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Usefulness of the European Epidemic Intelligence Information System in the management of an outbreak of listeriosis, Belgium, 2011

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A cluster of time-linked cases and the identification of a clonal strain suggest the occurrence of an outbreak of listeriosis in Belgium in 2011, presumably due to the consumption of hard cheese made with pasteurised milk and produced by a Belgium manufacturer. The outbreak clone was identified as *Listeria monocytogenes* serovar 1/2a, sensitive to arsenic and cadmium and of multilocus sequence typing MLST-type 37. Food investigation of this outbreak was facilitated by the European Epidemic Intelligence Information System and data exchanged between French and Belgium listeriosis surveillance systems.

Introduction

Listeria monocytogenes, a Gram-positive bacterium, is a ubiquitous organism in the environment and a facultative intracellular food-borne pathogen. Infections occur through ingestion of contaminated food. The bacterium causes listeriosis, which is characterised by bacteraemia or meningitis. Infection during pregnancy can lead to abortion. The incubation time of listeriosis is estimated from two to 88 days. Immunocompromised patients, the elderly, pregnant women and neonates are particularly at risk of developing symptomatic disease [1]. Due to its high mortality rate (approximately 25% of the patients) and hospitalisation rate (approximately 97% of the patients), timely and accurate isolate characterisation is essential to identify outbreaks [2].

The Belgian National Reference Centre for *Listeria* (BNRCL) receives annually between 40 and 70 strains of human clinical cases (53, 64 and 43 cases in 2008, 2009 and 2010, respectively), representing an annual incidence of three to six cases/million habitants. The vast majority of them are sporadic cases, infected with unrelated molecular strains. Contrary to the Flemish speaking community of Belgium, listeriosis is mandatorily notifiable in the French speaking community.

In the present study we report an outbreak of 12 cases of human listeriosis in Belgium in 2011. The strain linked to the outbreak was characterised by serotyping, metal resistance typing, pulsed field gel electrophoresis (PFGE) and multilocus sequence typing (MLST) [3,4]. The microbiological characteristics were then communicated within the European Union (EU) via the Epidemic Intelligence Information System (EPIS), a platform tool allowing national surveillance systems to exchange information regarding current or emerging public health threats with a potential impact in the EU. This allowed the identification of a hard cheese as a likely source of the outbreak.

Methods

Case definition

For this outbreak, a person was considered a case if the *L. monocytogenes* strain isolated from this person had the same *Apa*I/*Asc*I PFGE pattern as the outbreak strain as well as the serotype (1/2a) and MLST-type 37.

Outbreak investigation

Cases diagnosed with listeriosis received a standardised questionnaire aimed at detecting risk factors for *Listeria* and at collecting information about their food history in the two month before the onset of symptoms. The patients gave verbal consent to answer the questionnaire.

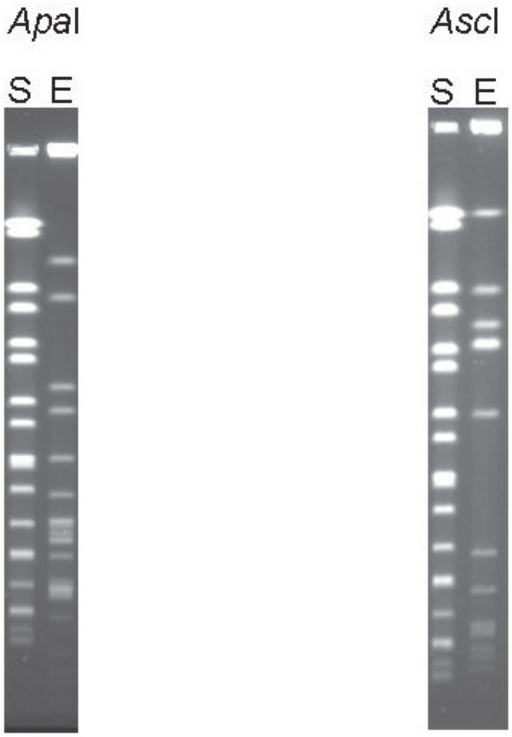
Listeria monocytogenes bacteria were isolated from blood and ascites fluid of patients by the clinical laboratories. The isolates were sent to the BNRCL for confirmation of the identification and typing.

Strain identification was carried out with API *Listeria* microgallery (bioMérieux, France). Serotyping was conducted according to a standard protocol using a commercial agglutination test (Denka Seiken, Tokyo, Japan)

for somatic (O) and flagellar (H) antigens [5]. Strain susceptibility to arsenic and cadmium was determined according to McLauchlin et al. [3]. Antibiotic susceptibility was tested by E-test (bioMérieux); the following antibiotics were studied (Susceptible/Resistant (S/R) breakpoints in µg/ml): ampicillin (2/4), amoxicillin (4/16), gentamicin (4/16), vancomycin (4/32), erythromycin (0.5/8), tetracycline (4/16), ciprofloxacin (1/4), chloramphenicol (8/32) and trimethoprim/sulphamethoxazole (2/4). Molecular typing was performed on all human isolates. Pulsed-field gel electrophoresis (PFGE) was done following the United States (US) PulseNet protocol after deoxyribonucleic acid (DNA) digestion with the *Apa*I and *Asc*I enzymes [6]. Band pattern analysis was performed with ImageMaster video documentation system (Amersham Pharmacia Biotech) and BioNumerics (Applied Math). Multilocus sequence typing was performed according to the method described by Ragon et al. [4], which is based on allelic analysis of seven housekeeping genes and enables the comparison of the obtained sequences to an online accessible database [7].

Figure 1

Pulsed-field gel electrophoresis *Asc*I and *Apa*I profiles of the outbreak of human listeriosis clone, Belgium, 2011



S: *Salmonella* Braenderup as reference, E: *Listeria monocytogenes* outbreak clone.

International enquiry

In order to find out if the outbreak strain had occurred in clinical samples or food isolates, in particular within the EU, the microbiological characteristics of the outbreak strain were communicated via EPIS, a communication platform established by the European Centre for Disease Prevention and Control (ECDC).

Results

Outbreak investigation

Between 4 February and 1 March, 2011 BNRCL received three clinical isolates of *L. monocytogenes* from respective patients hospitalised at a same hospital in Antwerp. The responsible strain was confirmed at BNRCL as *L. monocytogenes* serovar 1/2a and sensitive to arsenic and cadmium (SS). Molecular typing of the three clinical isolates showed a clonal origin based on their similar combined PFGE *Asc*I/*Apa*I profile (Figure 1) and MLST-type 37.

An investigation for possible nosocomial infection was immediately started at the hospital and was inconclusive. Meanwhile, BNRCL continued to receive clinical isolates, with the same microbiological and molecular characteristics from other hospitals in Belgium confirming the detection of an outbreak. A total of 12 isolates positive for the outbreak strain were identified as of June 2011, from 12 hospitalised patients, three of whom were known to have been initially hospitalised for other illnesses than listeriosis. Eleven of the isolates were derived from blood and one from ascites fluid. All were sensitive to the nine antibiotics tested.

The outbreak began in February when two respective patient isolates with the outbreak strain were received by BNRCL, it reached a maximum in March and April, with four respective positive isolates, and declined in May and June with one positive isolate respectively (Figure 2).

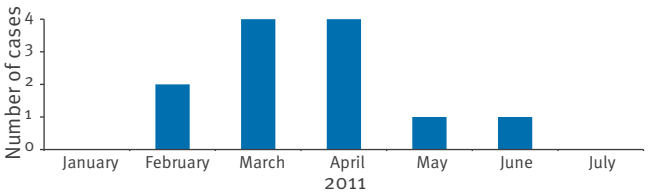
The patients' characteristics are presented in the Table. The overall mean age was 77.3 years (range: 56–86 years). Five patients were male and seven female. The mean age of the male patients was 82 years and the mean age of the female patients was 74.6 years. No pregnancy-related case was reported. An underlying disease was reported for eight patients while this was unknown for the others. During the period of the outbreak four patients died. For two of the deaths, the sepsis caused by the *Listeria* outbreak strain was a significant contributing factor, while for the remaining two the direct cause was underlying disease.

Six patients lived in the province of Antwerp; the remaining cases lived in five different provinces distributed almost nationwide (Figure 3).

In search of the source of infection, the BNRCL database was consulted. A hard cheese isolate was

Figure 2

Cases of listeriosis outbreak by month of diagnosis in the Belgian National Reference Centre for Listeria, Belgium, 2011 (n=12)



identified with similar microbiological characteristics as the outbreak clone. This food isolate was received at the BNRCL a year before, in conjunction with the monitoring programme of the Belgian Federal Agency for the Safety of the Food Chain.

International enquiry

The clinical strains typing results were submitted to EPIS of the Food and Waterborne Diseases and Zoonoses Programme of the ECDC, to investigate for the previous isolation of human/food strains with the same microbiological characteristics particularly in other EU Member States. The inquiry (Reference 2011-04-05-497) was created on 05 April 2011 and 13 countries replied. Twelve EU and European Free Trade Association (EFTA) countries and the US reported no similar unusual increases of listeriosis. At the same time of the Belgian outbreak, the French National Reference Centre for *Listeria* reported an indistinguishable food strain isolated subsequent to a food alert in the Département du Nord, an area, bordering Belgium. Food isolates with the same strain as the outbreak strain all originated from hard cheese made from pasteurised milk (called *Pavé du Nord*). The cheese was manufactured in Belgium and imported to France where it was sliced, packaged and sold in supermarkets. Enumeration of *L. monocytogenes* in this sliced and packaged hard cheese was low, around 20 cfu/g. In addition, two hard cheeses raw material samples had been analysed and found to meet the microbiolical safety criterium of less than 100 cfu/g of *L. monocytogenes* [8]. The Belgian cheese manufacturer and its distributor nevertheless decided to recall different batches of hard cheese from the national and international market, and issued a warning to the public. Four alert notifications were launched by the Rapid Alert System for Food and Feed (RASFF) of the European Commission, on the presence of *L. monocytogenes* in hard cheese: Three in Belgium (Alert Notification 2011.0374; 2011.0511; 2011.0619) and one in France (Alert Notification 2011.132).

At the Belgian cheese manufacture plant, an inspection was launched to identify the origin of contamination. The Federal Agency for the Safety of the Food Chain ordered the operator to send all isolated *L. monocytogenes* strains to the BNRCL for further typing. The BNRCL received two cheese isolates and three cheese surface swab strains with the same microbiological characteristic of the outbreak clone. The samples had been taken at the manufacture plant. Several cheese samples taken at one hospital with human cases proved negative for the presence of *L. monocytogenes*.

The strains isolated from the patients and from hard cheese were indistinguishable but it remained to be established if the patients had consumed the suspected food. To this aim, all patients (or their physicians) received a questionnaire, yet only four of the 12 patients responded. No information about the patients with a fatal outcome could be collected. No responders remembered having eaten hard cheese from the suspected manufacturer, yet the delay between disease and questionnaire filling was long (ranging from one to four months). Nevertheless, after the food inspection of the cheese manufacture plant and appropriate sanitary measures taken on site, no more cases with the outbreak clones was recorded at BNRCL.

Discussion

Centralised surveillance of the human *Listeria* cases is essential for the early detection of outbreaks and for the organisation of an immediate and appropriate response [9]. The investigation and control of foodborne outbreaks involve different actors and requires data centralisation from different sectors such as clinical medicine, epidemiology, food safety, risk communication and management. In this study, the outbreak

Table

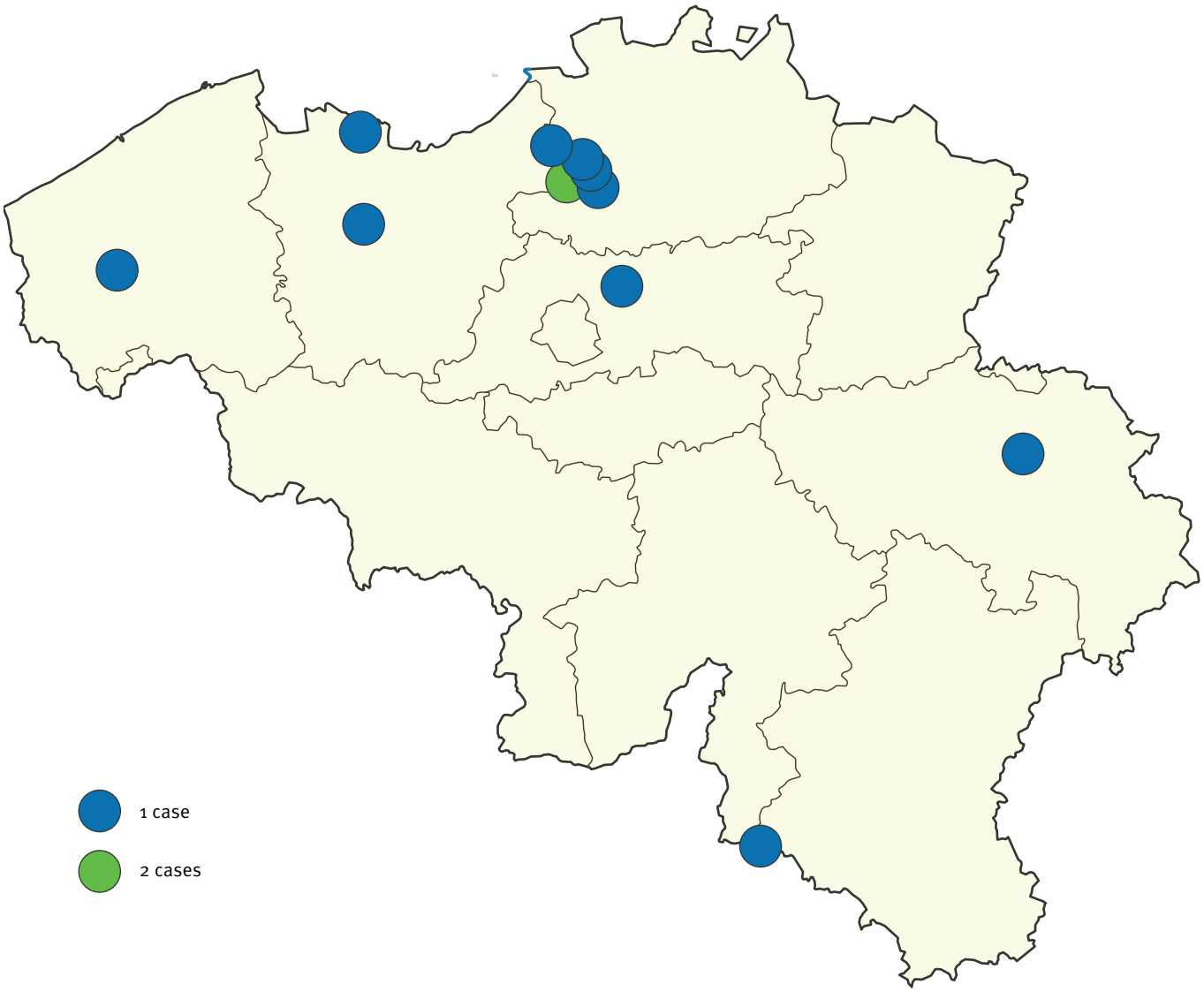
Characteristics of outbreak cases of listeriosis, Belgium, 2011 (n=12)

Case number	Isolation site of the strain	Clinical presentation	Comorbidity
1	Blood	NA	NA
2	Ascites fluid	Peritonitis	NA
3	Blood	NA	Respiratory insufficiency
4	Blood	Septicaemia and peritonitis	Liver insufficiency
5	Blood	Septicaemia	Multiple myeloma
6	Blood	Septicaemia	Bronchial carcinoma
7	Blood	Septicaemia	Chronic obstructive pulmonary disease
8	Blood	NA	NA
9	Blood	NA	NA
10	Blood	Septicaemia	NA
11	Blood	Septicaemia	Liver cirrhosis and type 2 diabetes
12	Blood	NA	NA

NA: Not available.

Figure 3

Geographic distribution of the outbreak cases of listeriosis, Belgium, 2011 (n=12)



was detected because the BNRCL received strains from clinical laboratories and performed subtyping of all the strains. Although Belgian clinical laboratories transfer their clinical isolates to the BNRCL favouring BNRCL to play a central role in the early detection of human clusters at the community and national level, this is done on a voluntary basis. It is therefore estimated that the BNRCL receives between 70 to 80% of the total number of isolated clinical strains, offering potential for an underestimation of the number of cases in this outbreak.

By means of this centralised data collection, additional information regarding trends, emerging agents, transmission routes, groups at risk and specific risk factors can be obtained in order to manage an outbreak and to eliminate the source of contamination.

Nevertheless, a challenge for outbreak management is to trace back the food source of infection. The long incubation time of listeriosis makes it difficult to successfully interview patients and identify the source of infection. The Cantaloupe outbreak in the US underlined also the difficulty to detect quickly foods which are not classically listed as a source of contamination in humans and at the origin of outbreaks [10]. Moreover, food investigation in outbreak management is difficult when an imported contaminated product is at the origin of national cases. In this study, food investigation was facilitated via EPIS and an alert was created on 5 April 2011, to which 13 countries replied. The same day information from France pointed to the Belgian cheese manufacturer, and this prompted the withdrawal of batches of the suspected cheese from the market. As the Netherlands also imported cheese from that manufacturer, contacts between the Dutch investigators

and the BNRCL were facilitated by the ECDC Food and Waterborne Diseases and Zoonoses network. No cases linked to this outbreak were reported by the Netherlands.

Within the epidemiological investigation about this outbreak, use of the food questionnaire proved to be unsuccessful, probably as it was not conducted soon enough after the diagnosis of listeriosis: only four patients responded and no one remembered having eaten hard cheese from the suspected cheese manufacture plant. This is quite understandable, also given the relatively old age of the patients, the long incubation time of the disease and the lapse of time between the onset of the illness and receiving the written questionnaire. Furthermore, unpackaged sliced hard cheese is not labelled at the retail level, making it more difficult for the consumer to link the information about the manufacturer with the cheese. To limit these types of problems it is important to question the patients verbally, immediately after the diagnosis of listeriosis. Unfortunately the Belgian questionnaire did not inquire patients on the consumption of hard cheese from pasteurised milk, although hard cheese from unpasteurised milk is included; hard cheese from pasteurised milk should be added to the questionnaire in the future.

In the food investigation part of this outbreak, there are only microbiological indications that hard cheese was the source of contamination. Complete DNA sequence of food and patient outbreak strains could be more conclusive. Results of the internal investigation of the cheese manufacturer suggested that the rind of the hard cheese was contaminated with *L. monocytogenes* originating from a machine that rotates the cheese during riping, which was shown to be contaminated. Meanwhile, measures were taken to disinfect this rotator. This observation underlined the fact that, as for example slicers in the ready-to eat meat industry, equipment may play an important role in *L. monocytogenes* contamination of a product [11].

It is very exceptional to assign hard cheese as the causative food of listeriosis cases, unlike soft cheese which is recognised as an at risk product [11]. Microbiological criteria for *L. monocytogenes* in hard cheese ripened or not, are established for healthy people (‹100 cfu/g) but, for hospitalised people, should be modified to absence. Even low levels of *L. monocytogenes* in hard cheese pose a risk to immunocompromised persons and this type of cheese is often served in hospitals or in elderly homes. In the United Kingdom, it was therefore recommended that food served to hospital patients be free from *L. monocytogenes* [12,13]. In our view as a result of this study, a clarification of European regulation on microbiological criteria for food served in hospital should be investigated to protect this particular type of consumer.

We believe that our results underline the need for mandatory notification of listeriosis in Member States in order to facilitate food and human outbreak investigations. In addition, our investigation shows the importance of continuous exchange of human and food data between EU Member States based on an established network, combined with molecular typing surveillance of listeriosis in Europe, based on harmonised and recognised methods for early detection and management of national or European outbreaks. Due to the international marketing of foods or raw food materials and the free movement of people between countries, we consider that the surveillance of listeriosis only at national level is currently insufficient to protect the consumer.

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Influenza-associated hospitalisations in Finland from 1996 to 2010: unexpected age-specific burden during the influenza A(H1N1)pdm09 pandemic from 2009 to 2010

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To assess the burden of influenza on the Finnish healthcare system, we analysed hospitalisations during 1996–2010 using the International Classification of Diseases codes potentially related to influenza and its complications from the national hospital discharge registry. To compare the influenza A(H1N1)pdm09 pandemic with previous influenza seasons in 1996–2009, we calculated hospitalisation rates by age- and diagnostic groups. We built a negative binomial regression model based on times series analysis to assess the impact of the pandemic. Influenza-associated hospitalisation rates were higher during the pandemic compared to pre-pandemic influenza seasons for 5–24 year-olds (incidence rate ratio (IRR): 1.52, 95% confidence interval (CI): 1.44–1.60) and 25–64 year-olds (IRR: 1.33, 95% CI: 1.29–1.36), but did not differ for persons aged ≥ 65 years (IRR: 0.98, 95% CI: 0.97–1.00). Hospitalisation rates exceeded the upper limit of the prediction line by 177% in 5–24 year-olds, 66% in 0–4 year-olds and 57% in 25–64 year-olds. During the influenza season of 2003/04, all age groups had higher-than-expected hospitalisation rates, whereas other seasonal peaks were only notable among persons aged ≥ 65 years. These age-specific differences in the hospital burden underscore the importance of the continuous surveillance of hospitalisations in order to evaluate immunisation priorities for seasonal influenza and pandemic preparedness including use of antiviral medication.

Introduction

The impact of the influenza A(H1N1)pdm09 pandemic on relevant public health indicators, such as laboratory-confirmed severe cases, has been widely reported in the European region [1] and also in Finland [2]. However, surveillance based only on laboratory-confirmed cases may underestimate the disease burden due to the low likelihood of testing in some clinical situations and the increased usage of rapid test methods with low sensitivity [3]. The availability of diagnostic tests and testing activity may vary between countries, and thus international comparisons must be done with caution.

Within the European monitoring of excess mortality for public health action [4], pooled results from eight European countries showed higher all-cause mortality in children during the influenza A(H1N1)pdm09 pandemic in comparison with the three previous years [5] but this finding was not detected in mortality data from the individual countries, including Finland. However, mortality does not reflect the whole burden of disease [6,7].

The impact of seasonal and pandemic influenza on healthcare systems, particularly inpatient care, can be assessed by using a wide range of influenza-associated conditions leading to hospitalisation. In the United States, two retrospective studies have used a list of influenza-associated discharge diagnoses to estimate excess hospitalisations due to influenza during seasonal influenza periods, where a comparison between seasons provided information on important virological factors, such as the dominant influenza virus subtype and vaccine match [6,8]. Using a similar methodology, Widgren et al. [9] described the hospital burden of influenza in Denmark during the pandemic and the previous five years and revealed a higher than expected hospitalisation burden in children and young adults aged 5–24 years, but no excess burden in persons aged 65 years and above.

In the present study, we describe observed numbers of influenza-associated hospitalisations in Finland by age

and influenza-associated diagnostic groups during the influenza A(H1N1)pdm09 pandemic in comparison with the 13 previous influenza seasons. We also present a prediction model for influenza hospitalisations during the pandemic, incorporating data from the nationwide laboratory-based surveillance of influenza and other seasonally circulating respiratory pathogens.

Methods

Data sources

In Finland (population 5.4 million in 2010), the National Hospital Discharge Register (HILMO) receives reports on all discharges from inpatient care providers on an annual basis. Each report includes a national identity code for the patient, the first three diagnoses given to the patient according to the International Classification of Diseases 10th revision (ICD-10) from 1996 and onwards, age, sex and place of residence, admission and discharge dates, name and place of attending hospital, type of service and medical specialty. Thus, the study base from which we obtained the data on hospitalisations consisted of all the discharges reported to HILMO from the entire country for the years 1996–2010. Yearly age-specific population data from Statistics Finland for the years 1996–2010 were used to calculate hospitalisation rates.

We obtained weekly numbers of seasonally circulating respiratory pathogens (influenza A and B, parainfluenza, adenovirus and respiratory syncytial viruses (RSV), *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and *Bordetella pertussis*) from the National Infectious Disease Register, to which all clinical microbiology laboratories electronically notify all positive findings (culture, antigen, serology and polymerase chain reaction (PCR)) for the aforementioned pathogens.

Definitions

We obtained data on influenza-associated hospitalisations from HILMO according to a list of ICD-10 discharge diagnoses and classified these into five diagnostic groups [6,8,9]: influenza, viral or unspecified pneumonia, bacterial pneumonia, febrile convulsions and acute respiratory distress syndrome (ARDS). A list of ICD-10 codes used with corresponding diagnostic groups is presented in Table 1.

Influenza seasons were defined as starting from week 30 to week 15 of the following year; this extended season was created to accommodate the influenza A(H1N1) pdm09 pandemic for which the onset and peak in influenza activity, as measured through laboratory-based surveillance, came much earlier than in the previous seasons [2,9]. Hospitalisations were analysed according to the following age groups: 0–4, 5–24, 25–64 and 65 years and above [9]. In the study database, the national identity code was replaced with a unique surrogate identifier; each individual's influenza-associated hospitalisations reported to HILMO within a six-week period were counted as one unique episode of influenza-associated hospitalisation [9].

Analyses and statistics

We calculated age-specific weekly hospitalisation rates per 100,000 population using unique hospitalisation episodes. We compared the hospitalisation rate during the influenza A(H1N1)pdm09 pandemic with the mean hospitalisation rate of pre-pandemic influenza seasons by calculating the age-specific incidence rate ratio (IRR) with a 95% confidence interval (CI).

We stratified the data on all the influenza-associated hospitalisations by age groups and the previously described five diagnostic groups for each season. We compared the stratum-specific numbers of hospitalisations during the pandemic with the median numbers for pre-pandemic influenza seasons by calculating the risk ratio (RR) with a 95% confidence interval (CI) for each age-specific diagnosis group using binomial regression.

Furthermore, we constructed a time series in which weekly age-specific unique hospitalisation episodes were plotted from week 1 of 1996 to week 15 of 2010. We

Table 1

Diagnostic group classification of International Classification of Diseases 10th revision discharge diagnoses used to identify influenza-associated hospitalisations from the National Hospital Discharge Register, Finland, 1996–2010

Diagnostic group	International Classification of Diseases, 10th revision discharge diagnoses
Influenza	G051F, G051O, H671B, J09, J091, J091A, J091B, J099, J10, J100, J101, J101A, J101B, J101C, J108, J108A, J108B, J108C, J11, J110, J111, J111A, J111B, J111C, J118, J118A, J118B, J118C, I411A
Viral or unspecified pneumonia	J12, J120, J121, J122, J128, J129, J18, J180, J181, J182, J188, J189
Bacterial pneumonia	J13, J139, J139A, J139B, J14, J149, J149A, J149B, J15, J150, J151, J152, J153, J154, J155, J156, J156A, J157, J158, J159, J16, J160, J168, J170, J170A, J170B, J170C, J170D, J170E, J170F, J170H, J171, J171A, J171B, J171C, J171D, J172, J172A, J172B, J172C, J172D, J173, J173A, J173B, J173C, J178, J178A, J178B, J178C
Febrile convulsions	R560
ARDS	J96, J960, J969

ARDS: acute respiratory distress syndrome.

Table 2

Incidence rates for influenza-associated hospitalisations during the influenza A(H1N1)pdm09 pandemic and the pre-pandemic influenza seasons 1996–2009, Finland

Influenza A(H1N1)pdm09 pandemic				Pre-pandemic influenza seasons 1996–2009				
Age group (years)	Total number	Incidence rate[a]	95% CI	Mean number/season	Incidence rate[a]	95% CI	IRR	95% CI
0–4	1,937	16.59	14.64–16.47	1,700	15.19	14.99–15.39	1.09	1.04–1.14
5–24	1,725	3.54	3.38–3.72	1,144	2.33	2.30–2.37	1.52	1.44–1.60
25–64	7,554	6.70	6.55–6.85	5,460	5.05	5.02–5.09	1.33	1.29–1.36
≥ 65	16,717	46.48	45.78–47.19	14,662	47.26	47.05–47.47	0.98	0.97–1.00
Total	27,933	13.36	13.20–13.52	22,965	11.53	11.48–11.57	1.16	1.15–1.17

CI: confidence interval; IRR: incidence rate ratio.

[a] Hospitalisation episodes per 100,000 of the age group population/week.

predicted age-specific hospitalisation rates during the influenza A(H1N1)pdm09 pandemic by applying a negative binomial regression model to the hospitalisation data from the pre-pandemic influenza seasons. In the model, we included weekly reports of seasonally circulating respiratory pathogens as covariates with a time lag of three weeks as suggested by simulations. We also included a seasonality index by months and long-term periodicity based on the observed periodicity for RSV (two years) and a range of periodicity observed for *Mycoplasma pneumoniae* (three years, seven years) [10]. Previously observed peaks in seasonal influenza were not removed since we believed that those events are expectable in influenza transmission and dynamics [6,8,11,12]. Observed age-specific hospitalisations during the pandemic were compared to the upper bound of the 99% CI of the corresponding age-specific prediction obtained from the model, which we expressed as relative differences (%) for each age group. All analyses were performed using Stata software version 10.1 (Stata corporation, College Station, TX, USA).

Ethical approval and data protection

The study protocol was approved by the ethics committee of the National Institute for Health and Welfare (THL), and the appropriate permission to use the data from HILMO, which is administrated by the THL, was acquired through an internal application and review process.

Results

A total of 535,862 influenza-associated hospitalisations were identified from 1996 to 2010; 440,922 of these were unique hospitalisation episodes.

Based on the analysis of unique hospitalisation episodes, the overall influenza-associated hospitalisation rate was 16% higher during the influenza A(H1N1)pdm09 pandemic as compared to the mean rate of pre-pandemic influenza seasons (Table 2). The hospitalisation rates differed by age groups: statistically significant excesses were observed in children and adults (age groups 0–4 years, 5–24 years and 25–64 years), whereas no excess was detected in persons aged 65 and above. The magnitude of excess hospitalisation was highest in 5–24 year-olds and 25–64 year-olds.

Based on the analysis of all the hospitalisations, discharge diagnoses of influenza, viral pneumonia and ARDS were more frequent during the pandemic as compared to pre-pandemic seasons, but discharge diagnoses of bacterial pneumonia and febrile convulsions were less frequent (Table 3). When analysing discharge diagnoses by age groups, influenza, viral pneumonia and ARDS remained more common during the pandemic as compared to pre-pandemic seasons in 0–4 year-olds, and influenza and viral pneumonia remained more common in age groups 5–24 and 25–64 years. In persons aged 65 and above, viral pneumonia and ARDS were more common during the pandemic than during pre-pandemic seasons. The number of hospitalisations with discharge diagnoses corresponding to ARDS during the pandemic was 726 for all age groups, and the median number was 540 in previous seasons (range, 248–760). The diagnoses of bacterial pneumonia and febrile convulsions remained less frequent during the pandemic as compared to the previous seasons in all age groups.

In the time series analyses, the model built on pre-pandemic hospitalisation data and notifications from the laboratory-based surveillance of seasonally circulating respiratory pathogens fitted well with the observed hospitalisation rates during the same period (Figure 1). Very small autocorrelations were left in the residuals, which showed only a minor effect on the prediction and its limits when all covariates were added to the model. A peak in influenza-associated hospitalisations in all four age groups was observed during the influenza season 2003/04. When extending the prediction line to the influenza A(H1N1)pdm09 pandemic, hospitalisation

Table 3

Influenza-associated hospitalisations by age- and diagnostic groups during the influenza A(H1N1)pdm09 pandemic and the pre-pandemic influenza seasons 1996–2009, Finland

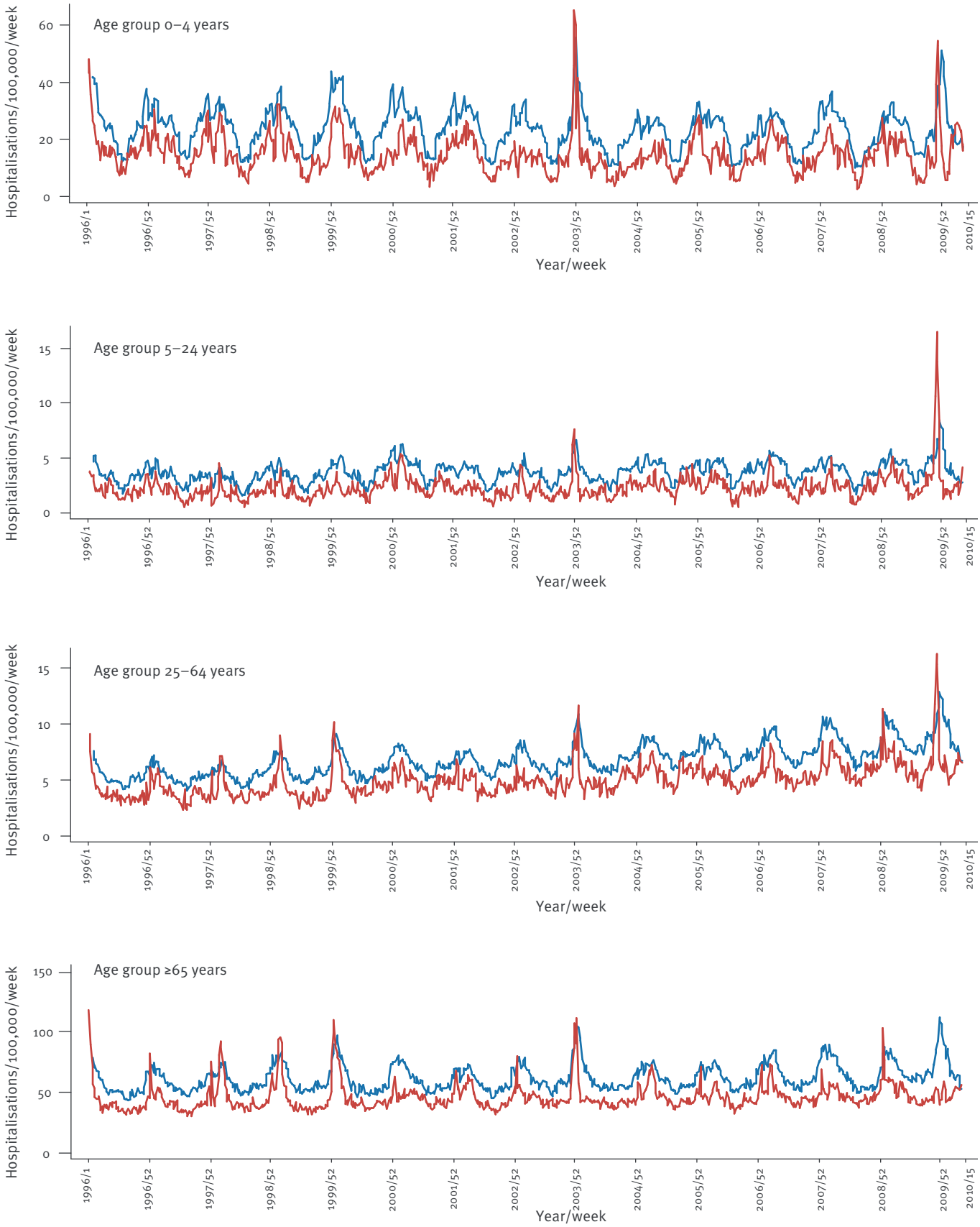
Age and diagnostic group	Number of hospitalisations in the influenza A(H1N1) pdm09 pandemic	Median number of hospitalisations in the pre-pandemic influenza seasons 1996–2009	Range in influenza seasons 1996–2009	Risk ratio[a]	95% CI	p
All age groups						
Influenza	1,826	580	358–1844	1.77	1.69–1.86	0.000
Viral or unspecified pneumonia	25,372	14,937	11,607–25,730	1.20	1.19–1.21	0.000
Bacterial pneumonia	6,799	9,089	7,366–10,811	0.59	0.58–0.60	0.000
Febrile convulsions	392	616	472–908	0.49	0.45–0.55	0.000
ARDS	726	540	248–760	1.10	1.02–1.19	0.011
0–4 years				**0.90**	**0.86-0.94**	**0.000**
Influenza	364	108	54–341	2.53	2.28–2.81	0.000
Viral or unspecified pneumonia	1,077	739	517–964	1.27	1.22–1.33	0.000
Bacterial pneumonia	232	353	264–537	0.55	0.48–0.62	0.000
Febrile convulsions	339	506	389–779	0.56	0.51–0.62	0.000
ARDS	11	4	2–12	2.10	1.11–3.99	0.023
5–24 years				**1.20**	**1.14–1.25**	**0.000**
Influenza	428	75	49–124	3.68	3.32–4.08	0.000
Viral or unspecified pneumonia	1,035	585	409–915	1.06	1.02–1.11	0.006
Bacterial pneumonia	398	444	376–650	0.56	0.52–0.62	0.000
Febrile convulsions	29	58	40–72	0.34	0.23–0.49	0.000
ARDS	16	17	11–23	0.64	0.39–1.06	0.083
25–64 years				**1.14**	**1.12–1.16**	**0.000**
Influenza	776	118	71–363	3.37	3.11–3.65	0.000
Viral or unspecified pneumonia	6,173	3,067	2,315–6,069	1.19	1.17–1.21	0.000
Bacterial pneumonia	2,169	2,546	2,228–3,066	0.59	0.57–0.61	0.000
Febrile convulsions	15	22	12–48	0.43	0.25–0.72	0.001
ARDS	299	217	105–320	0.99	0.88–1.11	0.814
≥ 65 years				**0.95**	**0.94–0.95**	**0.000**
Influenza	258	322	111–1176	0.48	0.42–0.54	0.000
Viral or unspecified pneumonia	17,087	10,766	7,936–17,782	1.22	1.21–1.23	0.000
Bacterial pneumonia	4,000	5,816	4,414–7,121	0.59	0.57–0.60	0.000
Febrile convulsions	9	15	8–29	0.49	0.25–0.96	0.038
ARDS	400	304	127–417	1.16	1.05-1.28	0.005

ARDS: acute respiratory distress syndrome; CI: confidence interval.

[a] Risk ratio per age- and diagnostic group during pandemic versus previous influenza seasons calculated from the binomial regression model.

Figure 1

Observed influenza-associated hospitalisation rates by age groups per 100,000 population of the respective age groups per week , Finland, 1996–2010 (n=440,922)



The red line represents the observed influenza-associated hospitalisation rates in Finland by age groups per 100,000 population of the respective age groups per week. The blue line represents the upper limit of the 99% confidence interval for the prediction line which was obtained from the negative binomial regression model using data from the pre-pandemic influenza seasons.

rates exceeded the upper bound of the prediction line in the age groups 0–4, 5–24 and 25–64 years, and the observed peak at week 46 in 2009 occurred earlier than predicted. The time series model predicted a similar peak in influenza-associated hospitalisations for individuals aged 65 and above, but no excess in hospitalisation rate was seen during the pandemic.

The hospitalisation rates varied between age groups (Figure 1). In the children aged 0–4 years, the rate peaked at 50/100,000 population of this respective age group/week during the influenza A(H1N1)pdm09 pandemic, as compared to 30/100,000 population of the respective age group/week in pre-pandemic peaks. In the age groups 5–24 years and 25–64 years, peak rate during the pandemic reached 15/100,000 population of these respective age groups/week, whereas the seasonal peak rates usually were below 5/100,000 population of these respective age groups/week. In the persons aged 65 and above, the hospitalisation rate during the pandemic did not exceed 50/100,000 population of this respective age group/week, whereas the seasonal peak rates in 1999/00, 2003/04 and 2008/09 were up to 100/100,000 population of the same respective age group/week.

During the peak week of the pandemic (at week 46, 2009), the observed hospitalisation rates exceeded the upper 99% CI of the predicted rates by 177% in 5–24 year-olds, 66% in 0–4 year-olds and 57% in 25–64 year-olds, but remained below the expected hospitalisation rate in people aged 65 years and above (Figure 2).

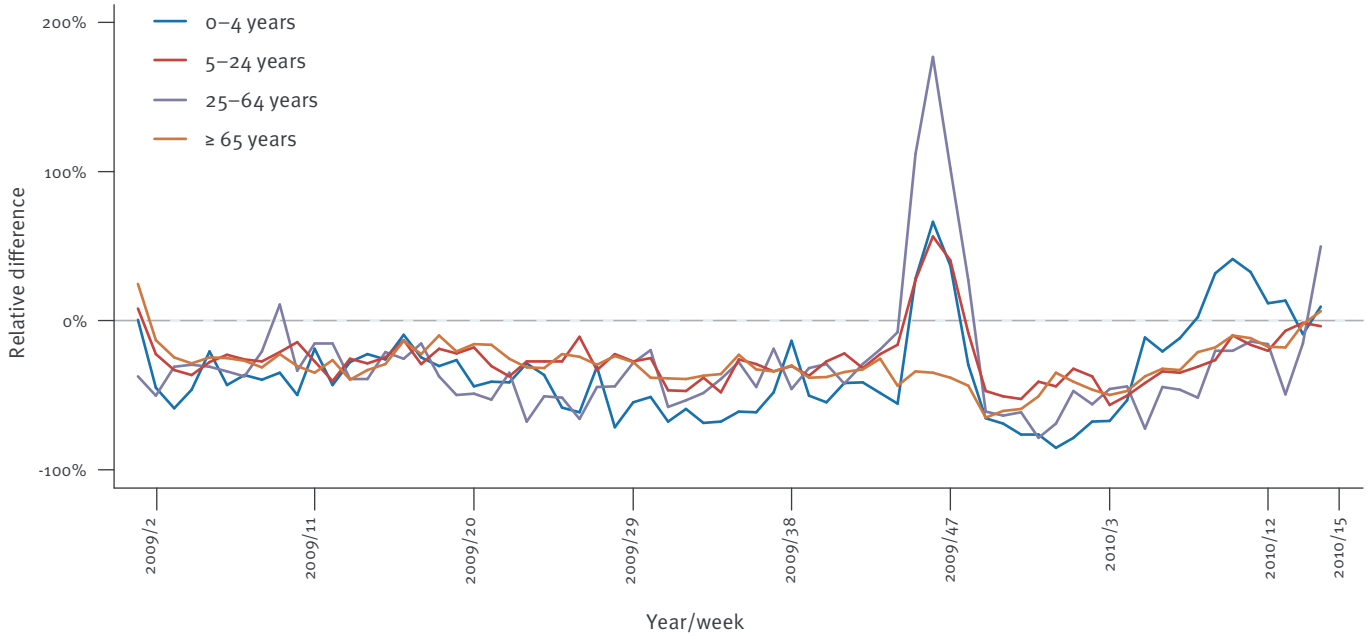
Discussion

Our study showed, based on the national hospital discharge register data, an increase in influenza-associated hospitalisation rates during the influenza A(H1N1) pdm09 pandemic in Finland as compared to the pre-pandemic seasons 1996–2009. The burden of the pandemic on hospitalisation rates was most pronounced in people aged 5–24 and 25–64 years, whereas there was no difference in persons aged 65 years and above.

The present study was initiated to provide national data on influenza-associated hospitalisations in Finland, using similar methodology as a study from Denmark [9]. As in Denmark, we found a higher than expected hospitalisation burden during the pandemic in persons aged 5–24 years, but the same phenomenon was also detected in persons aged 25–64 years. As shown by the absolute numbers and graphical presentation of the time series, there was no increase in the burden of hospitalisation in persons aged 65 years and above, which was also noted in Denmark. This is partly explained by the presence of cross-reacting antibodies against the Spanish influenza of 1918 or descendants

Figure 2

Relative difference between observed influenza-associated hospitalisations by age groups during the influenza A(H1N1) pdm09 pandemic and the upper limit of the 99% confidence interval for the prediction line based on pre-pandemic hospitalisation data, Finland, 1 January 2009–18 April 2010



The 99% confidence interval for the prediction line was obtained from the negative binomial regression model based on pre-pandemic hospitalisation data.

from this virus in this age group [13]. Another possible contribution to the differences between age groups and the two countries is the immunisation policy adopted against the pandemic influenza. In Finland, vaccination campaigns started with healthcare workers and risk groups before the peak in October 2009, then reached out to other target groups, such as children, and finally reached the general population around early January of 2010 [unpublished data THL]. The highest vaccination coverage was reached in 5–14-year-old children (76%) and the lowest in adults aged 20–29 (31%). In Denmark, vaccination against the pandemic influenza was offered to healthcare workers and risk groups including children aged three years or more in October 2009; the general population including healthy children were included in the vaccination programme at the end of February 2010 [14]. The differences in vaccination policies arose partly from unresolved questions regarding the effectiveness of immunisation in young children [15], but a growing body of literature supports the view that the burden of the disease was previously underestimated [16].

Our analyses by a list of ICD-10 codes previously used in the United States [6,8] and Denmark [9], revealed an increase in hospital discharges coded as influenza and viral or unspecified pneumonia, especially in children and adults. For the ARDS diagnostic group, an increase during the pandemic was observed in children and persons aged 65 and above, but due to the small numbers, these results should be interpreted with caution. The smaller numbers of hospital discharges coded as ARDS in our study as compared to the numbers found in Denmark [9] may reflect differences in clinical practice and the usage of ICD-10 codes between the two countries, which have similar population sizes (The Danish population is 5.5 million). Hospital discharges coded as bacterial pneumonia were fewer during the influenza A(H1N1)pdm09 pandemic as compared to the pre-pandemic seasons in all the age groups, including children and persons aged 65 and above, which are the two groups usually most vulnerable to secondary bacterial infections during seasonal influenza waves [17]. Febrile convulsions in children were also less frequent during the influenza A(H1N1)pdm09 pandemic, an observation also reported from Australia [18].

In the age-specific time series over the whole 14-year period, we observed seasonal influenza peaks in persons aged 65 and above and in children; these two age groups also showed the largest variation in the hospitalisation rate between seasonal peaks, except for the pandemic where the absence of excess in those aged 65 and above was a striking finding. The influenza season of 2003/04 represented the second most important peak in hospitalisations in all groups (and the highest peak in people aged 65 and above) and was dominated by an influenza A (H3N2) virus of the Fujian lineage which represented a major drift in the H3N2 virus causing poor match with the then available seasonal influenza vaccine [10].

Our study has several limitations. Firstly, we were unable to determine the possible impact of the increased awareness regarding influenza and its potential complications, especially among younger age groups, during the influenza A(H1N1)pdm09 pandemic, a phenomenon that could affect both diagnostic activity and the threshold for hospitalisation, resulting in higher numbers of influenza and influenza-associated ICD-10 codes appearing in the hospital discharge register. An English study limited to laboratory-confirmed cases of influenza during the pandemic revealed lower hospitalisation rates than in other countries, which can possibly be explained by differences in the threshold for hospital admission; however, hospitalisation was far more common in patients with pre-existing medical conditions [19]. Influenza infection causes the exacerbation of cardiopulmonary diseases, which could also be seen as an excess in hospitalisation rates [8]. Secondly, a weakness was related to the structure of the HILMO data as compared to the Danish hospital discharge register, since only the three first ICD-10 codes from each medical record were collected in the register, whereas the Danish register provided an unlimited number of ICD-10 codes [9]. Coding for influenza infection may be noted among the later diagnoses in patients suffering from multiple illnesses. However, in a study from the United States by Simonsen et al., only the code provided in the first position was considered [6]. Finally, we were not able to use the model for continuous monitoring, as hospital discharge data is collected by HILMO only annually; data delivery at least on a monthly basis would enable timely surveillance.

Our hospitalisation data covered the whole country, minimising bias due to regional differences in the population and the healthcare structure; the same coverage was obtained in the Danish study [9]. In contrast, we used age-specific population denominators, resulting in hospitalisation rates useful for international comparisons [6,8]. We used hospitalisation data from a total of 14 years when building the prediction model for the pandemic, and the resulting model thus accommodates information from various types of influenza seasons, including the 2003–2004 season with its high burden of disease. Furthermore, we added weekly numbers of seasonally circulating respiratory pathogens reported to nationwide laboratory-based surveillance as covariates to the model, and we obtained a very good fit of the prediction line for pre-pandemic seasons 1996–2009, as suggested by previous studies on influenza-associated mortality [7,20] and on overall influenza surveillance [11,21]. These covariates proved useful as we observed a second peak in hospitalisations among children aged 0–4 years in early 2010; after comparison with the time series of individual respiratory pathogens, we suspected this age-dependant observation to be due to a higher circulation of RSV.

In conclusion, the present study showed a differential burden of influenza-associated hospitalisations during

the influenza A(H1N1)pdm09 pandemic as compared to previous seasons by age and diagnostic groups. The availability of surveillance data describing the burden of influenza on healthcare systems for all age groups is important when assessing changes in influenza dynamics in future seasons and pandemics, when evaluating immunisation priorities and recommendations for use of antiviral medications [2,15,22]. The monitoring of influenza-associated hospitalisations is an important complementary approach to the surveillance of excess in all-cause mortality and the case-based surveillance of severe cases, but the data from the monitoring needs to be timely. Integration of epidemiological and microbiological data is an important part of the modelling process, which will require calibration in future studies that should also allow for international comparisons of hospitalisation rates.

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What really happens to tuberculosis patients classified as lost to follow-up in West Yorkshire?

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Tuberculosis (TB) patients who do not complete treatment pose a potential public health risk. In West Yorkshire, local clinicians suspected that this risk was overestimated by the national Enhanced Tuberculosis Surveillance system. We audited patients who failed to complete treatment and were categorised as lost-to-follow-up (LTFU) between 2004 and 2008, using a combination of hand searching existing records and obtaining additional information from clinicians. In the study period 2,031 TB cases with reported outcome were notified in West Yorkshire, 23% (n=474) did not complete treatment, and 199 (42%) of those were categorised as LTFU 12 months after notification. Of these 199, 49% (n=98) remained LTFU after the audit, 51% (n=101) were re-classified to the following categories: 24% (n=47) transferred abroad, 16% (n=31) recommenced and completed treatment, 6% (n=13) transferred to another clinic in the United Kingdom (UK), and 5% (n=10) died. These patients therefore no-longer posed a public health risk. Further training for clinicians to improve accuracy of outcome reporting has been initiated. Nationally, the collection of treatment outcome data needs to be strengthened and extending the follow-up for treatment outcome monitoring should be considered.

Background

The most important intervention for the control of tuberculosis (TB) is effective treatment of infectious cases [1]. Failure to complete treatment poses a significant public health risk through disease reactivation, increased transmission, and development of drug-resistance.

Treatment success measured by a standardised process of treatment outcome monitoring is one of the pillars of TB control. The World Health Assembly (WHA) passed a resolution in 1991, adopting the target to cure at least 85% of TB cases as one of two global targets [2]. In the European Union (EU), TB case notification rates are among the lowest in the world, declining by 15.2% between 2005 and 2010 [3]. However, there was a concurrent decline in treatment completion rates in the region, declining from 72.5% in 2005 to 68.7% in 2010 among new diagnosed cases, the lowest TB treatment success rate in the world and short of the WHA resolution target [3]. Eleven per cent of newly diagnosed laboratory-confirmed pulmonary cases are lost to follow-up (LTFU) [3]. There has been limited research into this phenomenon in the region and investigation is required to determine the underlying factors and implementing measures required to address it.

In England, the Chief Medical Officer adopted the WHA target in their TB Action Plan 2004 [4], and most recently, TB treatment completion has been included as a key indicator in the Public Health Outcome Framework for England [5].

The Enhanced Tuberculosis Surveillance System (ETS) collates detailed epidemiological, clinical and microbiological information on TB cases in England, Wales and Northern Ireland, including treatment outcomes. In line with World Health Organization (WHO) recommendations [6], treatment outcome is recorded 12 months after notification, and then again at 24 months for those who are still on treatment at 12 months. The Health Protection Agency publishes these results annually and measures performance against the national target of 85% treatment completion at 12 months from notification [4]. In 2010, the national treatment completion rate was 78% [7].

A UK study argued that the current categories used to monitor treatment outcome (Figure 1) are limited in capturing patients' true outcomes, as it is not collected properly in all cases [8]. Refining the categories used in the current surveillance system to focus on patients' final true outcomes could significantly improve the measured treatment completion rates [8]. This in turn would provide a more accurate picture of those patients who pose a genuine risk to public health.

In West Yorkshire, the treatment completion rate in 2008 was 75% [9], and 78% in 2009 and 2010 [10,11] well below the national average and target. The 25% not completing treatment include patients classified as LTFU, defined as the failure to obtain contact with

Figure 1

Current categories used in treatment outcome monitoring for tuberculosis in England, Wales, and Northern Ireland

TUBERCULOSIS TREATMENT OUTCOME SURVEILLANCE FORM
ENGLAND, WALES & NORTHERN IRELAND

This form should be completed 12 months after start of treatment, but can be filled in earlier for patients that have completed treatment, died, were misdiagnosed (not TB) or had their treatment stopped (and not restarted). For patients still on treatment at 12 months the form should also be completed at 24 months. For more information see the guidance notes attached / on reverse.

Section A. PATIENT INFORMATION

ID:	Surname:	Forename:	
Local ID:	Date of birth:	Age (years):	Sex:
Street:		Town:	
Post code:	PCT/Health board (residence): PCT		
Date of case report:	Date treatment started:	Patient's Consultant:	
Hospital:		Case manager:	

Section B. TRANSFER DETAILS

If the patient's care was transferred to another clinical team please give details, then – Go to section D

Clinician:.....

Hospital/Trust:.....

Section C. TREATMENT OUTCOME

Name and post of person completing this form:.....

Date of completion of this form: ...../...../.....

Did the patient complete a full course of therapy within 12/24 months of starting treatment?

1. ☐ **Yes** If Yes, **date of end of treatment**:...../...../.....
   treatment regimen used: ☐ standard (2 months HRZE and 4 of HR)
   ☐ other (please specify).....

2. ☐ **No — Patient did not complete treatment within 12/24 months because (please tick appropriate boxes):**
   ☐ **Treatment stopped**: ☐ Patient found not to have TB* (including atypical mycobacterial infection) **or**
   ☐ Other reason

   Or ☐ **Patient died** before or while on treatment (including post mortem diagnosis).
   If yes, **date of death**: ...../...../..... Please indicate whether:
   ☐ TB caused death **or**
   ☐ TB contributed to death **or**
   ☐ TB incidental to death **or**
   ☐ Relationship between TB and death unknown

   Or ☐ **Planned course of treatment exceeds 12 months** as a result of: ☐ initial drug resistance ☐ other

   Or ☐ **Planned course of treatment was interrupted** as a result of: ☐ intolerance / side effects ☐ poor compliance ☐ other

   Or ☐ **Planned course of treatment changed** as a result of: ☐ intolerance / side effects ☐ Initial drug resistance ☐ development of new drug resistance ☐ failure to culture convert ☐ poor clinical response to treatment ☐ other

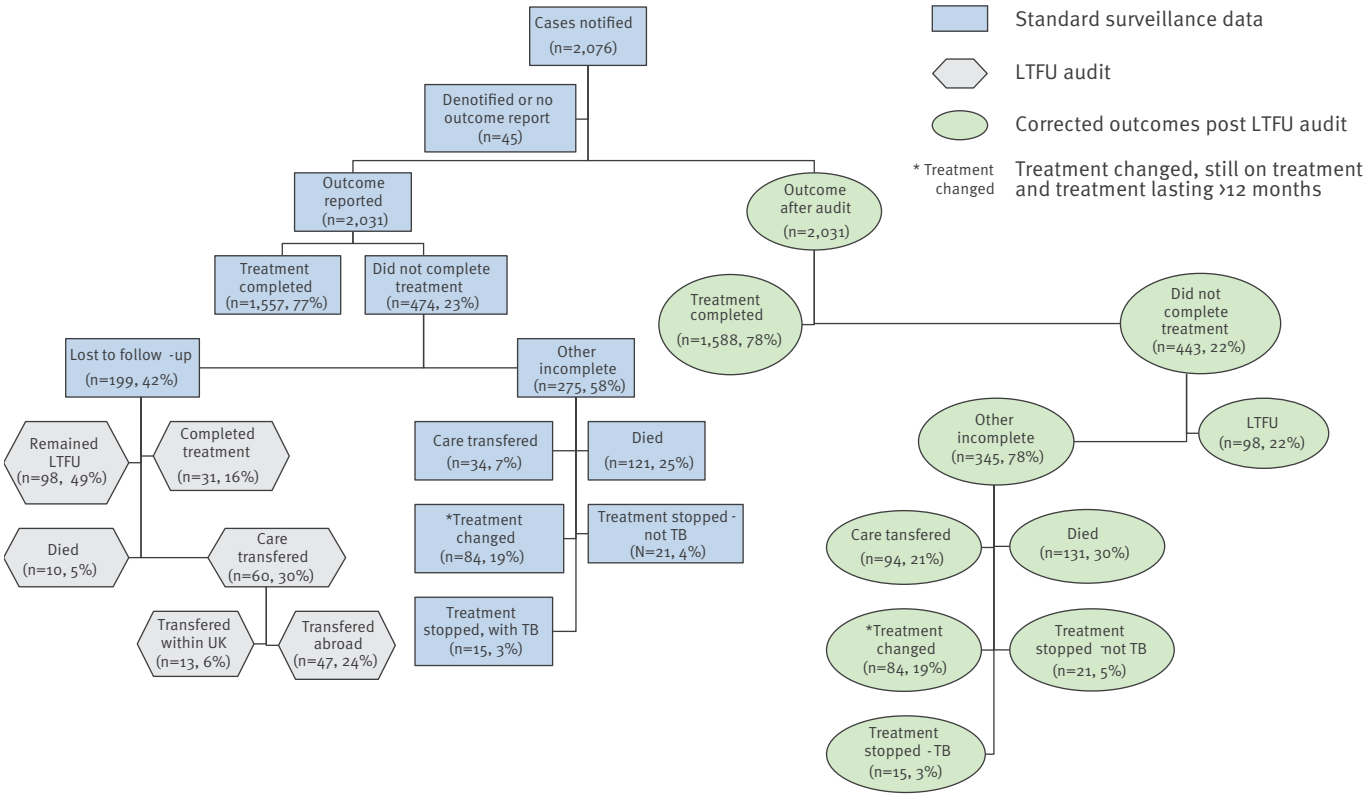
3. ☐ **Patient was lost to follow-up** before the end of treatment because: ☐ patient left the UK ☐ other

4. ☐ **Unknown** – only tick if treatment details are unavailable (e.g. lost patient notes)

* This case should be de-notified from the electronic surveillance system

Figure 2

Tuberculosis patient treatment outcomes before and after audit, West Yorkshire, September 2010–March 2011 (n=2,076)



LTFU: lost to follow-up; TB: tuberculosis, UK: United Kingdom.

the patient before the end of treatment [12], so that the treatment outcome is not known. Patients included in this category are considered to be a potential public health risk due to their unknown outcome, whereabouts or disease status. Alongside the published evidence on the categories used to classify treatment outcomes [8], the West Yorkshire TB Network were concerned that the LTFU category was being overused in the absence of more accurate descriptors and that in reality some of the patients who were classified as LTFU had completed treatment. This meant that the surveillance system reported treatment completion rates that were lower than clinicians would expect, and from a public health perspective the true risk to public health posed by LTFU patients was being overestimated based on current surveillance data. Our audit therefore focussed on addressing this issue to understand what really happens to TB patients classified as being LTFU.

Methods

The audit was conducted over a period of seven months from September 2010 to March 2011. Records of all TB cases notified in West Yorkshire between 2004 and 2008 were extracted from the ETS and treatment outcomes reviewed. Records for those classified as LTFU were extracted. Demographic and risk factor information was compared to patients classified as having completed treatment. Paper records for patients classified as LTFU, were hand searched. Any additional information contained in the free text section of the reporting form that had not previously been transferred to the ETS was gathered. Where no additional information was recorded on the outcome form, TB clinical teams who had been responsible for the treatment of the case were contacted to clarify the true outcome. The collated information was analysed using standard treatment outcome categories (Figure 1) and further relevant categories that were developed during the analysis based on the collected information, such as recommenced and completed treatment.

Results

Between 2004 and 2008 2,031 TB cases were notified in West Yorkshire (Figure 2). Of those, 474 (23%) were reported as not having completed treatment. Twelve months after notification, 199 (42%) of those not completing treatment were categorised as LTFU.

LTFU patients were more often male and older than those who completed treatment, although these

Table

Baseline characteristics comparing patients classified as lost to follow-up to those who had completed treatment

	LTFU n=199	Complete n=1,557
Male n (%)	110 (55)	795 (51)
Female n (%)	89 (45)	758 (49)
Unknown sex n (%)	0(0)	4 (0.3)
Median age in years (95% confidence interval)	35 (32–39)	33 (32–34)
% pulmonary TB (95% confidence interval)	48 (40–55)	48 (46–51)
Most common ethnic groups n (%)		
Pakistani	78 (39)	703 (43)
Black African	36 (18)	228 (15)
Indian	30 (15)	200 (13)
White	26 (13)	228 (15)

LTFU: lost to follow-up; TB: tuberculosis.

differences, along with ethnicity and site of TB were not statistically significant (Table).

The hexagonal boxes in Figure 2 show that of the 199 patients initially classified as LTFU, 98 (49%) remained LTFU after the audit. No further information was available relating to these patients' outcomes. Of the remaining 101 patients, 47 (24%) had transferred abroad, 31 (16%) had recommenced and completed treatment, 10 (5%) had died and 13 (6%) transferred to another UK clinic.

India and Pakistan were the countries most frequently reported as the destination for those transferring abroad (20/47), which is in keeping with the cultural background of TB cases in West Yorkshire, where over a third of reported cases have a Pakistani ethnic origin [9]. However, a wide range of destinations across Asia and Africa were also noted. Of the 47 patients who left the UK, only 10 (21%) were reported to have left with a full supply of treatment.

The circular boxes in Figure 2 show that after excluding cases inaccurately categorised, who recommenced and subsequently completed treatment, and those who transferred abroad, the proportion of all TB cases in West Yorkshire between 2004 and 2008 that were truly LTFU was not 10% (n=199/2,031) but 5% (n=98/2,031) of this five-year cohort.

Discussion

In West Yorkshire, between 2004 and 2008, more patients successfully completed treatment than existing surveillance data indicated, which implies that the risk to public health from treatment failure may have been over-estimated.

Some of this variation in reporting is due to the fact that reporting clinicians did not always select the appropriate option in the reporting form. This could have occurred for two reasons: the first is through classification error where clinicians had access to the correct information regarding the patients' outcome but completed the wrong section on the Treatment Outcome Monitoring (TOM) form; the second is that the clinician simply did not have the relevant information to hand at the time of completing the form, which resulted in misclassification. This second scenario is particularly relevant to the many patients reported as LTFU at 12 months who were subsequently found, recommenced and completed treatment or transferred to services abroad.

There is currently little literature examining the validity of the LTFU category in relation to national surveillance systems. A recent study by Ditah et al. [8] focused on the categories used for TB surveillance and consequently cannot be generalised to allow comparison with our work. Ditah et al's study analysed predominantly patients whose treatment was interrupted or lasted longer than a year. It did not explore what happened to patients who were LTFU, simply categorising these patients as 'treatment failures'. As a result, the study does not consider the public health risk posed by this group of patients.

There is a wider range of literature relating to the risk factors for failing to complete treatment for TB. These include social deprivation, illiteracy, history of incarceration, older age, white ethnicity, and a history of substance misuse [13-15]. Our audit was unable to consider these wider risk factors in depth due to incomplete data. The data we analysed predates the collection of this information in the ETS system. Further work looking at the distribution of these risk factors amongst TB cases LTFU should be a priority. Our results showed no significant differences in terms of sex, age, ethnicity, or site of TB between those who completed treatment and those who were classified as LTFU.

Our audit suggests that there is a need to consider refining treatment outcome reporting to more

accurately reflect risk to public health. Our results showed that 16% of patients initially classified as LTFU subsequently recommenced and completed treatment, often many months after the 12 month deadline. Whilst the current treatment outcome monitoring form (Figure 1) states clearly that for patients still on treatment at 12 months, the form should be also be completed at 24 months, this does not capture patients who had stopped treatment prior to 12 months, were classified as LTFU and then recommenced treatment after the 12-month period. Our results show similarities to a study conducted in London [16], which re-reviewed treatment outcomes at 24 months after treatment initiation. That study showed that the group of patients classified as treatment failure at two years constituted mainly patients transferring abroad, transferring to another clinic, and those that died. Our audit highlights that new information often becomes available for patients classified as LTFU after the 12-month deadline. Consideration should be given to extending the deadline for treatment outcome reporting or changing the 24-month follow-up to include not just patients continuing treatment for longer than 12 months, but LTFU patients as well.

Our audit also suggests that significant numbers of our patients had interrupted treatment, resulting in significantly extended treatment regimes. Treatment interruption contributes to increased drug resistance in TB patients [17]. This suggests that more effort should be made at the time of diagnosis to identify patients at risk of treatment interruption and to use enhanced case management protocols and incentives to mitigate this risk. This will require increased investment in TB clinical teams, specifically community-based TB nurses and case mangers.

Locally, an outcome of this audit has included further training for clinicians to improve accuracy of outcome reporting. Nationally and internationally, a sustained focus on, and awareness of, the importance of enhanced TB surveillance is essential in reducing the public health threat posed by LTFU cases.

Risk factors for poor treatment adherence were not routinely collected by ETS during the period audited, and as such only unvalidated information from TB nursing records was available. This information suggested that poor treatment adherence was predicted for some of these patients and that, had resources been available, many of these patients would have been put on enhanced case management regimes at the time of diagnosis, such as directly observed therapy. The national ETS system introduced the collection of information about social risk factors for all notified TB cases in 2009, and therefore completeness levels are low but improving [8]. Analysing this improving information and conducting further work to quantify the risk of a patient becoming LTFU is important and should be a priority for the Health Protection Agency and in the future, Public Health England.

This audit only considers outcomes for patients notified in West Yorkshire (population 2.2 million). It is therefore important to understand if treatment outcome reporting in West Yorkshire differs significantly from the national pattern. A total of 379 patients (4.6% of reported cases) were classified nationally as LTFU in 2009 [7]. This rate is closer to the corrected figure obtained after our audit, suggesting that the overestimation of LTFU may be a local concern. At European level, results from the England, Wales and Northern Ireland TOM are collated by the European Surveillance System (TESSy). A recent report raised concern regarding the variations in TOM definitions and data collection methods between EU Member States, which impact upon results reported by TESSy [18]. Our results therefore emphasise that further work is necessary to understand possible national variations and should also ensure that TOM outcomes reported from national surveillance systems are consistent between countries and, most importantly, reflect the true outcomes of patients.

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