PPS also met the objectives of Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC) [34].

Methods

Participating countries and hospitals

In January 2010, ECDC invited all national contact points for HAI surveillance and/or experts designated as national expert for the ECDC PPS to participate in the pilot PPS study and enter at least one institution qualified as acute care hospital according to national definitions. Two or more hospitals per country were preferred to allow testing of both the patient-based ('standard') and unit-based ('light') version of the protocol in the same country. In total, 23 countries (22 EU Member States and one EU enlargement country) participated in the survey with 66 hospitals and including 19,888 patients.

The number of hospitals per country was: Belgium (n=7 hospitals), Bulgaria (n=2), Croatia (n=2), Cyprus (n=3), Czech Republic (n=2), Estonia (n=2), Finland (n=16), France (n=3), Germany (n=1), Greece (n=1), Hungary (n=2), Italy (n=4), Latvia (n=2), Lithuania (n=3), Luxembourg (n=1), Malta (n=1), Poland (n=1), Portugal (n=2), Romania (n=1), Slovakia (n=2), Slovenia (n=2), Spain (n=5), and the United Kingdom, Scotland (n=1).

The national contact points acted as national PPS coordinators and invited hospitals to participate on a voluntary basis. As this was a pilot survey, we did not aim for a representative sample of hospitals in the countries. It was recommended to include both large and small hospitals in order to test the feasibility of the protocol in different settings. Information on the size and type (primary, secondary, tertiary and specialised) of each hospital was collected through a specific hospital questionnaire. National questionnaires were used to collect data on the number of acute care hospitals and beds for the entire country and by hospital type.

Case definitions

European case definitions for HAIs were used where these had been developed previously by HELICS or other European projects [35-38], whereas case definitions from the National Healthcare Safety Network (NHSN, formerly NNIS) at the United States Centers for Disease Control and Prevention (CDC) were used otherwise [39,40]. In the HAI section, data on microorganisms and the respective resistant phenotype were collected. Only results that were already available on the date of the survey were included.

For the purposes of this protocol, an infection was defined as active on the day of the survey when:

1. signs and symptoms were present on the date of the survey;
OR
2. signs and symptoms were no longer present but the patient was still receiving treatment for that infection on the date of the survey. In this case, the symptoms and signs occurring from the start of treatment until the date of the survey were checked to ascertain that the infection matched one of the case definitions of HAI.

An active infection was defined as healthcare-associated (associated to acute care hospital stay only, for the purpose of this protocol) when:

1. the onset of the signs and symptoms was on Day 3 of the current admission or later (with Day 1 the day of admission);
OR
2. the signs and symptoms were present at admission or became apparent before Day 3, but the patient had been discharged from an acute care hospital less than two days before admission;
OR
3. the signs and symptoms of an active surgical site infection were present at admission or started before Day 3, and the surgical site infection occurred within 30 days of a surgical intervention (or in the case of

surgery involving an implant, a deep or organ/space surgical site infection that developed within a year of the intervention);
OR
4. the signs and symptoms of a *Clostridium difficile* infection were present at admission or started before Day 3, with the patient having been discharged from an acute care hospital less than 28 days before the current admission.

For antimicrobial use, the Anatomical Therapeutic Chemical (ATC) classification system of the World Health Organization Collaborating Centre for Drug Statistics Methodology was used [41]. Antimicrobial agents for systemic use within the ATC groups A07AA (intestinal anti-infectives), D01BA (dermatological antifungals for systemic use), J01 (antibacterials for systemic use), J02 (antimycotics for systemic use), J04AB02 (rifampicin) and P01AB (nitroimidazole-derived antiprotozoals) were included. Antiviral agents and antimicrobials for the treatment of tuberculosis were not included.

As in the former ESAC hospital PPS protocol [23-26], antimicrobial treatment was recorded if, at the time of survey, the antimicrobial agent was still prescribed on the treatment chart. In the case of surgical prophylaxis, any single dose of an antimicrobial agent given within the 24-hour period before 8:00 am on the day of the survey was recorded. This time window for surgical prophylaxis allowed making the distinction between single dose prophylaxis, one day prophylaxis, or prophylactic doses given over more than one day.

Data collection and inclusion criteria

Two data collection protocols were available for use by participating hospitals. The first was patient-based: Denominator data, including risk factors, were collected for each individual patient irrespective of whether the patient had a HAI and/or received antimicrobials. The patient form for this protocol also included more detailed information, such as the presence of invasive devices, the specialty area of the patient's disease or consultant in charge of the patient and the McCabe score (the McCabe score classifies the severity of underlying medical conditions) [42]. The second protocol was unit-based: Denominator data were aggregated at ward level, and a patient form was used only for patients with a HAI and/or receiving antimicrobials. For both protocols, data were also collected at both ward level (ward name and specialty) and hospital level, including hospital type, size and whether or not any wards were excluded from the survey.

Each participating hospital had to choose one of the two data collection protocols. For each ward, all patients registered on the ward census before 8:00 am and not discharged from the ward at the time of the survey were assessed. Patients who were temporarily absent from the ward (e.g. for medical imaging, endoscopy, surgery) were included in the survey. Day admissions, outpatients (including patients attending the hospital for haemodialysis) and patients at the Accident and Emergency department were excluded. In addition, given that the agreed objective of the EU-wide ECDC PPS was to estimate the burden of HAIs and antimicrobial use in acute care hospitals only, long-term care units in acute care hospitals were excluded from the survey; however, long-term patients within an acute care ward were included. It was recommended that each participating hospital should include all eligible patients in the survey. Despite this recommendation, five of the 66 hospitals excluded one or several wards that were eligible for inclusion, because the hospital staff considered that being exhaustive was not needed for a pilot study.

The ECDC pilot PPS protocol recommended that personnel experienced in reading patient charts/notes and in identifying HAIs (e.g. infection control professionals, clinical microbiologists, infectious disease physicians) should act as survey team leaders in the hospitals. To obtain better information, collaboration with the clinical team in charge of patient care was recommended rather than exclusively reading the patient chart/notes and laboratory results. The number and type of healthcare workers (HCWs) performing the PPS in the hospital was assessed by questionnaire.

Data collectors in the hospital were trained by the national PPS coordinators to become familiar with the protocol and case definitions. Training material in English language was provided by ECDC through a contract with the Health Protection Agency, London (contract ECD.1842).

Time window

The ECDC pilot PPS had to be carried out any time between May and October 2010. The ideal duration of a 'point' prevalence survey is a single day but this was not feasible for the majority of participants due to the size of the hospital and/or the lack of trained personnel. To ensure feasibility of the survey, the maximum total time allowed to complete data collection in each hospital was three weeks and preferably not more than two weeks. Each individual ward, and if possible each respective department (e.g. all medical wards), had to be surveyed on the same day.

Data entry

Each country was free to organise its own system for data entry and processing, as long as all variables were collected in accordance with the ECDC methodology. It was not possible for a hospital to use a mixture of the patient-based and unit-based protocols. Most hospitals entered their data directly into an adapted version of the ESAC WebPPS located on the server of the University of Antwerp [24,25]. Only one country (Slovenia), participating with two hospitals, used its local software, whilst Belgium used the WebPPS installed on the server of the Belgian Scientific Institute for Public Health (WIV-ISP) in Brussels. Belgian data were uploaded on the WIV-ISP server and were

later incorporated into the European data set at the University of Antwerp. Data from Slovenia were converted by ECDC and then transferred to the University of Antwerp for incorporation into the central database.

Feasibility and workload

An additional feasibility questionnaire was sent to the national contact points of the 23 participating countries and to the corresponding 66 hospital contact points. At the national level, we requested information about whether a list of hospitals by type (primary, secondary, tertiary and specialised) and size was available, thus assessing the feasibility of a systematic sampling design using these variables in future surveys. National contact points were also asked to give any other feedback regarding the feasibility of obtaining a representative sample of hospitals in their country. In addition, data about the workload needed for training, data collection and data entry were requested both at the national and hospital level. The number and type of HCWs involved in the survey were also collected.

Data analysis

Data were analysed at the University of Antwerp and at ECDC using Stata 10.1 (StataCorp Texas, US). Binomial exact confidence limits were calculated where appropriate. Risk factor analysis was performed separately for HAIs and for antimicrobial use using multiple logistic regression. Presence of a peripheral and central vascular catheter were excluded from the multiple logistic regression model since the time relationship between insertion of a catheter and start of parenteral antimicrobial use cannot be deduced from the protocol. In both models, p values below 0.05 were considered as statistically significant. Individual hospital reports (Microsoft Excel spreadsheets) summarising the hospital's prevalence figures, compared to the aggregated prevalence figures of all participating hospitals in the country, were produced by ECDC using Stata 10.1 and sent to the national contact points for further distribution and feedback to the hospital contact points. We did not receive any feedback from the hospitals that these reports were not concordant with local hospital data.

Results

A total of 19,888 patients from 66 hospitals in 23 countries were included in the ECDC pilot PPS. Fifty hospitals used the patient-based protocol and 16 hospitals used the unit-based protocol.

Hospital characteristics were available for 65 hospitals. University or other teaching hospitals (defined as 'tertiary' hospitals in the protocol) represented 52.3% of participating hospitals, secondary hospitals 24.6%, primary hospitals 15.4% and specialised hospitals 7.7%, with an average hospital size of 614 beds, 431 beds, 215 beds and 300 beds, respectively. The overall average hospital size in the study sample was 483 beds (median: 400 beds). At national level, only 13 countries (representing 29 hospitals in the study sample) were able to provide national numbers of hospitals by type. Tertiary hospitals represented 7.7% of all acute care hospitals in these countries, secondary hospitals 31.1%, primary hospitals 49.3% and specialised hospitals 11.9%. The total number of hospitals in these 13 countries was 2,609 with on average 298

Table 1

Prevalence of healthcare-associated infections and antimicrobial use in surveyed patients, by specialty, during the ECDC pilot point prevalence survey, 2010 (n=19,888)

Specialty	Surveyed patients		Patients with HAI[a]		Patients with antimicrobial use[b]	
	n[c]	%[d]	n[c]	%[e]	n[c]	%[e]
Surgery	6,653	33.5	518	7.8	2,584	38.8
Medicine	7,833	39.4	505	6.4	2,888	36.9
Paediatrics	1,024	5.1	38	3.7	310	30.3
Intensive care	915	4.6	257	28.1	562	61.4
Obstetrics and Gynaecology	1,711	8.6	32	1.9	313	18.3
Geriatrics	502	2.5	33	6.6	117	23.3
Psychiatry	828	4.2	2	0.2	18	2.2
Other/mixed	422	2.1	23	5.5	83	19.7
All specialties	**19,888**	**100**	**1,408**	**7.1**	**6,875**	**34.6**

ECDC: European Centre for Disease Prevention and Control; HAI: healthcare-associated infection.

[a] Patients with a least one HAI.
[b] Patients receiving at least one antimicrobial agent.
[c] Number of patients in category.
[d] Percentage of total (column percent).
[e] Percentage within category (category percent).

beds (median: 261 beds), for a total population of 160 million inhabitants in 2010.

Healthcare-associated infections

Overall, 7.1% patients had at least one HAI, ranging from 0.2% in psychiatry to 28.1% in intensive care departments (Table 1). The prevalence of HAIs was 5.8% in primary hospitals, 6.3% in secondary hospitals, 7.4% in tertiary hospitals and 7.8% in specialised hospitals.

The most common type of HAI was pneumonia and other lower respiratory tract infections, representing 25.7% of all reported HAIs (Table 2). The second most frequently reported type of HAI was surgical site infection (18.9%), followed by urinary tract infection (17.2%), bloodstream infection (14.2%) and gastro-intestinal infection (7.8%). *Clostridium difficile* infections represented 1.4% of all HAIs. On average, there were 1.09 HAIs per infected patient (or a total of 1,531 HAIs in 1,408 patients with HAI). The median length of stay before onset of HAI acquired during the current hospitalisation (n=1,159) was 12 days (range: 4–65 days). Of 372 (24%) HAIs present at admission, 58% were associated with a previous stay in the same hospital.

For 59.1% of the HAIs, a positive microbiology result was available, ranging from 40.3% for gastro-intestinal infections to 94.0% in bloodstream infections (Table 3).

The most commonly isolated groups of microorganisms were Gram-negative non-*Enterobacteriaceae* in pneumonia (36.5%), *Enterobacteriaceae* in urinary tract infections (63.8%) and Gram-positive cocci in surgical site infections (54.3%). Overall, the most commonly isolated microorganism was *Escherichia coli* (15.2% overall, and 37.1% in urinary tract infections), followed by *Staphylococcus aureus* (12.1% overall and 21.5% in surgical site infections).

Carbapenem resistance was reported in 3.2% of *Enterobacteriaceae*, 23.4% of *Pseudomonas aeruginosa* and 20.4% of *Acinetobacter* spp. The percentage of meticillin-resistant *S. aureus* (MRSA) was 34.2% and that of glycopeptide-resistant *Enterococcus* spp. was 5.4%.

Antimicrobial use

A total of 6,875 patients (34.6%) received at least one antimicrobial agent at the time of the survey, ranging from 2.2% in psychiatry to 61.4% in intensive care departments (Table 1). The prevalence of antimicrobial use was 36.2% in primary hospitals, 32.1% in secondary hospitals, 35.7% in tertiary hospitals and 28.7% in specialised hospitals. Analysing the antimicrobial agents used by main indication (treatment, surgical prophylaxis and medical prophylaxis) revealed differences in the use of different antimicrobial classes (Table 4).

Pneumonia or other lower respiratory tract infection was the most common indication (29.2%) for antimicrobial treatment, and accounted for 31.6% of intentions for treatment of community infection, and 24.8% of intentions for treatment of hospital infection.

The most widely used antimicrobial agents at ATC 4th level were combinations of penicillins with beta-lactamase inhibitors (16.3%), mainly for treatment intention (18.0%). For surgical prophylaxis, first- and second-generation cephalosporins were mostly chosen: 26.8% and 20.0%, respectively. For medical prophylaxis, fluoroquinolones, primarily ciprofloxacin, were the most widely used antimicrobial agents.

Table 5 summarises the indications for antimicrobial use, their route of administration and whether the reason for antimicrobial use was indicated on the patient chart. Community infection was the most common treatment intention (41.3%), followed by hospital infection (24.0%). Surgical prophylaxis (17.3%) was prolonged for more than one day in 60.7% of cases. Medical prophylaxis accounted for 13.5% of antimicrobial use. The parenteral route of administration was used for 71.9% of administered antimicrobial agents. A reason was included in the chart of 69.3% of the patients on antimicrobials (Table 5).

Risk factors

Data from the 50 hospitals that used the patient-based protocol, including patient characteristics and risk factors, are shown in Table 6. Using multiple logistic regression, the presence of an HAI was independently associated with age (highest adjusted odds ratio in children under five years-old, $p<0.001$), male sex ($p<0.05$), length of stay before onset of HAI (p for trend<0.001), the McCabe score (p for trend<0.001), the number of invasive devices (urinary catheter and intubation) before onset of infection (p for trend<0.001) and surgery since admission ($p<0.001$). Antimicrobial use was independently associated with age (highest adjusted odds ratio in the age category 1–4 years, $p<0.001$), male sex ($p<0.001$), the McCabe score (p for trend<0.001), the number of invasive devices (urinary catheter and intubation, p for trend <0.001), length of stay in the hospital (p for trend<0.05) and surgery since admission ($p<0.001$).

Feasibility

Thirteen countries (Belgium, Bulgaria, Cyprus, Estonia, France, Greece, Italy, Lithuania, Malta, Portugal, Romania, Slovakia and Spain) responded to the national feasibility questionnaire. Fifty hospitals responded to the hospital feasibility questionnaire.

Overall, the average number of HCW involved in data collection, excluding ward staff, was six, with a maximum of 21. In five hospitals, one single HCW was involved in the data collection process. Ward staff was involved in 20 hospitals. On average per hospital, 3,7 different types of HCW were involved in the survey for

Table 2

Prevalence of healthcare-associated infections and antimicrobial use in surveyed patients, by specialty, during the ECDC pilot point prevalence survey, 2010 (n=19,888)

Type of infection	HAIs				Antimicrobial use (treatment only)[a]					
					All treatment intentions[b]		Treatment intended for community infection		Treatment intended for hospital	
	n patients[c]	% patients [95% CI][d]	n HAIs[e]	Relative % HAIs[f]	n intentions	Relative %	n intentions	Relative %	n intentions	Relative %
Pneumonia or other lower respiratory tract infection	392	2.0 [1.8–2.2]	394	25.7	1,328	29.2	922	31.6	382	24.8
Surgical site infection	290	1.5 [1.3–1.6]	290	18.9	–[g]	–[g]	–[g]	–[g]	–[g]	–[g]
Urinary tract infection	263	1.3 [1.2–1.5]	264	17.2	679	14.9	412	14.1	237	15.4
Bloodstream infection (BSI)[h]	216	1.1 [0.9–1.2]	217	14.2	219	4.8	67	2.3	145	9.4
Gastrointestinal infection	118	0.6 [0.5–0.7]	119	7.8	593	13.0	466	16.0	117	7.6
Skin and soft tissue infection	59	0.3 [0.2–0.4]	59	3.9	646	14.2	357	12.2	279	18.1
Bone or joint infection	38	0.2 [0.1–0.3]	39	2.5	154	3.4	92	3.2	60	3.9
Eye, ear, nose or mouth infection	47	0.2 [0.2–0.3]	47	3.1	211	4.6	170	5.8	41	2.7
Systemic infection[h]	40	0.2 [0.1–0.3]	40	2.6	668	14.7	318	10.9	334	21.7
Cardiovascular system infection	26	0.1 [0.1–0.2]	26	1.7	76	1.7	40	1.4	36	2.3
Central nervous system infection	15	0.1 [0.0–0.1]	15	1.0	67	1.5	54	1.8	12	0.8
Catheter-related infections without bloodstream infection	11	0.1 [0.0–0.1]	11	0.7	–[g]	–[g]	–[g]	–[g]	–[g]	–[g]
Reproductive tract infection	10	0.1 [0.0–0.1]	10	0.7	65	1.4	49	1.7	16	1.0
Missing/unknown	0	NA	NA	NA	65	1.4	39	1.3	25	1.6
Total	**1,408**	**7.1 [6.7–7.5]**	**1,531**	**100**	**4,552**	**100**	**2,919**	**100**	**1,539**	**100**

CI: confidence interval; ECDC: European Centre for Disease Prevention and Control; HAI: healthcare-associated infection; NA: not applicable.

[a] This table does not include antimicrobials used for prophylaxis or for unknown indications (shown in Table 5).

[b] The category "Treatment intended for infections acquired in long-term care facilities" represented 2.0% of all treatment intentions and is not shown in the table.

[c] Number of patients with HAI (site-specific number)

[d] Percentage of patients with HAI (site-specific prevalence)

[e] Number of HAIs.

[f] Percentage of total number of HAIs (relative percentage)

[g] For used antimicrobials, the types of infection 'surgical site infection' and 'catheter-related infection without bloodstream infection' were not specifically recorded and could be included within the category 'skin and soft tissue infection'.

[h] Includes catheter-related infections with positive blood culture, and neonatal bloodstream infections and clinical sepsis. For used antimicrobials, some bloodstream infections (bacteraemia) may have been included in the category 'systemic infection'.

Table 3

Distribution of microorganisms isolated in healthcare-associated infections, by main type of infection, ECDC pilot point prevalence survey, 2010 (n=1,165)

	All types of infection	Pneumonia or other lower respiratory tract infection	Surgical site infection	Urinary tract infection	Bloodstream infection	Gastrointestinal infection
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
HAIs and microorganisms						
HAIs, total	1,531 (100)	394 (25.7)	290 (18.9)	264 (17.2)	200 (13.1)	119 (7.8)
HAIs with microorganisms	905 (59.1)	191 (48.5)	172 (59.3)	187 (70.8)	188 (94.0)	48 (40.3)
Microorganisms, total	1,165 (100)	249 (100)	247 (100)	210 (100)	228 (100)	65 (100)
Major groups of microorganisms						
Gram-positive cocci	410 (35.2)	46 (18.5)	134 (54.3)	39 (18.6)	95 (41.7)	21 (32.3)
Enterobacteriaceae	404 (34.7)	80 (32.1)	58 (23.5)	134 (63.8)	79 (34.7)	18 (27.7)
Gram-negative bacteria, non-*Enterobacteriaceae*	226 (19.4)	91 (36.5)	36 (14.6)	29 (13.8)	30 (13.2)	7 (10.8)
Fungi	69 (5.9)	23 (9.2)	5 (2.0)	7 (3.3)	17 (7.5)	4 (6.2)
Top 15 microorganisms (accounting for (92.4% of total number microorganisms)						
Escherichia coli	177 (15.2)	24 (9.6)	29 (11.7)	78 (37.1)	29 (12.7)	10 (15.4)
Staphylococcus aureus	141 (12.1)	26 (10.4)	53 (21.5)	2 (1.0)	26 (11.4)	5 (7.7)
Pseudomonas aeruginosa	131 (11.2)	44 (17.7)	24 (9.7)	21 (10.0)	17 (7.5)	6 (9.2)
Enterococcus spp.	114 (9.8)	4 (1.6)	33 (13.4)	32 (15.2)	21 (9.2)	11 (16.9)
Coagulase-negative staphylococci	97 (8.3)	3 (1.2)	33 (13.4)	3 (1.4)	38 (16.7)	1 (1.5)
Klebsiella spp.	94 (8.1)	22 (8.8)	7 (2.8)	30 (14.3)	25 (11.0)	3 (4.6)
Candida spp.	56 (4.8)	15 (6.0)	3 (1.2)	6 (2.9)	16 (7.0)	3 (4.6)
Enterobacter spp.	49 (4.2)	13 (5.2)	10 (4.0)	6 (2.9)	10 (4.4)	1 (1.5)
Acinetobacter spp.	49 (4.2)	18 (7.2)	5 (2.0)	5 (2.4)	9 (4.0)	1 (1.5)
Streptococcus spp.	45 (3.9)	13 (5.2)	11 (4.5)	2 (1.0)	4 (1.8)	4 (6.2)
Proteus spp.	35 (3.0)	5 (2.0)	6 (2.4)	15 (7.1)	4 (1.8)	0 (0)
Anaerobic bacilli	24 (2.1)	1 (0.4)	5 (2.0)	0 (0)	5 (2.2)	11 (16.9)
Serratia spp.	17 (1.5)	11 (4.4)	1 (0.4)	0 (0)	5 (2.2)	0 (0)
Other *Enterobacteriaceae*	17 (1.5)	3 (1.2)	0 (0)	1 (0.5)	4 (1.8)	3 (4.6)
Stenotrophomonas maltophilia	16 (1.4)	11 (4.4)	3 (1.2)	0 (0)	1 (0.4)	0 (0)
Citrobacter spp.	15 (1.3)	2 (0.8)	5 (2.0)	4 (1.9)	2 (0.9)	1 (1.5)

ECDC: European Centre for Disease Prevention and Control; HAI: healthcare-associated infection.

The table only shows details for the main infection types. The total also includes all other HAI types.

Table 4

Distribution of antimicrobial agents (ATC 4th and 5th levels) by main indication for use, ECDC pilot point prevalence survey, 2010 (n=9,588 antimicrobial agents)

	All indications	Treatment	Surgical prophylaxis	Medical prophylaxis
	n (%)	n (%)	n (%)	n (%)
Antimicrobial agents, total	**9,588 (100)**	**6,365 (100)**	**1,654 (100)**	**1,293 (100)**
Top antimicrobial agents at ATC 4th level (accounting for 93.1% of use)				
Combinations of penicillins, incl. beta-lactamase inhibitors (J01CR)	1,566 (16.3)	1,147 (18.0)	217 (13.1)	145 (11.2)
Fluoroquinolones (J01MA)	1,293 (13.5)	948 (14.9)	133 (8.0)	168 (13.2)
Second-generation cephalosporins (J01DC)	900 (9.4)	475 (7.5)	330 (20.0)	76 (5.9)
Third-generation cephalosporins (J01DD)	701 (7.3)	521 (8.2)	94 (5.7)	67 (5.2)
First-generation cephalosporins (J01DB)	599 (6.2)	121 (1.9)	444 (26.8)	23 (1.8)
Carbapenems (J01DH)	583 (6.1)	503 (7.9)	25 (1.5)	37 (2.9)
Imidazole derivatives (J01XD)	494 (5.2)	278 (4.4)	151 (9.1)	51 (3.9)
Glycopeptide antibacterials (J01XA)	449 (4.7)	365 (5.7)	41 (2.5)	31 (2.4)
Aminoglycosides (J01GB)	427 (4.5)	277 (4.4)	72 (4.4)	69 (5.3)
Triazole derivatives (J02AC)	424 (4.4)	246 (3.9)	11 (0.7)	153 (11.8)
Penicillins, extended spectrum without anti-pseudomonal activity (J01CA)	289 (3.0)	200 (3.1)	18 (1.1)	65 (5.0)
Combinations of sulfonamides and trimethoprim, incl. derivatives (J01EE)	252 (2.6)	70 (1.1)	7 (0.4)	163 (12.6)
Lincosamides (J01FF)	232 (2.4)	183 (2.9)	38 (2.3)	11 (0.9)
Macrolides (J01FA)	185 (1.9)	144 (2.3)	4 (0.2)	26 (2.0)
Beta-lactamase-resistant penicillins (J01CF)	160 (1.7)	138 (2.2)	16 (1.0)	5 (0.4)
Nitroimidazole derivatives (P01AB)	134 (1.4)	102 (1.6)	17 (1.0)	9 (0.7)
Beta-lactamase-sensitive penicillins (J01CE)	133 (1.4)	90 (1.4)	9 (0.5)	32 (2.5)
Other antibacterials (J01XX)	102 (1.1)	80 (1.3)	4 (0.2)	11 (0.9)
Top antimicrobial agents at ATC 5th level (accounting for 70.8% of use)				
Amoxicillin and enzyme inhibitor (J01CR02)	1,045 (10.9)	696 (10.9)	193 (11.7)	104 (8.0)
Cefuroxime (J01DC02)	866 (9.0)	466 (7.3)	318 (19.2)	63 (4.9)
Ciprofloxacin (J01MA02)	844 (8.8)	607 (9.5)	100 (6.0)	113 (8.7)
Metronidazole (J01XD01)	493 (5.1)	277 (4.4)	151 (9.1)	51 (3.9)
Cefazolin (J01DB04)	473 (4.9)	57 (0.9)	396 (23.9)	12 (0.9)
Piperacillin and enzyme inhibitor (J01CR05)	432 (4.5)	374 (5.9)	19 (1.1)	36 (2.8)
Ceftriaxone (J01DD04)	396 (4.1)	282 (4.4)	52 (3.1)	47 (3.6)
Vancomycin (parenteral) (J01XA01)	376 (3.9)	310 (4.9)	36 (2.2)	26 (2.0)
Meropenem (J01DH02)	375 (3.9)	322 (5.1)	9 (0.5)	29 (2.2)
Fluconazole (J02AC01)	319 (3.3)	201 (3.2)	11 (0.7)	96 (7.4)
Levofloxacin (J01MA12)	310 (3.2)	246 (3.9)	13 (0.8)	34 (2.6)
Gentamicin (J01GB03)	265 (2.8)	151 (2.4)	62 (3.7)	46 (3.6)
Sulfamethoxazole and trimethoprim (J01EE01)	235 (2.5)	66 (1.0)	7 (0.4)	150 (11.6)
Clindamycin (J01FF01)	228 (2.4)	183 (2.9)	34 (2.1)	11 (0.9)
Imipenem and enzyme inhibitor (J01DH51)	141 (1.5)	120 (1.9)	11 (0.7)	7 (0.5)

ATC: Anatomical Therapeutic Chemical; ECDC: European Centre for Disease Prevention and Control; HAI: healthcare-associated infection.

The category "Unknown indication" represented 2.9% of the total and is included in the first column.

Table 5

Antimicrobial use: prevalence, indication, route of administration and reason in patient charts/notes, ECDC pilot point prevalence survey, 2010 (n=6,875 patients)

	Patients with antimicrobial use[a]		Antimicrobial agents	
	n	%[b] [95% CI]	n	Relative %[c]
Total	**6,875**	**34.6 [33.8–35.4]**	**9,588**	**100**
Indication				
Treatment	4,500	22.6 [22.0–23.3]	6,365	66.4
Intended for community infection	2,919	14.7 [14.1–15.2]	3,957	41.3
Intended for hospital infection	1,539	7.7 [7.–-8.1]	2,300	24.0
Intended for other healthcare-associated infection	94	0.5 [0.4–0.6]	108	1.1
Surgical prophylaxis	1,396	7.0 [6.7–7.4]	1,654	17.3
Single dose	336	1.7 [1.5–1.9]	357	3.7
One day	265	1.3 [1.2–1.5]	293	3.1
More than one day	810	4.1 [3.8–4.4]	1,004	10.5
Medical prophylaxis	979	4.9 [4.6–5.2]	1,293	13.5
Unknown indication	211	1.1 [0.9–1.2]	276	2.9
Route of administration				
Parenteral	5,098	25.6 [24.9–26.3]	6,891	71.9
Oral	2,218	11.2 [10.7–11.6]	2,648	27.6
Other/unknown	49	0.2 [0.2–0.3]	49	0.5
Reason in patient charts/notes				
Yes	4,819	24.2 [23.6–24.9]	6,647	69.3
No	2,171	10.9 [10.5–11.4]	2,939	30.7
Unknown	2	0.0 [0.0–0.0]	2	0.0

CI: confidence interval; HAI: healthcare-associated infection.

[a] Patients receiving a least one antimicrobial agent.
[b] Prevalence of antimicrobial use in each category.
[c] Percentage of total number of antimicrobials (relative frequency).

Table 6

Prevalence of healthcare-associated infections and antimicrobial use, by patient risk factors (standard patient-based protocol only, 50 hospitals), ECDC pilot point prevalence survey, 2010 (n=14,329)

	Surveyed patients		Patients with HAIs[a]		Patients with antimicrobial use[b]	
	n[c]	%[d]	n	%[e]	n	%[e]
All patients	**14,329**	**100**	**1,072**	**7.5**	**5,201**	**36.3**
Age group (years)						
<1	746	5.2	58	7.8	181	24.3
1–4	267	1.9	18	6.7	135	50.6
5–14	393	2.7	12	3.1	148	37.7
15–24	699	4.9	30	4.3	228	32.6
25–34	1,224	8.5	34	2.8	313	25.6
35–44	1,160	8.1	75	6.5	385	33.2
45–54	1,527	10.7	106	6.9	570	37.3
55–64	2,325	16.2	212	9.1	939	40.4
65–74	2,582	18.0	241	9.3	1,012	39.2
75–84	2,481	17.3	202	8.1	903	36.4
≥85	925	6.5	84	9.1	387	41.8
Sex						
Female	7,267	50.7	456	6.3	2,364	32.5
Male	7,062	49.3	616	8.7	2,837	40.2
Length of stay (days)[f]						
1–3	4,622	32.3	104	2.3	1,352	29.3
4–7	3,916	27.3	300	7.7	1,608	41.1
8–14	2,824	19.7	272	9.6	1,137	40.3
>14	2,966	20.7	396	13.4	1,104	37.2
Surgical intervention since hospital admission						
No	10,089	70.4	569	5.6	3,163	31.4
Yes	4,240	29.6	503	11.9	2,038	48.1
McCabe score						
Non-fatal	9,705	67.7	491	5.1	3,088	31.8
Ultimately fatal	3,666	25.6	430	11.7	1,645	44.9
Rapidly fatal	791	5.5	143	18.1	419	53.0
Missing/unknown	167	1.2	8	4.8	49	29.3
Central vascular catheter						
No	12,621	88.1	651	5.2	4,033	32.0
Yes	1,594	11.1	411	25.8	1,117	70.1
Missing/unknown	114	0.8	10	8.8	51	44.7
Peripheral vascular catheter						
No	7,455	52.0	389	5.2	1,565	21.0
Yes	6,763	47.2	674	10.0	3,592	53.1
Missing/unknown	111	0.8	9	8.1	44	39.6
Urinary catheter						
No	11,702	81.7	612	5.2	3,594	30.7
Yes	2,512	17.5	452	18.0	1,558	62.0
Missing/unknown	115	0.8	8	7.0	49	42.6
Intubation						
No	13,734	95.8	888	6.5	4,775	34.8
Yes	486	3.4	173	35.6	369	75.9
Missing/unknown	109	0.8	11	10.1	57	52.3

ECDC: European Centre for Disease Prevention and Control; HAI: healthcare-associated infection.

[a] Patients with a least one HAI.
[b] Patients receiving at least one antimicrobial agent.
[c] Number of patients in category.
[d] Percentage of total (column percent).
[e] Percentage within category (category percent).
[f] Length of stay until onset of HAI in case of HAI during current hospitalisation.

data collection and 1.3 for data entry. Eighteen hospitals were surveyed by an external team (either national or regional coordination staff) (Table 7).

A large variation among responding countries was identified in the workload associated with the PPS. The calculation of workload included preparation and training before the actual PPS, as well as data collection and data entry. National PPS coordinators provided on average 12.4 hours (median: 6 hours) of training to the hospital staff and spent on average an additional 6.5 hours (median: 4 hours) on answering questions during the survey. The time needed for collection and entry of data for 100 patients, was estimated at about four working days (ca. 32 hours) with the patient-based protocol and about 2.5 working days (ca. 20 hours) with the unit-based protocol. This means that performing the survey with the unit-based protocol took about 37.5% less time than with the patient-based protocol.
The feasibility of the data collection was also evaluated by the analysis of missing data in the database. At the national level, 11 of 23 countries were unable to provide national hospital denominator data by hospital type as defined in the protocol. At hospital level however, the hospital type was always available and the number of beds was only missing for one hospital. Ward level data were complete because all fields were mandatory in the software. Similarly, some patient level data (age, sex, hospital admission date and medical specialty of the patient's disease or the consultant), infection data and antimicrobial use data were mandatory in the software. For the other, non-mandatory variables of the patient-based protocol (n=14,329 patients), the percentage of missing values ranged from less than 1% for the presence of invasive devices, 1.2% for McCabe score, and 1.9% for surgery since admission, to 7.6% for surgery in the previous 30 days.

Discussion

The ECDC pilot PPS of HAIs and antimicrobial use was successfully performed from May to October 2010 in 66 acute care hospitals from 23 countries. In total, 19,888 patients were surveyed. The number of participating hospitals was higher than the anticipated minimum of 25 hospitals. The collected data allowed for the estimation of the prevalence of HAIs and antimicrobial use, which was the primary objective set by ECDC. Both the patient-based protocol, preferred by the majority (76%) of hospitals, and the unit-based protocol (applied by 24% of hospitals) provided the necessary data.

Main study limitations

An important limitation of our study is that the hospitals participating in this ECDC pilot PPS were not representative of the total hospital patient population in the EU. Hospitals were not randomly selected, and

Table 7

Type of healthcare workers involved in data collection and data entry for the ECDC pilot point prevalence survey, 2010 (n=50 hospitals)

Type of healthcare worker	Hospitals where this type of healthcare worker was involved		Involved in data collection		Involved in data entry	
	n	%[a]	n	%[b]	n	%[b]
Infection control nurse	25	50	25	100	9	36
Infection control physician or equivalent	31	62	31	100	12	39
Ward nurse	18	36	18	100	0	0
Ward physician	15	30	15	100	0	0
Infectious disease physician	12	24	12	100	3	25
Hospital microbiologist	6	12	6	100	3	50
Medical specialist trainee	10	20	10	100	2	20
Hospital pharmacist	6	12	6	100	1	17
Infection control link nurse	5	10	5	100	1	20
Data nurse	4	8	3	75	2	50
Nurse aid	1	2	0	0	1	100
Medical student	1	2	1	100	0	0
Other hospital staff	10	20	6	60	6	60
National PPS coordination staff	13	26	12	92	6	46
Regional PPS coordination staff	5	10	5	100	2	40
Other	6	12	4	67	3	50

ECDC: European Centre for Disease Prevention and Control; PPS: point prevalence survey.

[a] Percentage of total number of responding hospitals (n=50).
[b] Percentage of number of healthcare workers in category.

tertiary or teaching hospitals were overrepresented in the study sample (52.3% instead of less than 10%, according to available national hospital statistics). This selection had consequences both for the results of the feasibility test of the protocol and for the interpretation of the epidemiological results of the study (see below).

In addition, since inference from the epidemiological study results to the total acute care hospital population in Europe was not an objective of the pilot study, we did not apply any statistical methods that could take into account the effects of the hierarchical design of the study (e.g. regions within countries, hospitals within regions, wards within hospitals, and types of patients within wards). Methods such as multilevel modelling for risk factor analysis and complex survey analysis to adjust confidence intervals for the prevalence estimates at the national and EU level will be used to analyse the EU-wide PPS of HAIs and antimicrobial use that was conducted in 2011–12. The pilot study database was also used to estimate the expected design effect (DEFF) for different average sizes of hospitals (patient clusters) in order to estimate the required sample size for each country in the EU-wide PPS [14]. The overall DEFF in the pilot PPS was 5.3 for the prevalence of HAIs and 22.7 for the prevalence of antimicrobial use, indicating indeed that the sample design for representative samples at the national level should be adjusted for the important clustering of the main survey outcomes within the hospitals.

Feasibility study

A minority of respondents to the feasibility questionnaire mentioned that the participating included hospitals in their country had had experience in performing PPSs and that it is unlikely that randomly selected hospitals would be able to participate in an ECDC EU-wide PPS. ECDC therefore provided training material to help national contact points improve the skills of hospital staff during preparation of the future EU-wide PPS. Part of this training material was already available before the pilot PPS and was used to organise the training of the hospital contact points in the current study.

Training is also of key importance for the standardisation of data collection in participating hospitals, including interpretation of the case definitions. The large variation in the number and type of HCWs involved in data collection for this pilot PPS (Table 7) illustrates the challenge of standardising data collection for an EU-wide PPS. For example, failure to consult the clinical team in charge of patient care during data collection, as recommended in the protocol, may impact on the ascertainment of variables such as the medical specialty of the patient's disease or of the consultant in charge of the patient (patient/consultant specialty), the McCabe score, the physician's motive for prescribing antimicrobials, or even the signs and symptoms of a suspected HAI. The fact that ward staff was not involved in the data collection in more than half of the hospitals may indeed indicate that physicians were not sufficiently consulted. Also, the fact that in 18 of the 66 hospitals the survey was performed by an external team may indicate that the pilot PPS was not always performed in real-life conditions since this scenario is unlikely to be a feasible option for the ECDC EU-wide PPS or a full-scale national PPS.

Another frequently mentioned feasibility issue was the difficulty to categorise hospitals at the national level according to the hospital types defined in the protocol (primary, secondary, tertiary and specialised). Information on hospital categories used in the different countries are needed for the future EU-wide PPS to ensure that all categories are represented proportionally in the national representative sample. In addition, national denominator data (e.g. number of hospitals and discharges per year) by hospital type would be needed (i) to extrapolate the PPS results by hospital type (category-specific burden estimates), and (ii) to adjust the national and EU burden estimates in case hospital types are not proportionally represented in the national samples. Only 13 of 23 countries were able to provide some categorisation of their national list of hospitals according to the categories of the protocol, using the national hospital type categories.

Therefore, for the purpose of drawing a representative systematic sample of hospitals for the EU-wide PPS, the standardised EU types of hospitals were replaced by the national hospital categories in the final protocol of the ECDC EU-wide PPS. This means that, for the analysis of the data collected in the ECDC EU-wide PPS, it will not be possible to stratify or adjust the estimates of the burden of HAIs and antimicrobial use (based on extrapolation to the total national denominator data) according to types of hospitals.

Patient-based versus unit-based protocol

Despite a higher workload, the patient-based protocol was used more often than the unit-based protocol, thus allowing a better description of patients and invasive procedures. During an expert meeting held in Brussels in November 2010, it was recommended that PPSs of HAIs and antimicrobial use should be carried out at least once every five years, and the patient-based protocol was selected as the preferred methodology for future PPSs [43]. This expert recommendation is anticipating the fact that, because of hospital changes and medical advances, a patient-based protocol would be required to allow for detailed adjustment for patient case-mix. The patient-based protocol allows for assessment of the prevalence of HAIs and antimicrobial use according to the presence or absence of various risk factors and enables categorisation of hospitals by patient case-mix at national and/or European level. Indeed, adjustment for patient case-mix has been used in other studies, including for outcomes in intensive care [44,45] and surgical patients [46], and for comparing HAI rates [47]. Patient-based PPSs can also be used to identify patient-related factors that influence

the prevalence of HAIs and thus help focus surveillance and infection prevention initiatives [48].

The unit-based protocol, however, will be kept, to offer a less labour-intensive option for countries and hospitals where human resources are limited. This protocol might also be more appropriate for very large hospitals and in situations that require repeated PPSs at short intervals. A limitation is that its only denominator variable is the number of patients per ward, for the total ward and for the specialty of each patient's disease within each ward. This only allows an estimation of the prevalence of HAIs and antimicrobial use by ward or patient's disease specialty.

The ECDC pilot PPS also aimed at identifying any issue with the methodology that required modification, e.g. availability of data for any of the collected variables, or applicability of the case definitions for HAIs, before finalising the patient-based and unit-based protocols for the ECDC EU-wide PPS that was started in May 2011. Denominator data in the unit-based protocol did not require any modification whereas, for the patient-based protocol, the only variable that was difficult to obtain was 'surgery in the previous 30 days'. This variable also overlapped with 'surgery since admission' which was less difficult to determine. It was therefore decided that, for the ECDC EU-wide PPS, the data for the variable 'surgery in previous 30 days' would eventually not be collected [14]. With respect to case definitions for HAIs, a major change was the decision to add the case definition of clinical sepsis in adults, because possible bloodstream infections for which microbiological results were not yet available at the time of the PPS would otherwise remain unreported.

Epidemiological results

The two sections of the ECDC pilot PPS, i.e. HAIs and antimicrobial use, were independent of each other and did not follow the same definitions: data on HAIs were recorded following standardised epidemiological case definitions, whilst the indication for antimicrobial use was based on clinical judgment by the treating physician. For example, a patient could have been registered in the antimicrobial use section as receiving antimicrobials with the intention to treat a hospital infection, but the same patient did not fulfil the case definition for HAI and therefore was not included as having a HAI in the HAI section. Conversely, a patient may have presented the symptoms and signs of a HAI, but not have been treated with an antimicrobial. Hence, among other things, the different proportions for hospital-acquired pneumonia in Table 2.

While the protocol for the EU-wide PPS foresees a representative systematic random sample of hospitals in the participating countries [14], the data collected through this ECDC pilot PPS were not representative of the epidemiology of HAIs in the EU and the results must be interpreted with caution. The HAI prevalence of 7.1% (inter-quartile range: 4.2–9.4%) observed in our study is likely to be slightly overestimated because of the overrepresentation of tertiary hospitals which had a higher prevalence of HAIs (7.4%) than secondary and primary hospitals. Nevertheless, the overall HAI prevalence in this pilot PPS is comparable to that reported in other European studies [9,11,12] and to the European prevalence of HAIs of 7.1%, estimated by ECDC based on a review of 30 national or multicentre PPSs in 19 countries in its Annual Epidemiological Report for 2008 [1]. The range of reported prevalence results in studies that used CDC definitions for HAIs in non-EU countries, ranged from 4.9% in Mauritius in 1992 to 19.1% in Malaysia in 2001 [30]. Such a wide range in the prevalence of HAIs could be explained by differences in methodology and patient case-mix, and should not immediately be interpreted as an indication of variations in performance.

The distribution of isolated microorganisms in patients with HAI in this pilot PPS was also similar to that previously reported in the review of national or multicentre point prevalence surveys, with *E. coli* being most frequent [1]. The fact that only 59.1% of the HAIs were documented by microbiological results was also in line with previous findings [9,49,50] and was expected because, with few exceptions, case definitions of HAIs are primarily based on clinical criteria.

With respect to antimicrobial use, the ECDC pilot PPS showed a prevalence about 5% higher than shown by previous ESAC hospital PPSs using an identical methodology [23,25,26]. Nevertheless, the ranking order of the most used antimicrobials was comparable to that observed in ESAC hospital PPSs, with the various beta-lactams (penicillins, cephalosporins and carbapenems) accounting for more than half of all antimicrobials used. Other PPSs have reported a wide range of prevalence of antimicrobial use in acute care hospitals due to varying inclusion criteria [23].

A final aspect that should be considered for the interpretation of the epidemiological results of this and future surveys is the fact that the ECDC pilot PPS was not performed on a single day. For feasibility reasons, hospitals were allowed to organise the PPS within a period of three weeks, with the only restriction being that a ward had to be surveyed on a single day. In practice, hospitals and countries performed the pilot PPS survey from May until October 2010. For the EU-wide PPS, ECDC agreed with the national PPS coordinating centres in November 2010 on three possible periods to organise the first national PPS using the ECDC methodology [43]. These periods (May–June 2011, September–October 2011 and May–June 2012) were selected to avoid the winter period because of the higher incidence of respiratory tract infections and the summer holiday period because shortage of staff and lower activity in the hospital during this period could influence the practical organisation as well as the main outcomes of the survey. Despite these considerations, the potentially long time span between the different

surveys may influence comparability of the results between hospitals, regions or countries, e.g. because of rapidly changing incidences of HAIs with epidemic pathogens or the implementation of local or national infection control measures.

In conclusion, the ECDC pilot PPS methodology was successfully implemented by the national contact points, the hospital contact points and the HCWs involved in data collection and entry in the participating hospitals, without any major feasibility issues that could have led hospitals to cancel their participation. The pilot PPS showed that the aim of estimating the burden of HAIs and antimicrobial use in European acute care hospitals was realistic, irrespective of the protocol used. The patient-based protocol, even if more resource-intensive, was used more widely and provided more detailed and valuable data than the unit-based protocol. It was therefore selected as the preferred option for the ECDC EU-wide PPS of HAIs and antimicrobial use.

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Evidence-Based Medicine applied to the control of communicable disease incidents when evidence is scarce and the time is limited

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Control of acute communicable disease incidents demands rapid risk assessment, often with minimal peer-reviewed literature available but conducted in the public's view. This paper explores how methods of evidence-based medicine (EBM) can be applied in this scenario to improve decision making and risk communication. A working group with members from EBM organisations, public health institutions and the European Centre for Disease Prevention and Control used a six-stage framework for rapid risk assessments: preparation, risk detection/verification, risk assessment, development of advice, implementation, and evaluation. It concluded that data from observational studies, surveillance and modelling play a vital role in the evidence base. However, there is a need to further develop protocols and standards, to perform, report and register outbreak investigations more systematically and rigorously, and to allow rapid retrieval of the evidence in emergencies. Lack of evidence for risk assessment and advice (usual for new and emerging diseases) should be made explicit to policy makers and the public. Priorities are to improve templates for reporting and assessing the quality of case and outbreak reports, apply grading systems to evidence generated from field investigations, improve retrieval systems for incident reports internationally, and assess how to communicate uncertainties of scientific evidence more explicitly.

Introduction

Public health agencies responsible for the control of public health emergencies are expected to work according to the best standards of scientific evidence. They need to be explicit about the source, type, quality, scope and completeness of the evidence, so that policy makers, politicians and the public can understand the evolving nature of evidence, its strengths and limitations [1]. Even in the acute situation of infectious disease emergencies such as an influenza pandemic, agreed protocols for developing policy and advice should be followed. However, there are two important challenges: reliance upon limited field investigations and population surveillance data, and the speed with which evidence has to be identified and synthesised.

In 2010 the European Centre for Disease Prevention and Control (ECDC) set up a working group to review the potential utility of currently used evidence-based medicine (EBM) tools and risk assessment tools in realistic communicable disease outbreak scenarios, and to propose new tools [2]. A group of experts from 12 countries working in EBM and public health institutions or at ECDC, with a broad range of experience in public health methodology and infectious diseases, were appointed to give guidance on how to strengthen the scientific work at ECDC by adapting and applying EBM methods that were practical and applicable in the environment of infectious diseases and public health.

In this paper we report the conclusions on how to apply the principles of EBM in situations where rapid risk assessment is needed.

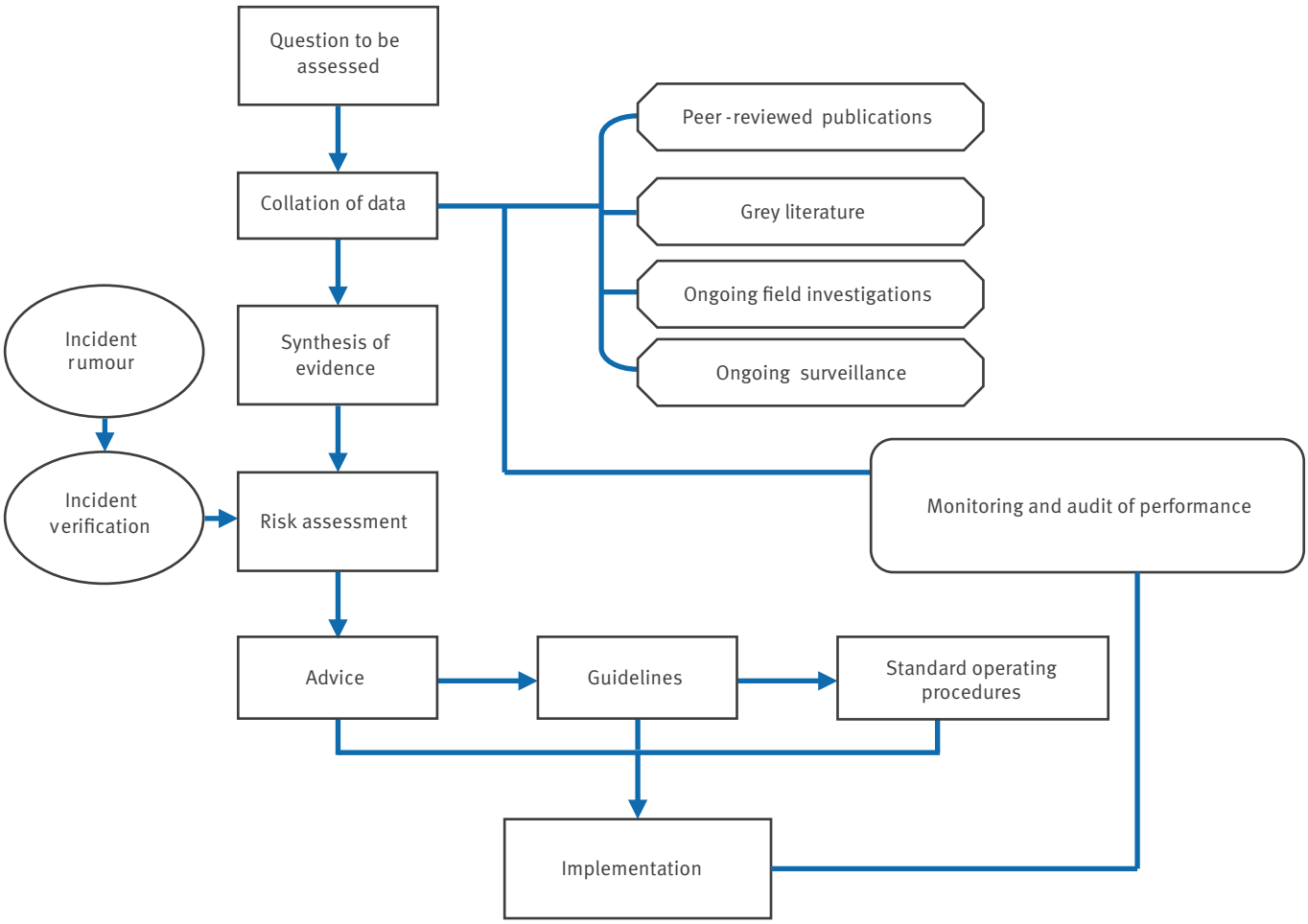
Methods and results

The working group presented the experiences of Member States in providing evidence-based guidance in circumstances when time was short, including the influenza pandemic in 2009 [3] and the Q fever epidemic in the Netherlands [4]. Consensus within the group was reached through informal group processes, through plenary and smaller group discussions, and by review of draft texts by the members and work colleagues in their institutions. The group members are listed at the end of the article.

The development of evidence for control of any incident, outbreak or pandemic was conceptualised as a knowledge cycle in which data are collated from surveillance and field investigation reports and peer-reviewed literature, rapidly appraised and used to

Figure 1

Evidence cycle in outbreak recognition, investigation, control and review



assess risks, develop advice and implement control measures. Continued surveillance, monitoring and auditing further consolidate the evidence base and allow refinement of risk assessment and evaluation of the effectiveness of interventions (Figure 1). Usually in the acute incident the knowledge cycle is entered at the risk assessment stage, when a report of an incident has to be verified, evidence collated and synthesised, and the risk assessed.

We identified six stages that need to be considered when preparing a rapid risk assessment under time constraints, and the need for improvement in each. They are summarised in the Table and described in detail below.

Stage 1: Preparatory phase

Alerting and surveillance systems should be set up that are regularly reviewed for fitness for purpose [5]. For newly emerging infections, the published data available to carry out systematic reviews will necessarily be very limited. It is therefore vital that critical summaries of evidence about epidemiology and control of these diseases are kept up to date and accessible internationally, including specifying key gaps in knowledge and suggesting appropriate models for risk assessment. Outbreak investigations are vital for defining epidemiological characteristics of specific pathogens (e.g. reproduction number) and can be used to evaluate the success of interventions [6,7]. However, to the best of our knowledge there are no agreed international standards for outbreak investigation and reporting. The value of field investigations would be greatly improved if a standardised framework for conducting, reporting, and synthesising data from outbreak investigations was used. Such standards exist for strengthening the reporting of observational studies in epidemiology (STROBE) [8], for the transparent reporting of evaluations of non-randomised designs (TREND) [9], and for meta-analysis of observational studies (MOOSE) [10]. Fine-tuning and evaluation for their application to outbreak situations has been undertaken for hospital

outbreaks (the outbreak reports and intervention studies of nosocomial infection (ORION) statement) [11]. For outbreak reports to be useful to others in a timely way, there needs to be an international repository of such reports and international agreement to make data rapidly available to investigators.

We identified tools and decision aids that we think would greatly improve public health decision making in acute outbreak situations.

- Up-to-date critical summaries of evidence from epidemiology and control of infectious diseases;
- Quality standards for performance and reporting of surveillance and field investigations;
- An international database of outbreak reports, accessible for all and with a user-friendly search function.

Stage 2: Incident verification

The critical step at this stage is to recognise the alert signal among the background noise of information. The agreed terminology outlining the epidemic intelligence process is the following:

- A signal needs to be filtered;
- An event needs to be validated;
- A validated event needs to be analysed.

In order to reduce the risk of bias, reproducible, transparent and explicit incident verification protocols should be followed. The process of verification requires rapid international communication networks of communicable diseases units. Algorithms should include trigger levels for upscaling, and stopping rules, to allow control agencies to agree that further investigation or more detailed risk assessment are not considered appropriate so that resources can be prioritised efficiently [12].

Tools required for this stage:

- International alerting and verification systems (e.g. the European Union's Early Warning and Response System [13]),
- Effective communication platforms (e.g. The European Union's Epidemic Intelligence Information System [14]).

Stage 3: Assessment of risk

This stage follows the verification of a threat and should address specific population groups at risk of more severe disease/outcome (e.g. pregnant women, the elderly, young children and immune-compromised individuals), and those at increased risk of exposure (e.g. healthcare workers). For rare, new and emerging infections there may be little or no peer-reviewed literature, and assessments will depend on field investigations, data from ongoing surveillance, and communication with experts in other countries. A comprehensive international database of outbreaks does currently not exist. Systematic methods for rapid searching and appraisal need to be developed that are appropriate to the time scales involved.

In order to reduce bias and to provide transparent quality assurance, risk assessment protocols and algorithms should be followed, and these should explicitly include frameworks for the synthesis of different types of evidence in relation to public health questions (e.g. risk of influenza A(H1N1) infection to pregnant women at different stages of pregnancy), admit to gaps and uncertainties in the evidence and possible alternative explanations of findings. Evidence should be classified by type (e.g. case report, population surveillance, field investigation) and study quality assessed through evidence-based checklists or tools such as the graphic approach to epidemiology (GATE) instrument for critical

Table

Conceptual stages in rapid risk assessment and proposed evidence-based medicine tools

Stage	Task	Tools
Stage 1	Preparatory phase	Summaries of evidence from epidemiology and infectious disease control Quality standards for performance and reporting of surveillance and field investigations An international database of outbreak reports
Stage 2	Incident verification	Alerting and verification systems Effective communication platforms
Stage 3	Assessment of risk	A protocol for rapid searching for relevant peer-reviewed and grey literature Checklists and templates for rapid appraisal of the evidence An international database on incidents and reports A rapid risk assessment procedure and tool
Stage 4	Developing advice	Guidance on developing advice Uncertainty tables
Stage 5	Implementation	A checklist of key points to address in risk communication
Stage 6	Monitoring and evaluation	A protocol for review and audit

appraisal [15] and rapid risk assessment algorithms [16].

Tools required for this stage:

- A protocol for rapid searching for relevant peer-reviewed and grey literature,
- Checklists and templates for rapid appraisal of the evidence,
- An international database on disease incidents and outbreak reports,
- A rapid risk assessment procedure and tool.

Stage 4: Developing advice

Guidance will need to recognise explicitly the situational context and the population groups to which it is applied, but should seek to follow agreed EBM principles as embodied in, for example, the guidelines evaluation tool AGREE II (appraisal of guidelines for research and evaluation) [17]. The grading of recommendations applicability, development and evaluation (GRADE) instrument was developed to evaluate and make explicit the steps from evidence to recommendations about treatments of diseases, but these principles also apply when a public health decision is to be made under time constraints [18]. An essential part of developing advice is to state clearly what are the options for interventions and the expected relative merits of different options, as well as openness in dealing with uncertainty [19]. Following the principles of EBM under pressure of time will usually reveal a higher level of uncertainty about the conclusions and recommendations than medium- or long-term risk assessments. We are aware that it is difficult, especially for public health agencies, to translate scientific uncertainty into policy advice [20]. Stakeholders expect certainty and clear answers. However, we also believe that scientific uncertainty should be included in the assessment and the decision-making process as information, not ignored [21].

The working group considered the added value to communicable disease incident control of integrating principles from the discipline of risk analysis, as embodied, for example, in the Codex Alimentarius [22]. If we consider the Public health decision making process as a predictive model, uncertainties can arise both from the potential errors associated with the structure of the model (such as the context of the outbreak, modes of transmission and potential control measures for new infections) and from uncertainties in the values of the model parameters (incomplete data or measurement errors) [23]. These uncertainties are an integral part of scientific judgment and should be reflected in communication with policy makers and the public.

Tools required:

- Guidance on developing advice, including assessment of the quality of evidence;
- Uncertainty tables addressing uncertainties arising directly from the data and from the model/ process used to capture and interpret the data.

Stage 5: Implementation

For effective implementation, advice must be framed by requirements of the target groups. Public perception and communication of risk must therefore be considered. Various governments and international organisations have published guidelines on risk communication which embrace the need for consistent, credible and high-quality information to be shared with the public [24,25]. In acute scenarios, the rapidly changing picture and accumulation of intelligence needs to be explained, and caveats about interim advice clearly admitted.

Tools required:

- A checklist of key points to address in risk communication.

Stage 6: Monitoring and evaluation

The last stage is monitoring the implementation of control measures. It is increasingly recognised by public health agencies that they should have in place systems for learning lessons from incidents and continuously improving performance [26]. Therefore, incidents should be reviewed systematically to identify the lessons for better management of future incidents, and to identify new knowledge about the causative agent and the risks to the population. This would be aided by the use of standardised audit tools [27] and protocols [28] that should be followed to give a rapid but systematic approach to identifying lessons within a framework of organisational accountability.

Tools required:

- Protocols for review and audit of lessons to be learned from of incidents.

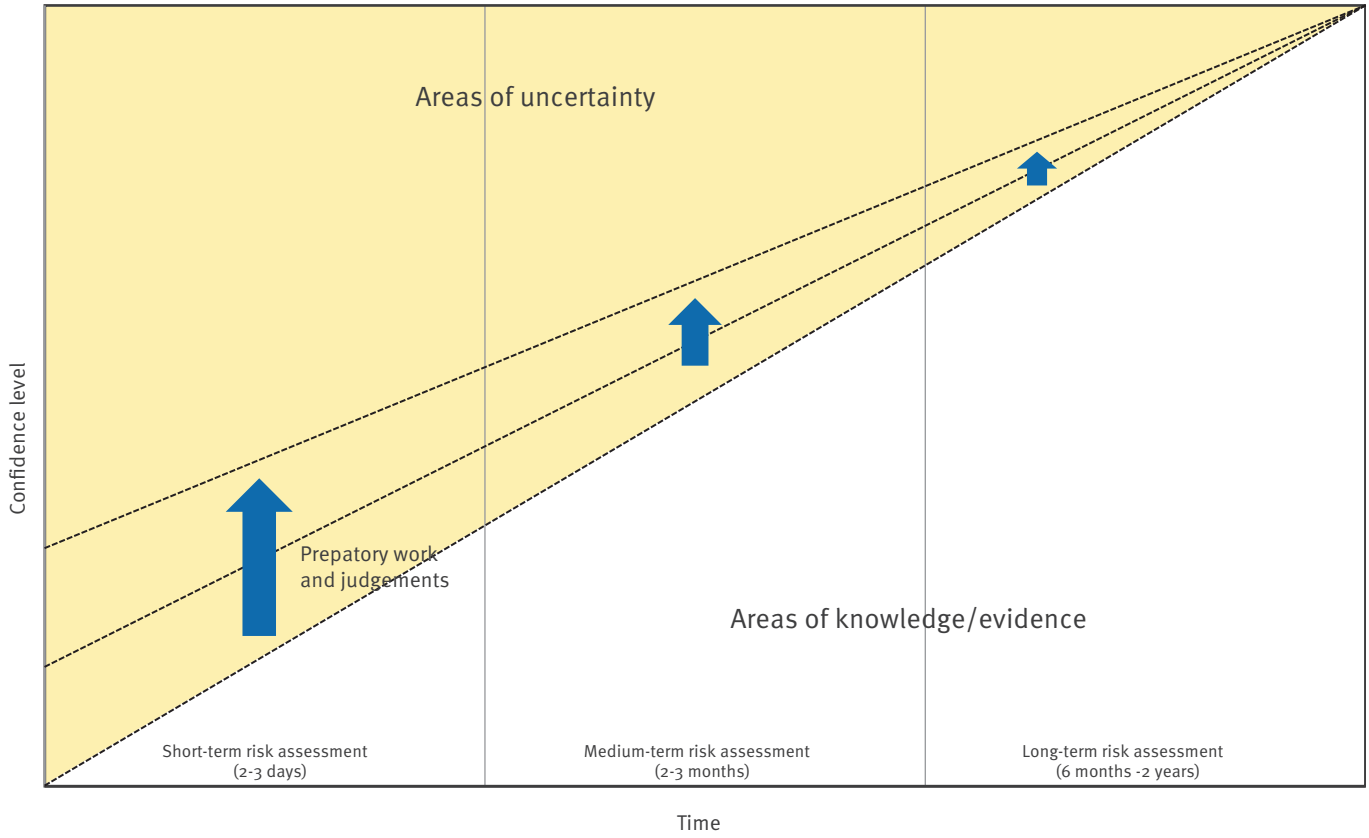
Discussion

The validity, credibility and success of public policy and risk management of public health threats are increasingly being seen as dependent upon the use of the best available scientific evidence developed through a transparent and open process [1]. To this end, a working group set up by ECDC has assessed the potential value of a more widespread use of strategies from evidence-based medicine in communicable disease control.

The EBM movement started as an application of epidemiological and public health principles in clinical practice; the application to public health threats is a more recent trend [28]. We recognise that there are important distinctions between evidence-based strategies applied to the review and appraisal in clinical medicine and the reality of public health policy making and communicable disease control, not least the lack of a strong evidence base and the pressure of time. In the sister discipline of risk analysis it is also increasingly being recognised that public health decision making is generally a result of a more complex interaction of the best available evidence from research and other epidemiological sources, with judgements made on needs,

Figure 2

Conceptual model of the relationship between uncertainty and time in risk assessments



resources, local circumstances, and ethical, legal and societal implications [29].

We see considerable merit in an integrative approach bringing risk analysis methods together with the epidemiological principles of EBM. For example, the EU Scientific Committee for New and Emerging Health Risks uses the expression 'lines of evidence' to characterise different sources and levels of evidence and information [29]. They consider lines of evidence that lie at the bottom of the EBM hierarchy. The highest levels of evidence from systematic reviews of randomised trials are seldom available in acute communicable disease incidents and advice has to be derived from observational studies underpinned by microbiological and virological principles. Sometimes advice has to be based on analogy and modelling, using laboratory research, animal experiments and mathematical modelling of outbreak data. When empirical data in an outbreak emerge, they first appear in expert committee papers and conference presentations, well before peer-reviewed publication, making it difficult to identify that knowledge systematically and quickly. But as with higher-level forms of evidence, the quality of such studies, their collation and interpretation should be guided by EBM methods. This demands the application of rigorous, standardised and systematic ways of handling evidence so that the risk of bias is minimised and assumptions are made explicit.

The application of risk analysis methods is particularly important when dealing with the uncertainties implicit in rapid decision making. It is important to acknowledge that the level of confidence in the conclusions reached is typically inversely related to the time that has passed since the start of the event (Figure 2).

The confidence level which can be achieved for short-term risk assessments is largely dependent upon the preparatory work done. "*Constraints, uncertainties and assumptions having an impact on the risk assessment should be explicitly considered at each step in the risk assessment and documented in a transparent manner. Expressions of uncertainty or variability in risk estimates may be qualitative or quantitative, but should be quantified to the extent that is scientifically achievable*" [22]. The applicability and relevance of standard EBM methods increases with time as the outbreak investigations proceed, but at any particular time there is also the necessity to consider the application of the

precautionary principle, and to be clear that lack of evidence of harm is not interpreted as evidence for no harm [30]. The principles of EBM, working rigorously, systematically and transparently and according to best available evidence, should apply at all times.

Next steps

In order to improve the management of outbreaks of communicable disease across Europe, the working group developed a conceptual framework and a potential set of tools and checklists that need to be developed to deal with the twin pressures of timeliness of risk assessment and lack of evidence. We hypothesise that these tools would improve outbreak management and thereby reduce the human and resource costs of outbreaks. They would also provide a clear auditable trail of decision making that would allow continuous learning from outbreaks. We envisage that the tools described above, collected together with worked examples in the format of a work book, could provide a uniform, consistent methodology for health protection practitioners. The international health protection community should work together to take this agenda forward and in particular identify leadership and responsibilities for developing the tools and for setting up and managing the archives and databases identified as a necessary part of EBM applied to outbreak control. Led by the Robert Koch Institute and based on a tender from ECDC, a multidisciplinary team has started to develop and pilot a systematic, transparent and comprehensive evidence assessment framework for rating the evidence and strength of recommendations in the area of infectious disease prevention and control.

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European Antibiotic Awareness Day: a five-year perspective of Europe-wide actions to promote prudent use of antibiotics

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Following the European Union (EU) Council Recommendation on prudent use of antimicrobial agents in human medicine in 2001, and the success of national campaigns, i.e. Belgium and France, the European Centre for Disease Prevention and Control (ECDC) decided to establish the European Antibiotic Awareness Day (EAAD) on 18 November as platform to support national campaigns across Europe. This article provides an overview of EAAD tools, materials, and activities developed during the first five years. It shows that EAAD has been successful due to good cooperation between ECDC and national institutions, strong political and stakeholder support and evidence-based development of campaign materials. EAAD has provided a platform for pre-existing national campaigns and encouraged similar campaigns to develop where neither political support had been secured, nor financial support had been available. As a result, participating countries have continuously expressed strong support for ECDC to continue its work on EAAD. This has been endorsed by a steadily increasing number of countries participating and the growing interest of varied professional and stakeholder organisations. We conclude that EAAD should continue to act as catalyst for discussion and as mechanism to raise awareness of the public and prescribers about prudent use of antibiotics.

Introduction

The emergence and spread of antibiotic resistance, is recognised as a global problem. Its immediate consequence is that, only a limited number of antibiotics, and sometimes even no antibiotic, is available for the treatment of infections caused by resistant bacteria. Other direct consequences for patients include delayed administration of appropriate antibiotic therapy, longer stays in hospitals, higher healthcare costs and poor patient outcomes [1]. Worldwide action is thus necessary to avert an impending threat to human health [2].

Of the steps that need to be taken to address antibiotic resistance, we believe that improving antibiotic use is the most important action needed to greatly slow the development and spread of antibiotic-resistant bacteria. Antibiotics are frequently used inappropriately or when they are not needed, in both humans and animals.

Following adoption of the European Union (EU) Council Recommendation on the prudent use of antimicrobial agents in human medicine in November 2001, which stated that EU Member States should inform the general public of the importance of prudent use of antimicrobial agents and the success of some national campaigns, such as Belgium and France, the European Centre for Disease Prevention and Control (ECDC) decided in 2008 to establish the European Antibiotic Awareness Day (EAAD) on 18 November as a platform for providing support to national campaigns across the region [3].

Since 2008, numerous health-related and professional organisations, as well as the European Commission and the World Health Organization Regional Office for Europe (WHO/Europe), have partnered with ECDC in preparing communications materials and planning activities targeting both communities and hospitals for EAAD. In 2012, under the banner of EAAD, national campaigns to inform about prudent antibiotic use took place in 43 European countries, with the target audiences selected by campaign organisers at national level, including both general public and prescribers.

This perspective describes the development of materials and tools during the past five years, and provides a review of the activities and achievements of EAAD. It also presents results from the annual questionnaire provided by participating countries and from an independent monitoring of the media coverage.

Development of materials and tools for the campaigns

ECDC endeavoured throughout the year 2008 to provide participating countries with a core set of tools, including a common name 'European Antibiotic Awareness Day' and logo, key messages, a dedicated website and communications materials targeting parents and carers of young children [4,5]. The various steps in preparation for the first EAAD that took place on 18 November 2008 were previously published [6].

In the following years, EAAD has focussed on primary care prescribers (2009) and hospital prescribers (2010). In each case, campaign messages and materials were developed following evidence-based processes, i.e. results of systematic reviews and subsequently they were reviewed by the EAAD Technical Advisory Committee and tested in focus groups representing the target audience in question. The campaign materials included a dedicated EAAD website, logos and visuals i.e., hedgehog mascot and TV and web spots, advertorials and on line banners, factsheets and prescribing check lists, patient brochures, template letters and presentations. All campaign materials were made available on the EAAD website [7].

In 2011 and 2012, the focus of EAAD shifted to consolidation, with new activities to support the national campaigns at a process level as opposed to the development of new content [8,9]. Given the global financial crisis and competing priorities, a number of countries reviewed government support for the annual campaigns. ECDC chose to strengthen its support to the participating countries by providing strategies and tools to support the delivery of the existing key messages and materials including a social media toolkit, and to foster impact evaluation strategies, and a pilot training course on development, implementation and evaluation of prudent antibiotic use campaigns.

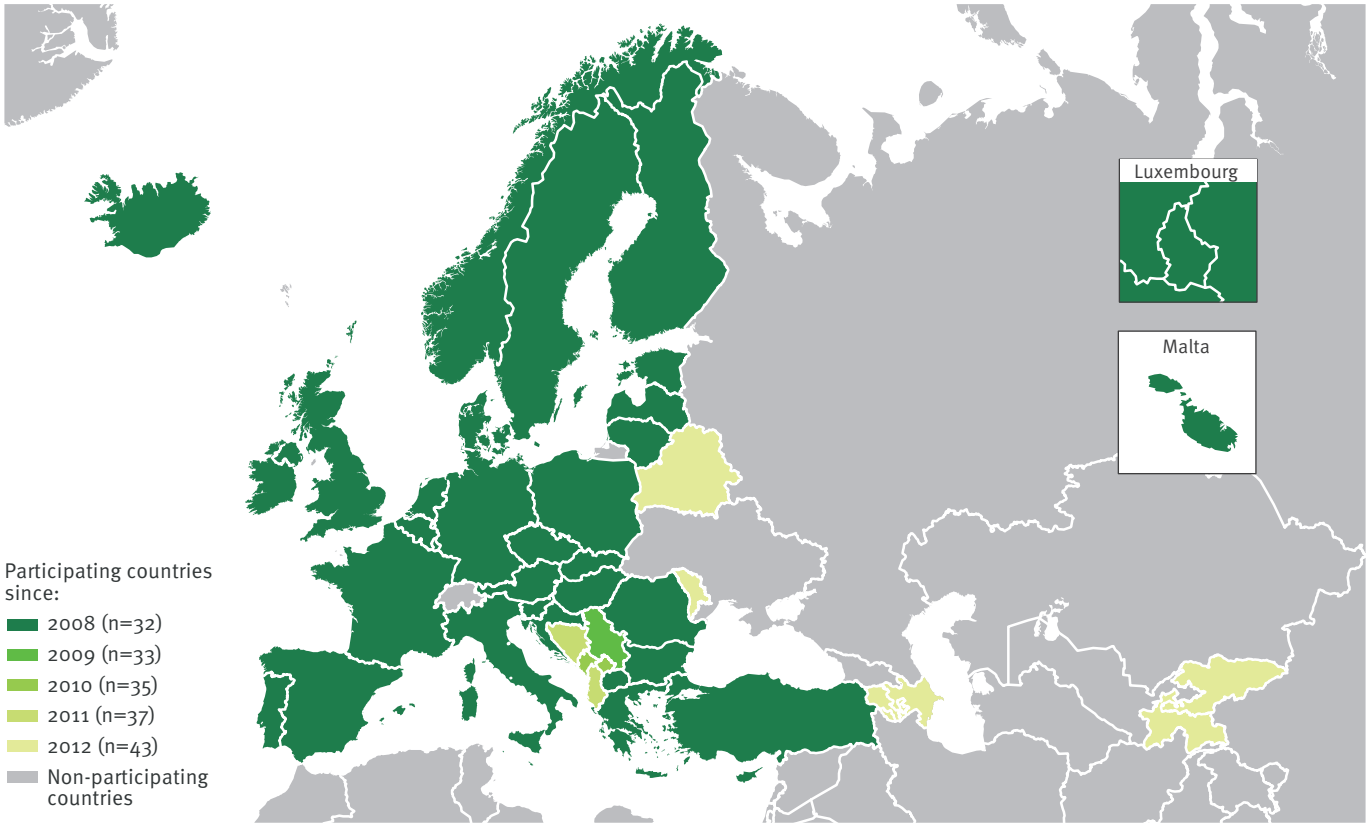
Each year, participating countries answered a questionnaire providing feedback to ECDC on their national activities for EAAD. The scope of this questionnaire is to gather information about the national campaigns: e.g. type and number of the activities, chosen target audience governmental support and EAAD material used to support those activities. In addition since 2010, an independent monitoring of the media coverage of EAAD in terms of print, online and social media is performed.

Coverage of the campaigns

Since 2008, the number of European countries participating in the EAAD has increased year on year. In 2008, all EU Member States plus Norway, Iceland, Croatia,

Figure

Countries participating in the European Antibiotic Awareness Day, 2008–2012



the Former Yugoslav Republic of Macedonia and Turkey participated making a total of 32 countries. Between 2009 and 2012, this number increased to 43 countries, firstly with the addition of other EU enlargement countries: Albania, Bosnia and Herzegovina, Kosovo*, Montenegro and Serbia [10,11]. In 2012, through cooperation with WHO/Europe, Armenia, Azerbaijan, Belarus, Kyrgyzstan, Moldavia and Tajikistan also participated (Figure).

Thirty-two countries initially participated to EAAD in 2008; one additional country in 2009, two additional countries in 2010; in 2011 two further countries joined and six more in 2012. Thus in 2012, a total of 43 European countries participated and in 2013, the number countries reached 45 (unpublished data).

Each participating country has carried out at least one activity targeting the general public, primary care prescribers or hospital prescribers (Table 1). The target audiences have predominantly followed the theme set by ECDC at European level, i.e. twenty-seven of 33 participating countries targeted primary care prescribers in 2009 and 31 of 35 countries targeted hospital prescribers in 2010 [12]. In the subsequent years of consolidation, ECDC has seen a continued focus on all three target audiences with in 2012, 36 of 43 countries organising activities targeted at the general public, 34 at primary care prescribers and 30 at hospital prescribers (Table 1).

Governmental support

Government support has been an essential element in funding and endorsing national campaigns. This support was universal in 2008, but then probably due to financial constraints and/or competing priorities (e.g. the 2009 influenza A(H1N1)pdm pandemic), a number of countries were not able to secure on-going government support for the annual campaigns. In 2009, 23 countries had government support, of which 14 were able to secure funding for their national campaigns as part of this support. The level of government funding further decreased and in 2010 only nine countries remained with government funding. This number increased again by 2012, with 30 countries then receiving support, of which 15 received financial support, from their governments (Table 2).

As government support varied in 2009 and 2010, campaign planners considered a broader scope of alternative groups to provide support and funding, such as professional groups and non-governmental organisations. By 2010, 16 countries reported cooperation with professional groups, such as medical associations and professional healthcare organisations. In 2011 and 2012, this number increased to 27 and 35 countries, respectively, of which 10 countries and 19 countries, respectively, reported receiving sponsorships (Table 2).

Print, online and social media coverage

ECDC has consistently monitored print and online press coverage of EAAD in all 24 official EU languages since 2010. In 2010 and in 2011, 476 and 611 articles related to EAAD were published, respectively, during a four-month period between 15 October and 15 February. In 2012, 446 articles related to EAAD were published in 47 countries worldwide during a two-month monitoring period between 18 October and 28 December. This coverage represented a range of 42 to 72 million visits of news online and a print reach of 18 to 77 million persons.

The EAAD website (http://ecdc.europa.eu/en/EAAD/Pages/Home.aspx) includes communications materials in all EU languages [7]. Analysis of the EAAD website showed around a 200% increase in web traffic i.e., during the week of 18 November each year compared to the previous one. The most visited EAAD pages were the country activities, toolkits, multimedia news release (for English version), as well as the factsheets and national campaigns (for the multilingual websites).

Since 2011, ECDC has increasingly used social media (e.g. Twitter, Facebook) to convey EAAD messages. In 2012, EAAD was mentioned in 1,773 tweets, with over of 3.7 million impressions reached. In 2012, ECDC with WHO/Europe and the European Commission held a joint Twitter chat on 20 November reaching 2.5 million impressions (out of the 3.7 million stated above). EAAD was also mentioned 58-times in the monitored period in blogs, e.g. European Medical Students' Association. The postings focused on the EAAD and the use of antibiotics.

From 2009 to 2012, ECDC broadcasted a TV spot raising awareness on antimicrobial resistance and EAAD on a pan-European TV channel (Euronews), reaching an average of 14 million EU citizens each year and among them an average of 1.5 million people working in the healthcare and medicine sector in Europe.

Discussion

In 2007, when the idea of a European-level initiative to raise awareness about the importance of prudent use of antibiotics was agreed, ECDC hosted two meetings of national antimicrobial resistance (AMR) focal points, nominated by the Member States. In these meetings in September 2007 and March 2008, the form that the initiative should take and the benefits that it could bring were discussed as well as draft campaign materials, and feedback was given. In the end, the initiative was conceived as a day (EAAD) upon which national campaigns could be launched and where the power of many could amount to more than the power of one [6,13–16]. Our analysis after five editions of EAAD, shows that it obviously responded to a need at European level.

The EAAD has provided a platform for pre-existing national campaigns and encouraged similar campaigns to develop in other countries where neither political support had been secured, nor financial support been

Country	National activities													
	Training	Scientific/professional conference	Publication of articles in medical journals	Distribution of brochures or other materials	Mailing	Communications on treatment recommendations	Advertisements	Press conference	Press release	Public relations activities	Activities targeting schools	Exhibition	Gimmicks	Other
European Union														
Austria		●●●	●●	●				●●●	●●●	●				●●
Belgium		●	●●●	●●	●●	●●●		●●●	●●●●		●	●	●	●
Bulgaria	●●●	●●●●	●●●	●	●●●	●		●●●●	●●●	●●		●		
Croatia		●●●●●	●●	●●●●	●	●		●●●●	●	●●●	●		●	●●●
Cyprus	●●●	●●●		●●●	●	●	●	●●	●●●●	●●●		●		●●
Czech Republic	●	●●●	●●●	●●●	●●●	●●		●●	●●●	●●		●●	●	●●
Denmark		●●●●	●●			●			●●					●●
Estonia		●	●●●●	●●	●●●●	●	●●	●●●	●●●●	●	●			
Finland								●	●●					●●
France	●	●	●	●●		●			●	●				●●
Germany	●●	●●●●●	●●●●						●●●					●●
Greece	●●●	●●	●●●	●●		●●		●●●	●●●	●●●				●●
Hungary		●●●●●	●●	●●●	●●		●	●●●●	●●●●	●●●				
Ireland		●	●	●●●	●●●	●●	●	●●●●	●●●	●●●			●	●●
Italy		●●●		●				●●	●●	●●●	●●			●●●●
Latvia	●	●●●	●●●		●			●	●●	●●				
Lithuania	●	●●●	●●●	●	●		●		●●●	●●	●●●			●●
Luxembourg		●	●	●	●●	●	●	●●	●●	●				●
Malta		●●●	●	●	●●		●	●●	●●	●●				●●
Netherlands			●	●●	●			●	●●●					●●
Poland	●●●●●	●●●●●	●●●●●	●●●●●	●	●●●●	●●●	●●●	●●●●	●●●	●●●	●●●●		●●
Portugal		●●●	●	●●		●●	●	●	●●●	●●●	●●●	●		●
Romania	●	●●●●	●●●	●●	●●●●	●●●		●●●	●●●	●●●				●●
Slovakia	●	●●●	●	●	●	●		●●●	●●●	●	●			
Slovenia	●●	●●●	●●●●		●			●●	●●●	●●				●●●
Spain		●●●●●	●●●●	●●●●	●●●●	●	●●●●	●●●	●●●●	●●●	●●	●●●		●
Sweden		●●	●●●	●	●			●●	●●●					●●●
United Kingdom	●●	●●●●	●●●●	●●●	●●●	●●			●●	●●	●●	●●		●●●●●
European Economic Area														
Iceland		●		●●	●	●●			●●●					●●
Norway	●	●●●	●●●	●●●	●●	●●			●●	●				●●●
Other countries														
Albania		●●●	●	●●		●●	●	●●	●	●●		●		
Bosnia and Herzegovina	●●	●●	●	●●	●	●●	●	●●	●●	●●				
Former Yugoslav Republic of Macedonia		●●●●●	●●●●●	●●●			●	●●●●●	●●●	●●●				●●
Kosovo*	●	●●●		●●●●	●●●●			●●	●●●	●●●				●
Montenegro		●●								●				●●
Serbia	●●	●●	●●		●●●	●		●●●●	●●●	●●●				●●●
Turkey	●●	●●●●		●●●●	●●	●		●●●●	●●●	●●	●●●			●●●

Each dot corresponds to one activity-year.

* This designation is without prejudice to positions on status, and is in line with United Nations Security Council Resolution 1244/99 and the International Court of Justice Opinion on the Kosovo declaration of independence.

	Campaign materials															
	Factsheet	Check list	Advertorial	Online banner	Presentation	Screen saver	Gimmicks	Posters	Leaflets	Patient dialogues	Letters to stakeholders	Web-based materials	Brochures	Television or web spots	Advertisements in print media	Other
		•						•	•		•	•				••
					•			••••	••••		••••	••••		••••		•
	••	•		•	•			••	••	•	•••	••••	•			
	••	••			•			••••	••••		•••	•		•••	••	•
	•••			••	••			•••	••••	•	••	•••	•••	•	•	••
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	•								•		••••	••••		••		•
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	••••	•			••	••		••••	••••	•	•••	••••	•	••		
	•••	••			•••	•		•••	•••		•••	•••	•	•	••	•••
	••							••				••••	•	•	••	••
	•				•						•	•••		••		
	•••			••	••			•••	•••		••	••••	••	••	••	•••
	••							••	••		•••	•	•	•	•	••
	•	•						••	•••		•	•	••	••		••
	••	•						••	•	•	••	•••	••			
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	••				•			•••	•••	•	••	••••	•••	•••	••	•
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					•			•	••		•	••		•	•	••
	••				••			•••	••		•••	••		••		••
	•••	•••	•••	•••	•••	•		••••	••••	•	•••••	••••	•••	••		•
	••				•			••			•••		•••	•		••
	•••	•••	•••	•••	••	••		••••	••••	•	••••	••••	••	••	•	•••
	••				•							•••	•			•
	••				•			••	•••		•••	••	•	••	•	•
	••							••	••		••			•		
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	••••	••			•••			••	•••	•	••••		•			
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	••••	••	••	•	••	••		•••		••	••••	•••		••••		••

Table 2

Overview of government and stakeholders' support received per country, European Antibiotic Awareness Day campaigns, 2008–2012

Country	Government support		Stakeholder support									
	Political support	Financial support	Health professionals	Pharmacies	Patient groups	Non-governmental organisations	Non-pharmaceutical companies	Pharmaceutical companies	Professional societies	Insurance system	Other	WHO/Europe or WHO country office
European Union												
Austria	••••	••	•••	••		•	••	•	••	•	•	
Belgium	••••	•••••	••	•••••			•	•	••••	••••		
Bulgaria	••		••	•		•••	•	•	•••			•
Croatia	•	•••••	•••••	•••••		••••		•	•••			•
Cyprus	••••	•••	••	•			•	•		••		
Czech Republic	••••		••	••••	•		•		••••	••	••	•
Denmark	•	••	••	•					•		••	
Estonia	•		•••						•			
Finland	••	•	•									
France	••••	•••	•						•••	•••	•	
Germany	••••	•••	••						•••		•	
Greece	••	••	•					•	••••		•	
Hungary	••••	••										•
Ireland	•••	••	••••	•••	••				•••		•	
Italy	••••	••	•••						••••		•	
Latvia	••		••			••			•			•
Lithuania	•••••	••	•	•		••	•		••		••	
Luxembourg	•••	•••	••	•••						•••	•	
Malta	••••	••	•••	•					•		•	
Netherlands	••	••	••••	•		••	•			•		
Poland	•••••	•••••	•••	•••		•••••	•		•••••	•	•••	
Portugal	••		••••	••		•	•	•	••		•	
Romania	••••	••	••••			•			•••••		••	
Slovakia	••	•••	•••			••			•	•••	•	
Slovenia	•••	•••	••••						••••	••		•
Spain	•••	•	••••	•••	•				•••		•	
Sweden	••••		••••					•	••		••	•
United Kingdom	•••••	••••	•••••	•••	••	•			••••		••	
European Economic Area												
Iceland	••	•	••									•
Norway	•••	••••	••	•					•		•	
Other countries												
Albania	••	•	••	•		•			•			•
Bosnia and Herzegovina	••		••	•				•	•			
Former Yugoslav Republic of Macedonia	•••••	••	•••••	•		•••••			••••	•	••	•
Kosovo*	••••		••					•	••••			•
Montenegro	••		••						••		•	•
Serbia	••		•••						••			•
Turkey	•••••	•••	••••	••					••••	•••		•

Each dot corresponds to one activity-year.

* This designation is without prejudice to positions on status, and is in line with United Nations Security Council Resolution 1244/99 and the International Court of Justice Opinion on the Kosovo declaration of independence.

available. As a result, year on year, in their reply to the annual questionnaire, countries have expressed their strong support for ECDC to continue its work on the EAAD. This has also been highlighted by a steadily increasing number of countries participating and the growing interest of varied professional and stakeholder organisations.
Evaluation of EAAD in terms of understanding its impact on antibiotic consumption and on antibiotic resistance is difficult because (i) the effects will vary depending on the country as a result of variations in the extent and the intensity of the national campaign in each country and (ii) these effects are unlikely to be immediate as shown from previous national campaigns in some Member States. In addition, it is important to remember that since the campaigns have been applied heterogeneously at national levels, according to local needs and resources, a one size fits all impact analysis evaluation is not appropriate.

Regular opinion polls, i.e. 'Special Eurobarometers' on antimicrobial resistance commissioned by the European Commission, however, should help identify improvements in the knowledge, perception and self-reported attitudes of Europeans with antibiotics [17,18]. Additionally, the effects on antibiotic consumption and on antibiotic resistance in the European countries most active in the campaigns should become visible in the data reported to the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) and the European Antimicrobial Resistance Surveillance Network (EARS-Net), respectively [19–21]. By providing training support on the development, implementation and evaluation of prudent antibiotic use campaigns, ECDC hopes that common evaluation indicators can now be developed at European level and implemented as part of national campaigns from 2014 onwards.

In 2013, ECDC and its partners launched the 6th edition of EAAD on 15 November 2013, with the emphasis that 'Everyone is responsible' for addressing antibiotic resistance and for using antibiotics more prudently, during a European Commission press conference [22]. During this press conference, the results of a recent 'Special Eurobarometer' on the attitudes and knowledge of Europeans about antibiotics, were presented together with a review of new research initiatives related to antimicrobial resistance and the latest surveillance data on resistance trends [21,23]. In particular, the 'Special Eurobarometer' on antimicrobial resistance showed a 5% decrease between 2009 and 2013, in the percentage of Europeans who took antibiotics during the past year and an increasing awareness of Europeans that antibiotics do not kill viruses [18]. These are positive developments that may reflect the continuous efforts made by Member States in the framework of EAAD. This is also the rationale for an annual EAAD to support to national campaigns.

In 2013, ECDC arranged for a first extended global Twitter conversation with its partners in the United States (US), Canada and Australia, and in connection with an EAAD Twitter chat organised jointly with the European Commission and WHO/Europe using the hashtag #EAAD. Dedicated EAAD Twitter (@EAAD_EU) and Facebook (http://facebook.com/eaad.eu) accounts have been set up for the first time. The full evaluation of the 2013 edition of EAAD is currently ongoing. In reply to the annual questionnaire sent by ECDC to evaluate the activities in 2013, 22 of 41 responding countries highlighted that there was a change in their country that could be attributed to the momentum created by EAAD.

Looking to the future, self-medication with antibiotics has been identified as a new focus for EAAD 2014. Concerns about antimicrobial resistance and the need for a more prudent use of antibiotics are of global significance and are progressively being raised on political agendas. A growing number of countries and regions across globe, including the US, Canada and Australia, have aligned the timing of their activities to that of EAAD and the week of 18 November is increasingly being recognised as the moment to raise awareness about prudent use of antibiotics. This is a strong encouragement for the coordinators of the EAAD to continue acting as a global catalyst for discussion and raising awareness about prudent use of antibiotics.

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* This designation is without prejudice to positions on status, and is in line with United Nations Security Council Resolution 1244/99 and the International Court of Justice Opinion on the Kosovo declaration of independence.

Conflict of interest

None declared.

Authors' contributions

Sarah Earnshaw - lead author, drafted article; Giovanni Mancarella - co-lead author, drafted article; Andrea Mendez - evaluation; Boyana Todorova - EAAD website; Marybelle Stryk - EAAD social media; Anna-Pelagia Magiorakos - EAAD patient stories and introduction; Enrico Possenti - EAAD audiovisuals; Signe Gilbro - EAAD multi-lingual content; Herman Goossens - EAAD Technical Advisory
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Weekly, print and online. In German.
http://www.rki.de/DE/Content/Infekt/EpidBull/epid__bull__node.html

Greece

HCDCP Newsletter
Hellenic Centre for Disease Control and Prevention (HCDCP/KEELPNO), Athens
Monthly, online. In English and Greek.
http://www2.keelpno.gr/blog/?lang=en

Hungary

Epinfo (az Országos Epidemiológiai Központ epidemiológiai információs hetilapja)
National Center For Epidemiology, Budapest
Weekly, online. In Hungarian.
http://www.oek.hu/oek.web?to=839&nid=41&pid=7&lang=hun

Iceland

EPI-ICE
Landlæknisembættið
Directorate Of Health, Seltjarnarnes
Monthly, online. In Icelandic and English.
http://www.landlaeknir.is

Ireland

EPI-INSIGHT
Health Protection Surveillance Centre, Dublin
Monthly, print and online. In English.
http://www.hpsc.ie/hpsc/EPI-Insight

Italy

Notiziario dell'Istituto Superiore di Sanità
Istituto Superiore di Sanità, Reparto di Malattie Infettive, Rome
Monthly, online. In Italian.
http://www.iss.it/publ/noti/index.php?lang=1&tipo=4

Bolletino Epidemiologico Nazionale (BEN)
Istituto Superiore di Sanità, Reparto di Malattie Infettive, Rome
Monthly, online. In Italian.
http://www.epicentro.iss.it/ben

Latvia

Epidemiologijas Bileteni
Sabiedribas veselibas agentura
Public Health Agency, Riga
Online. In Latvian.
http://www.sva.lv/epidemiologija/bileteni

Lithuania

Epidemiologijos žinios
Užkreciamuju ligu profilaktikos ir kontroles centras
Center for Communicable Disease Prevention and Control, Vilnius
Online. In Lithuanian.
http://www.ulac.lt/index.php?pl=26

Netherlands

Infectieziekten Bulletin
Rijksinstituut voor Volksgezondheid en Milieu
National Institute of Public Health and the Environment, Bilthoven
Monthly, print and online. In Dutch.
http://www.rivm.nl/infectieziektenbulletin

Norway

MSIS-rapport
Folkehelseinstituttet, Oslo
Weekly, print and online. In Norwegian.
http://www.folkehelsa.no/nyhetsbrev/msis

Poland

Meldunki o zachorowaniach na choroby zakazne i zatruciach w Polsce
Panstwowy Zaklad Higieny,
National Institute of Hygiene, Warsaw
Fortnightly, online. In Polish and English.
http://www.pzh.gov.pl

Portugal

Saúde em Números
Ministério da Saúde,
Direcção-Geral da Saúde, Lisbon
Sporadic, print only. In Portuguese.
http://www.dgs.pt

Romania

Info Epidemiologia
Centrul pentru Prevenirea si Controlul Bolilor Transmisibile, National Centre of Communicable Diseases Prevention and Control, Institute of Public Health, Bucharest
Sporadic, print only. In Romanian.
Sporadic, print only. In Romanian.
http://www.insp.gov.ro/cnscbt/index.php?option=com_docman&Itemid=12

Slovenia

CNB Novice
Inštitut za varovanje zdravja, Center za nalezljive bolezni, Institute of Public Health, Center for Infectious Diseases, Ljubljana
Monthly, online. In Slovene.
http://www.ivz.si

Spain

Boletín Epidemiológico Semanal
Centro Nacional de Epidemiología, Instituto de Salud Carlos III, Madrid
Fortnightly, print and online. In Spanish.
http://revista.isciii.es

Sweden

Folkhälsomyndighetens nyhetsbrev
Folkhälsomyndigheten, Stockholm
Weekly, online. In Swedish.
http://www.folkhalsomyndigheten.se/

United Kingdom

England and Wales

Health Protection Report
Public Health England, London
Weekly, online only. In English.
https://www.gov.uk/government/collections/health-protection-report-latest-infection-reports

Northern Ireland

Communicable Diseases Monthly Report
Communicable Disease Surveillance Centre, Northern Ireland, Belfast
Monthly, print and online. In English.
http://www.cdscni.org.uk/publications

Scotland

Health Protection Scotland Weekly Report
Health Protection Scotland, Glasgow
Weekly, print and online. In English.
http://www.hps.scot.nhs.uk/ewr/

European Union

"Europa" is the official portal of the European Union. It provides up-to-date coverage of main events and information on activities and institutions of the European Union.
http://europa.eu

European Commission - Public Health

The website of European Commission Directorate General for Health and Consumer Protection (DG SANCO).
http://ec.europa.eu/health/

Health-EU Portal

The Health-EU Portal (the official public health portal of the European Union) includes a wide range of information and data on health-related issues and activities at both European and international level.
http://ec.europa.eu/health-eu/

European Centre for Disease Prevention and Control

European Centre for Disease Prevention and Control (ECDC)
The European Centre for Disease Prevention and Control (ECDC) was established in 2005. It is an EU agency with aim to strengthen Europe's defences against infectious diseases. It is seated in Stockholm, Sweden.
http://www.ecdc.europa.eu

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