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# Influenza outbreaks in nursing homes with high vaccination coverage in Navarre, Spain, 2011/12

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In the 2011/12 season, three influenza outbreaks were studied in nursing homes with high vaccination coverage in Navarre, Spain. Attack rates ranged from 2.9% to 67%. Influenza A/Stockholm/18/2011(H3N2) virus strain was isolated from the three outbreaks. Vaccination should be complemented with other hygiene measures in nursing homes. Early detection of influenza outbreaks in nursing homes can aid in their control.

Four influenza-like illness (ILI) outbreaks have been detected in nursing homes in Navarre, Spain, during the 2011/12 wave of seasonal influenza. Three of these outbreaks were reported rapidly after the detection of the first cases. These outbreaks were investigated by the epidemiological surveillance unit in the region in order to identify the causes, to implement control measures and to give recommendations for preventing outbreaks in other nursing homes.

## Background

People living in nursing homes are more vulnerable to influenza infection due to their advanced age, the presence of major chronic diseases, and to the fact that they live together in close vicinity. Accordingly, there is broad consensus on the advisability of annual influenza vaccination for persons living in such conditions [1-3]. Routine vaccination of residents and caregivers can keep these homes from being affected by waves of seasonal influenza. However, in some seasons, when vaccine effectiveness is low because of the mismatch with the circulating virus, this measure is not enough, and more or less extensive outbreaks can occur [4-6].

## Investigation of the outbreaks

The three early detected outbreaks were studied by gathering information directly from the physicians who attended the cases and analysing the information from individual case reports of ILI. Following the European Union case definition [7] ILI was defined as the sudden onset of any general symptom (fever or feverishness, headache or myalgia) in addition to any respiratory symptom (cough, sore throat or shortness of breath). Vaccination data were obtained from clinical records in the nursing homes and were validated by the regional vaccination registry.

A number of cases were selected for swabbing from each outbreak according to different criteria: a random sample of ILI patients, hospitalised patients or all ILI cases (Table). Nasopharyngeal swabs were tested for detection of influenza virus by real time reverse transcription polymerase chain reaction (RT-PCR) and cell culture using a Madin-Darby canine kidney (MDCK) cell line. Isolates were sent to the National Reference Centre, National Center for Microbiology, Majadahonda, Spain, for influenza genotyping.

## Description of the 2011/12 influenza season in Navarre

Influenza surveillance in Navarre is based on automatic reporting of ILI cases from all primary healthcare centers and hospitals. In addition, a sentinel network of 83 primary care physicians and paediatricians take swabs from all their ILI patients for virological surveillance.

In the 2011/12 season, the influenza wave in the general population of Navarre exceeded the epidemic incidence threshold between 9 January and 18 March 2012, with the peak incidence in the third week of February (from 13 to 19 February).

Approximately 59% of the non-institutionalised population aged 65 and over in Navarre had received the inactivated influenza vaccine. By 1 April, the cumulative ILI attack rate in the non-institutionalised population was 2.1% overall, and 0.9% in those aged 65 and over. Preliminary estimates of vaccine effectiveness in preventing confirmed influenza cases are around 50% [8].

About 58% (368/640) of the throat swabs from patients in the sentinel physician network were positive for influenza by culture or RT-PCR, with a clear predominance of influenza A(H3N2) (94%). Fifty-six of these strains have been characterised: 43 were A/Stockholm/18/2011(H3N2) and 13 were A/Iowa/19/2010(H3N2).

## Description of the outbreaks in nursing homes, Navarre 2011/12

The three nursing home outbreaks are described in the table. All three nursing homes had carried out an influenza vaccination campaign in October 2011, reaching coverage from 82% to 97%. Problems concerning the vaccine lot, its conservation or administration were ruled out by consulting the vaccination registry and through discussions with the staff responsible for vaccination.

The influenza outbreaks occurred between week 4 and week 8 of 2012, coinciding with the epidemic wave in the region (Figure).

Influenza virus A(H3N2) was identified in all the three outbreaks, and the genotyped strains were characterised as A/Stockholm/18/2011(H3N2), coinciding with the strain most frequently found in the non-institutionalised population during this season. The attack rates were much higher in nursing homes (range 2.9% to 67%) than those in the general population aged 65 and over (0.9%). The attack rates in vaccinated persons ranged between 2.6% and 66%. The attack rates did not differ significantly between vaccinated and non-vaccinated persons in any of the nursing homes. During the outbreak investigation 57 ILI patients were detected with vaccine failure, 13 of whom had laboratory-confirmed influenza. In vaccinated persons, the time between vaccination and onset of ILI symptoms ranged between 92 and 142 days. Overall, 5% of the ILI cases (3/63) in the three nursing homes required hospitalisation, and death occurred in 3% of those affected (2/63), all of them in vaccinated persons with previous major chronic conditions.

## Control measures

As soon as the outbreaks were detected, hygiene measures (respiratory hygiene, hand hygiene, use of face masks) were intensified and cases were isolated to control the spread of the infection. The virus spread quickly in the first nursing home affected, and the intervention occurred when a large proportion of the residents had already become ill. In the other two nursing homes, the measures were applied early, helping to keep the attack rate at a lower level. Although antivirals were available, prophylaxis was not used in any nursing home. An alert was issued at regional and national level and hygiene measures were recommended in order to prevent possible future outbreaks in other nursing homes.

## Discussion

Influenza outbreaks in nursing homes with high vaccination coverage were detected in Navarre in the 2011/12 season. The attack rates did not differ significantly between vaccinated and unvaccinated persons, and 13 vaccine failures were laboratory confirmed. The results may indicate insufficient vaccine effectiveness to contain the spread of the influenza virus in nursing homes during this season. A recent study has reported moderate vaccine effectiveness in the 2011/12 season in Spain and suggests a limited match between vaccine and circulating influenza viruses [8].

To prevent influenza outbreaks in nursing homes, high rates of vaccination coverage should be achieved in residents and caregivers, and contacts of sick visitors and workers with residents should be restricted. Despite these measures outbreaks may occur, therefore epidemiologic and virologic surveillance systems in nursing homes should be instituted to report on influenza circulation in the resident population, and to allow early notification of suspected outbreaks [5-6].

Early identification of outbreaks of airborne diseases facilitates adequate decision making for their control. When an influenza outbreak is suspected in an institutionalised setting, it is recommended to intensify measures to avoid transmission: covering the mouth and nose when sneezing, frequent hand washing or use of alcohol-based hand sanitizers, use of face masks, separation of sick persons from the rest of the residents, reducing visits and reducing staff movement between different areas of the building. Antiviral drug treatment in cases and in persons exposed may also be useful [5-6].

Some limitations should be acknowledged in the study of these outbreaks. Information on ILI cases and vaccination status among nursing homes' workers and frequent visitors was not systematically collected. The design and the size of the study were not adequate to obtain estimates of the vaccine effectiveness. However, the high attack rate in vaccinated persons and the number of vaccine failures suggest reduced vaccine protection in these nursing homes.

In conclusion, influenza vaccination should be complemented with other hygiene measures in institutionalised settings. Early detection of influenza outbreaks in nursing homes can aid in their control.

### Acknowledgments

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## Table

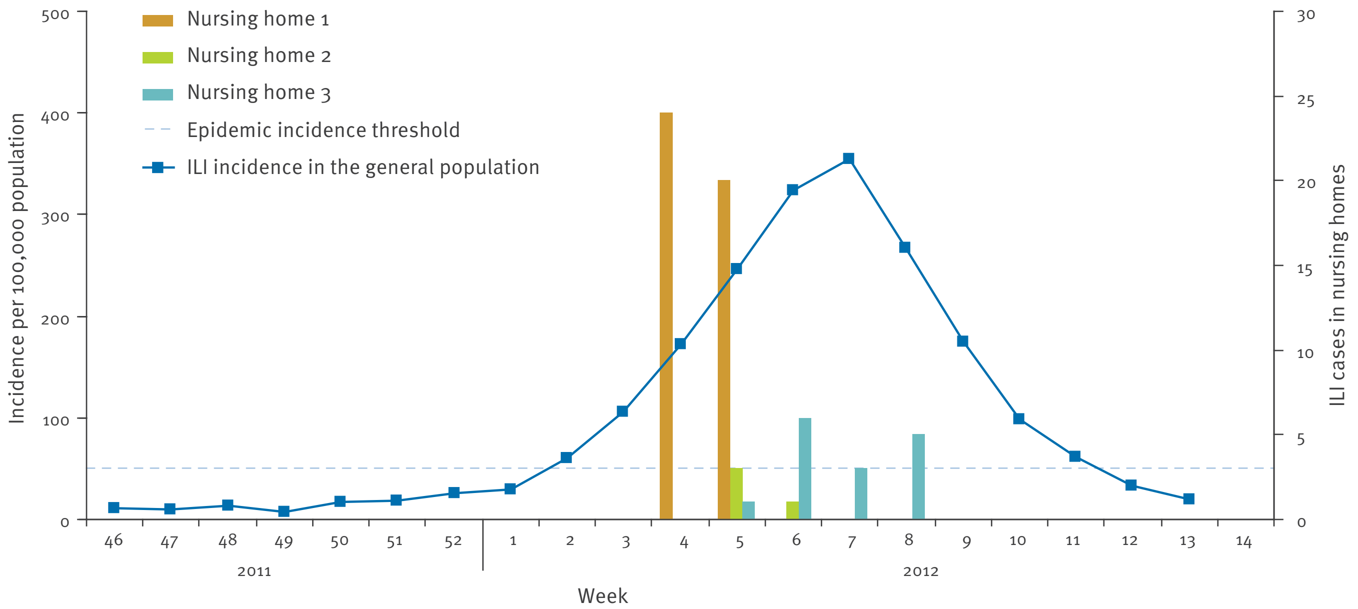
Characteristics of the influenza outbreaks and nursing homes studied, Navarre, Spain, 2012

| | Nursing home 1[a] | Nursing home 2[b] | Nursing home 3[a] |
|---|---|---|---|
| Resident population (n) | 66 | 22 | 523 |
| Women | 52 | 13 | 329 |
| Mean age (range) | 80.3 (42-97) | 81.2 (59-97) | 86.4 (62-104) |
| 2010/11 influenza vaccine coverage | 97% | 91% | 82% |
| Cases of influenza-like illness (n) | 44 | 4 | 15 |
| Influenza attack rate (total) | 67% (44/66) | 18% (4/22) | 2.9% (15/523) |
| Vaccinated | 66% (42/64) | 20% (4/20) | 2.6% (11/426) |
| Unvaccinated | 100% (2/2) | 0% (0/2) | 4.1% (4/97) |
| Comparison of attack rates in vaccinated and unvaccinated persons[c] | P=0.549 | P=0.549 | P=0.496 |
| Epidemic period (2012) | 24 Jan–1 Feb | 30 Jan–6 Feb | 2 Feb–3 March |
| Mean time between vaccination and symptom onset (days) | 99 | 103 | 127 |
| Swabbing criteria | Random sampling of cases | Hospitalised case | All cases |
| Nasopharyngeal swabs (n) | 7 | 1 | 15 |
| Identification of influenza virus | 6 | 1 | 8 |
| Vaccinated/unvaccinated | 6/0 | 1/0 | 6/2 |
| Virus strains | A/Stockholm/18/2011(H3N2) | A/Stockholm/18/2011(H3N2) | A/Stockholm/18/2011(H3N2) |
| Influenza-related hospitalisations (n) | 2 | 1 | 0 |
| Influenza-related deaths (n) | 1 | 1 | 0 |

[a] Urban area (city with 200,000 inhabitants approximately).
[b] Rural area (village with 1,000 inhabitants approximately).
[c] Two-tailed Fisher's exact test.

## Figure

Incidence of influenza-like illness (ILI) cases in the general population and ILI cases in nursing homes, by week, Navarre, Spain, 2011/12



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# Excess mortality among the elderly in 12 European countries, February and March 2012

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In February and March 2012, excess deaths among the elderly have been observed in 12 European countries that carry out weekly monitoring of all-cause mortality. These preliminary data indicate that the impact of influenza in Europe differs from the recent pandemic and post-pandemic seasons. The current excess mortality among the elderly may be related to the return of influenza A(H3N2) virus, potentially with added effects of a cold snap.

In most winter seasons, excess all-cause mortality among the elderly is observed in Europe. The extent of this excess varies considerably between seasons and between countries [1-5]. Most often, this excess has been attributed to seasonal influenza illness, especially in seasons dominated by A(H3N2) virus subtype, but other factors such as cold weather and infections resulting from other respiratory agents also play a role [1-8].

Since the beginning of February 2012, an increased number of excess deaths among the elderly has been observed in a number of European countries that carry out weekly monitoring of all-cause age-specific mortality.

The aim of this article is to describe the occurrence of this recently observed excess mortality in Europe and consider potential explanations in order to encourage other countries to assess their situation and share experiences.

## Monitoring all-cause mortality in Europe

Since autumn 2009, monitoring of weekly all-cause mortality has been carried out in up to 16 countries across Europe. This was initially part of the European monitoring of excess mortality for public health action (EuroMOMO), a project funded first by the European Union Health Programme [9] and later, European mortality monitoring received funding from the European Centre for Disease Prevention and Control (ECDC). The public health value of the project was underlined in the 2009 influenza pandemic, when these excess mortality outputs became important for European risk assessments [10-12].

A common statistical algorithm is used in EuroMOMO-participating countries to generate weekly indicators for age group-specific excess mortality that are comparable across countries. The algorithm is a time-series Poisson regression model with number of weekly deaths as a dependent variable adjusting for trend and seasonal variation. The algorithm also corrects for the delay observed between data collection and data processing in each country.

The main indicators generated are:
- total weekly number of deaths corrected for delay in registration;
- expected weekly number of deaths (baseline);
- weekly number of excess deaths (defined as observed number minus the expected number of deaths);
- standard deviation around the baseline (z-score);
- total mortality (all age groups) and mortality stratified into age groups (<5, 5–14, 15–64 and ≥65 years).

Standard deviation scores (z-scores) are used to standardise outputs and enable comparison of mortality patterns between different populations and between different time periods. Excess mortality above two z-scores from the baseline is considered above the normal level of the standard variation of data. Details of the EuroMOMO algorithm can be found elsewhere [13].

Data outputs from individual partner countries are compiled by the Statens Serum Institut in Denmark. Data analysed for this paper included all-cause mortality from week 1 (2 January) up to and including week 11 (18 March) 2012. A total of 14 countries submitted data: Belgium, Denmark, Finland, France, Germany (Hessen region), Greece (regions of Athens, Keratsini, Magnisia and Kerkira), Hungary, Ireland, the Netherlands, Portugal, Spain, Sweden, Switzerland and the United Kingdom (UK) (England and Wales).

Data on influenza activity were derived from the ECDC weekly influenza surveillance overview [14], EuroFlu [15] and from personal communication with national influenza surveillance representatives. Increased influenza activity was defined as medium or high influenza intensity, as reported through these channels.

## Results

All-cause mortality among the elderly (individuals aged ≥65 years) has been above two z-scores from the baseline for two consecutive weeks or more in Belgium, Portugal and Spain from week 5, in France and the Netherlands from week 6, in Finland, Hungary, Sweden and Switzerland from week 7. In the UK mortality among the elderly has been above 2 z-scores in weeks 7–8 and 11–12. Ireland reported a one-week peak of a z-score above 2 in week 9 and Greece in week 10. Denmark and Germany reported no excess mortality.

Although data from week 11 may be influenced by reporting delay, it appears that mortality has peaked and is now decreasing in Belgium, Finland, France, Portugal, Spain, Sweden and the Netherlands.

In Spain and Portugal, mortality has been above two z-scores from the baseline for two and three weeks, respectively, in the age group 15–64 years of age. Otherwise, there has been no sign of excess mortality in other age groups studied (0–4, 5–14 years).

In Portugal, Spain, France, Switzerland, Finland, Hungary, Ireland and Greece excess mortality among the elderly coincided with or followed after reported increased influenza activity (Figure 2). In Belgium, Sweden and the Netherlands, excess mortality seemed to precede, at least partly, reported increased influenza activity. In the UK, there was excess mortality but no reported increased influenza activity and in Germany, there was reported increased influenza activity but no excess mortality. Denmark, which has observed no excess mortality to date, reported no increased influenza activity. Among the countries that observed excess mortality, only the UK did not see medium or high influenza activity at least in parts of the same time period.

## Discussion

As in previous winter seasons, a number of European countries are experiencing increased mortality in the elderly population. Unlike the past two seasons, the excess mortality this year coincided in most countries with late increased influenza activity. An impact of influenza on the elderly is not unexpected, as this year is dominated by influenza A(H3N2): according to the ECDC weekly influenza surveillance overview of 30 March 2012, 95% of the influenza A viruses detected from sentinel and non-sentinel sources this season were type H3N2 [17]. In contrast, influenza A(H1N1) pdm09 was the prevailing type in the past two years. The pandemic virus more or less spared the elderly – although some countries, such as the UK, did observe excess mortality in middle-aged adults likely to be attributable to influenza A(H1N1)pdm09 activity [4,10,18].

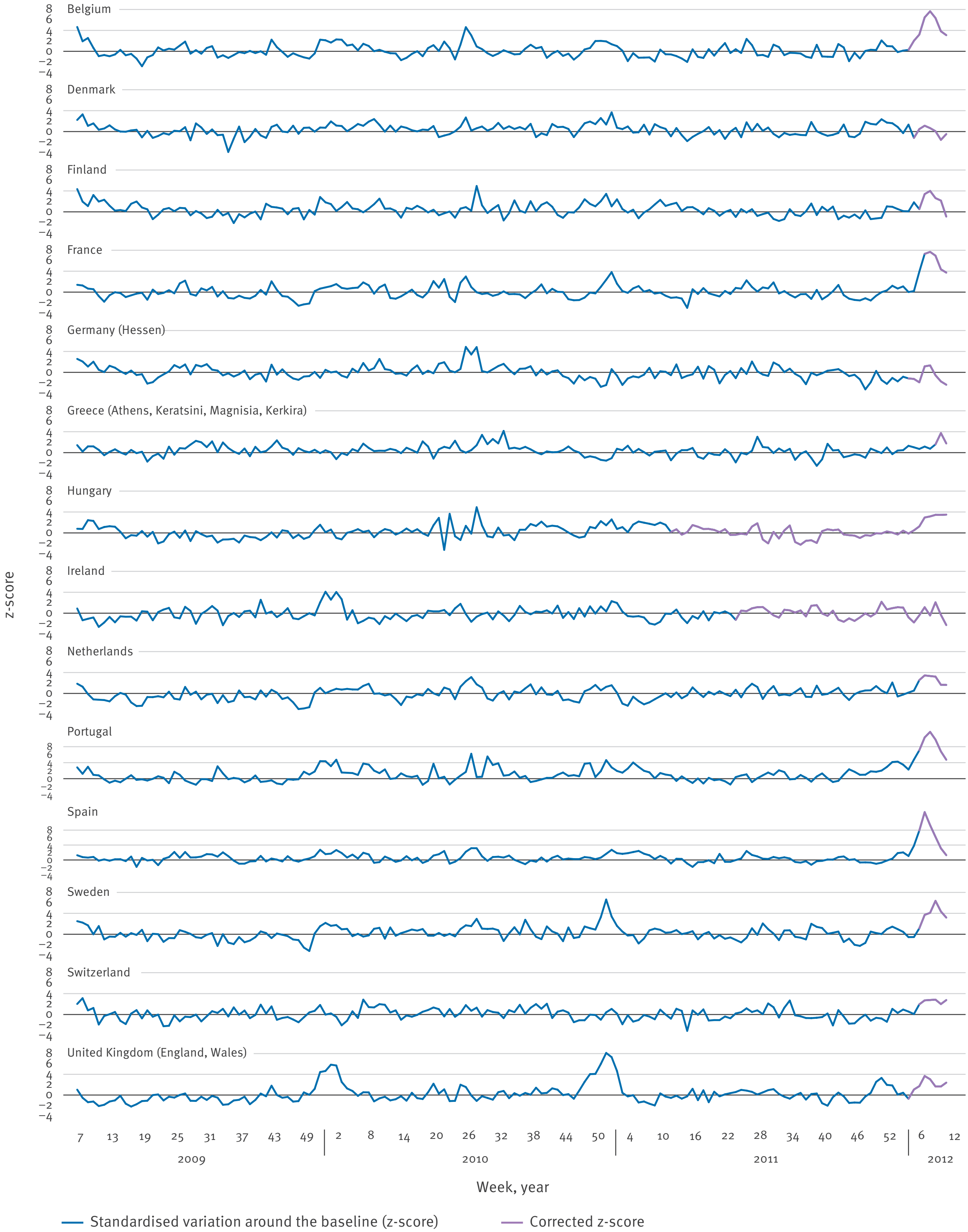
There are, at present, differences in observed excess mortality between European countries using the EuroMOMO algorithm. The available influenza data do not offer an exhaustive explanation for these differences. In most countries, excess mortality coincided or followed after reported increases in influenza activity. This pattern has been regularly observed in the pre-pandemic years [1-5,8] and corroborates the association of influenza (in particular influenza A(H3N2)) and excess deaths in the elderly. In particular, in the present season there are reports that some of these influenza A(H3N2) viruses are an imperfect match with the A(H3N2) strain included in the current vaccine; however, the contribution of this to the epidemiology of the observed excess mortality is unclear at this stage [19].

The data presented in Figure 2 suggest that the overlap between influenza activity and excess mortality was discordant in a few countries. There are several possible explanations for this observation. Firstly, the different patterns may suggest that other factors contribute to the occurrence of excess mortality. Indeed, there was a cold spell across Europe during weeks 4 to 6 this year throughout Europe, which might add to excess mortality in some countries, but not in others. It is well known that periods of extreme cold are associated with excess mortality [1,4,7,20,21]. In Spain, Belgium and the Netherlands, excess mortality could be observed before influenza transmission increased: we hypothesise that the cold spell could have been a contributing factor in those countries.

Secondly, the current definition of increased national influenza activity is based on a risk assessment by each European country. As a consequence, there are subjective differences in how this is interpreted. This may also partially explain the apparent discordance between observed excess mortality and reported level

**Figure 1**

Weekly mortality among those aged ≥65 years in 14 EuroMOMO countries as standardised deviations from the baseline (z-scores), week 7 2009–week 11 2012 (9 Feb 2009–18 March 2012)




EuroMOMO: European monitoring of excess mortality for public health action.
Corrected z-scores are z-scores corrected for delay in death registration.

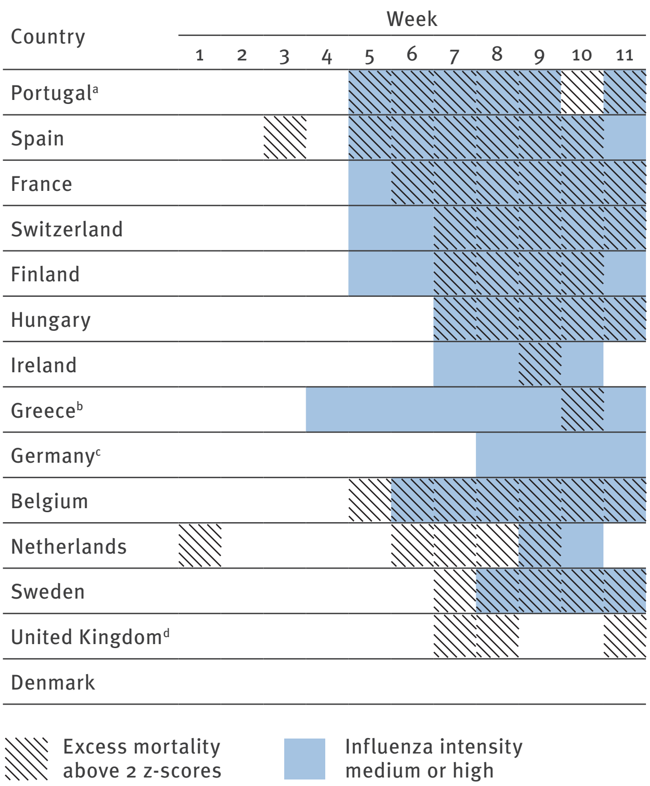
of influenza activity seen in some counties. It highlights the importance of developing more standardised objective measures of influenza activity. Finally, it is possible that infections other than influenza may contribute to excess mortality among the elderly in some countries.

The occurrence of potential risks at similar times – i.e. the cold snap and increased influenza activity – this winter season highlights the difficulty of disentangling the effects of different causes of excess mortality. Studies have shown that multivariate regression models can be successfully used to better quantify the impact of mortality risks such as influenza viruses, other respiratory viruses as well as extreme weather conditions [1,4,22,23].

In order to assess the public health impact of influenza at the population level, it is important to develop a common European approach to estimate the number of excess deaths associated with influenza. By including relevant and standardised indicators of influenza activity, virological data, vaccination data, climatic data and other respiratory infection data, it will be possible to perform a timely regression analysis to estimate excess mortality associated with influenza. We recommend that a standard approach should be developed with the results summarised at the end of the influenza season when final data are available. However, it is also important on an ongoing basis to collate, analyse, interpret and disseminate mortality data in order to inform public health actions. As cause-of-death in most countries will not be available in a timely fashion, this has to be carried out based on all-cause mortality data, and has to be interpreted in a qualitative method as in the present paper. On the basis of our preliminary data, we hypothesise that the epidemiology of the impact of influenza in Europe differs in the 2011/12 season from the recent pandemic and post-pandemic seasons, with excess mortality in the elderly caused by the return of influenza A(H3N2) virus, potentially with the added effects of a cold snap.

### Figure 2

Excess mortality above two z-scores above baseline among those aged ≥65 years and increased influenza intensity, in 14 EuroMOMO countries, by week, weeks 1–11 (2 January–18 March) 2012




EuroMOMO: European monitoring of excess mortality for public health action.

[a] Mortality data from [16].
[b] Athens, Keratsini, Magnisia, Kerkira.
[c] Hessen.
[d] England, Wales.

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# Influenza A(H1N1)pdm09 in England, 2009 to 2011: a greater burden of severe illness in the year after the pandemic than in the pandemic year

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Influenza pandemics are often perceived as single-year events, but the burden of previous influenza pandemics has in reality been spread over a number of years. The aim of this paper is to compare the burden of influenza in the pandemic year 2009/10 with that in the year immediately after (2010/11) in England. We compared four measures of disease. There was a greater burden of severe illness in 2010/11 compared with 2009/10: more deaths (474 vs 361), more critical care admissions (2,200 vs 1,700), and more hospital admissions (8,797 vs 7,879). In contrast, there were fewer general practice consultations in 2010/11 compared with 2009/10 (370,000 vs 580,000). There was also much less public interest in influenza, as assessed by number of Google searches. This is a worrying finding, as by the time of the second influenza season, much had been learnt about the potential impact of the influenza A(H1N1)pdm09 virus and an effective vaccine developed. We suggest that a widespread assumption of 'mildness' led to insufficient ongoing action to prevent influenza and hence to avoidable influenza-related deaths. This offers a lesson to all countries, both for future influenza seasons and for pandemic preparedness planning.

## Introduction

The public perception of influenza pandemics tends to be as single-year events. Contingency plans also assume that a new virus emerges and sweeps through the population, causing infection and death over a single year [1-4]. History, however, tells a different story. Previous pandemics have involved waves over multiple years, each causing pronounced mortality [1]. The 1968/69 pandemic was described as the 'smouldering pandemic'. In England and other European countries, its burden was greater in the 1969/70 influenza season than in the 1968/69 season [5].

When illness associated with the influenza A(H1N1)pdm09 virus (initially dubbed 'swine flu') was detected in April 2009, the public health response in England was intensive. In an initial containment phase, all contacts of cases were identified and treated with antiviral medication, to minimise spread of the virus. Schools were closed or partially closed. When increasing levels of influenza put serious pressure on the capacity of general practices to cope, a novel telephone and Internet-based system was introduced to mitigate this. This system, the National Pandemic Flu Service, ensured the public had ready access to antivirals. A widespread social marketing campaign, 'Catch it. Bin it. Kill it', emphasised the importance of hygiene measures (cough etiquette, hand washing) [6]. The pandemic also received extensive media coverage.

Fortunately the virus, and the pandemic, was milder than many had initially feared. Some criticised the government measures in the United Kingdom as a costly overreaction [7,8], though a formal inquiry into the management of the pandemic called the overall response 'highly satisfactory' [9].

In contrast, in the year after the pandemic, early comments from both from the Health Protection Agency and Department of Health were generally reassuring about the likely impact of influenza in the coming weeks [10,11]. The usual national advertising campaign to promote the seasonal influenza vaccine was not run [12]. When the number of severe cases rose and there were influenza-related deaths, the government was consequently criticised for complacency [13].

This study uses a number of objective measures to assess how the burden of influenza A(H1N1)pdm09 in the year after the pandemic compared with that in the pandemic year itself.

## Methods

Using published sources, we compared the burden of influenza in the pandemic year (2009/10) with that in the following year (2010/11) using four measures that were replicable across the two years. We also assessed public interest in influenza and antiviral usage over the same time period.

## General practice consultations

The Royal College of General Practitioners (RCGP) has undertaken surveillance of influenza-like illness (ILI) (clinically defined) in general practice for over 40 years. The system uses around 100 sentinel general practices across England, covering a population of approximately 800,000. The system extracts summary information (based on read codes [14]) from general practice electronic records. This is used to estimate the rate of ILI consultations in the population of England as a whole. These estimates, by age and week of consultation, were supplied by the RCGP Research & Surveillance Centre. We used these, together with mid-2009 population estimates from the Office for National Statistics [15], to estimate the total number of ILI consultations in England in each year.

## Hospital admissions

Information on hospital admissions was extracted from Hospital Episode Statistics (HES) [16]. This database contains details of all admissions to National Health Service (NHS) hospitals in England. Admission details are coded locally and uploaded to a central database. Two particular codes are used for influenza-related admissions: International Classification of Diseases (ICD) codes J10: influenza due to other identified influenza virus or J11: influenza, virus not identified). Instances of these codes were extracted by age and by week of hospital admission.

## Intensive care admissions

During the pandemic and the following year, all acute NHS hospitals reported both influenza-related critical care bed occupancy data (in 'bed-days') and the number of critical-care beds occupied at 8 a.m. on Wednesday mornings by age group to the Department of Health. These data recorded both suspected and confirmed cases of influenza. Suspected cases were those who were being treated for influenza on the basis of clinical suspicion but awaiting laboratory microbiological confirmation. Confirmed cases were those in whom the diagnosis had been confirmed by a specific microbiological test.

A national surveillance system in the pandemic year calculated the mean influenza-related length of stay in critical care as seven days [17]. We therefore estimated the number of admissions to critical care by dividing the total number of reported critical care bed days by seven. Critical care bed occupancy data were only recorded from 12 July 2009 to 21 February 2010 and from 20 December 2010 to 20 January 2011.

## Deaths

During the pandemic year, a special reporting system provided details of influenza-related deaths to England's Chief Medical Officer [18-20]. Deaths were considered influenza-related if the virus had been laboratory-confirmed, if influenza was recorded on the death certificate, or both. During the following year, the Health Protection Agency ran a similar system. Its definition of an influenza-related death was slightly narrower, requiring both laboratory confirmation and the recording of influenza on the death certificate [21].

## Public interest in influenza

A proxy chosen for public awareness of – and interest in – influenza was Google data on the rate at which particular search terms were used in its Internet search engine. We downloaded data describing the volume of searches for the term 'flu' by week in the United Kingdom. The absolute number of searches was not made available, thus the data describe the relative volume between weeks.

## Defining the influenza season

In England, the influenza season runs from the start of October to the start of April, with peak activity typically in December and January [22]. As the pandemic virus circulated outside the usual influenza season, however, we defined the pandemic year as starting when general practice consultations due to ILI first rose above 30 per 100,000 people per week, the threshold for normal seasonal influenza activity. In the year following the pandemic, we defined the start as being the usual start of an influenza season, i.e. the start of October. For both years, we defined the season end as the end of February. Thus the two seasons analysed were 29 June 2009 to 28 February 2010 (pandemic year) and 4 October 2010 to 27 February 2011 (second year).

## Antiviral prescribing data

Data describing the number of antiviral medication (oseltamivir and zanamivir) courses dispensed by pharmacists in the community in England were provided by the NHS Business Services Authority. Equivalent data were published by the National Pandemic Flu Service, describing the number of courses dispensed through this service, which was established specifically for the pandemic. Data on the number of courses of antiviral medication (oseltamivir or zanamivir) dispensed were published by the National Pandemic Flu Service.

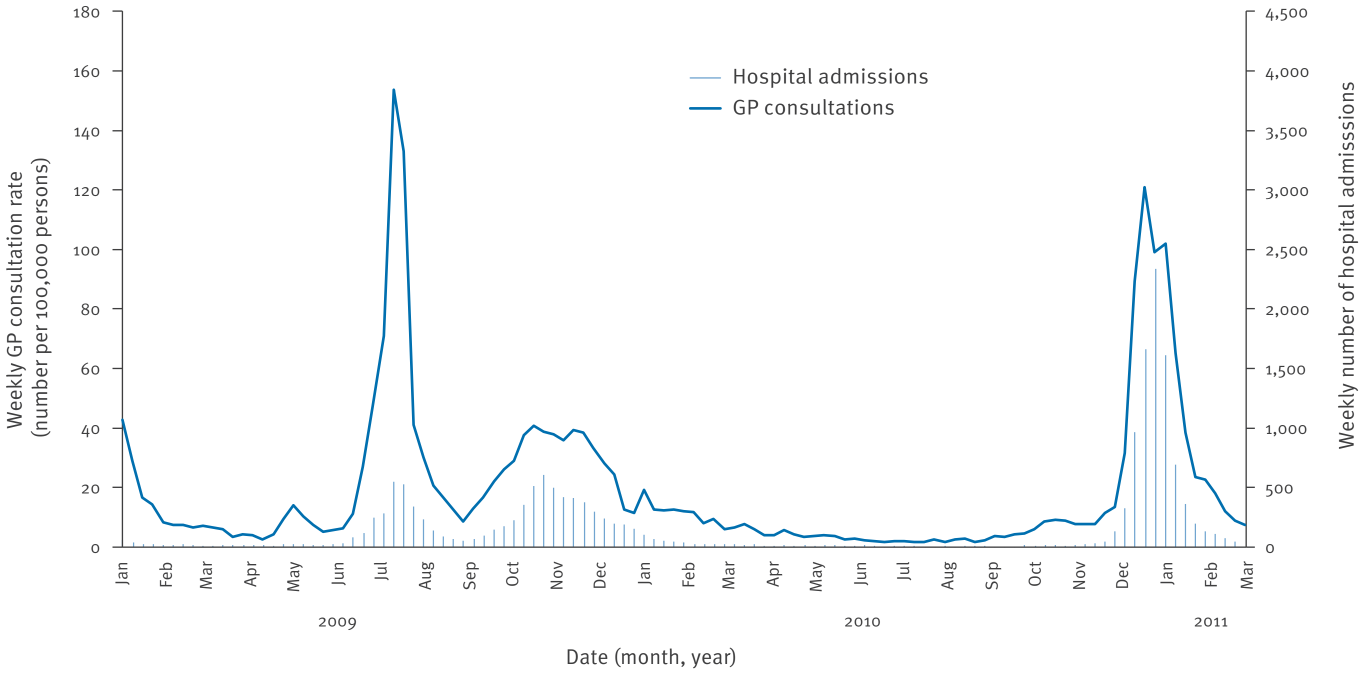
Oseltamivir and zanamivir are prescription-only medications. An electronic record of all prescriptions processed by community pharmacists is sent to the central NHS Prescription Services, in order for the pharmacist to receive reimbursement. These data are pooled to produce the total number of prescriptions of each discrete pharmaceutical item listed in the British National Formulary [23]. Although the data do not include private prescriptions, by including all prescriptions issued by the NHS, they will include the vast majority of prescriptions issued in the community in England.

# Results

Three distinct waves of influenza activity occurred during the two-year period (Figures 1 and 2): two during the pandemic year (2009/10) and a single wave in the second year (2010/11).

**Figure 1**

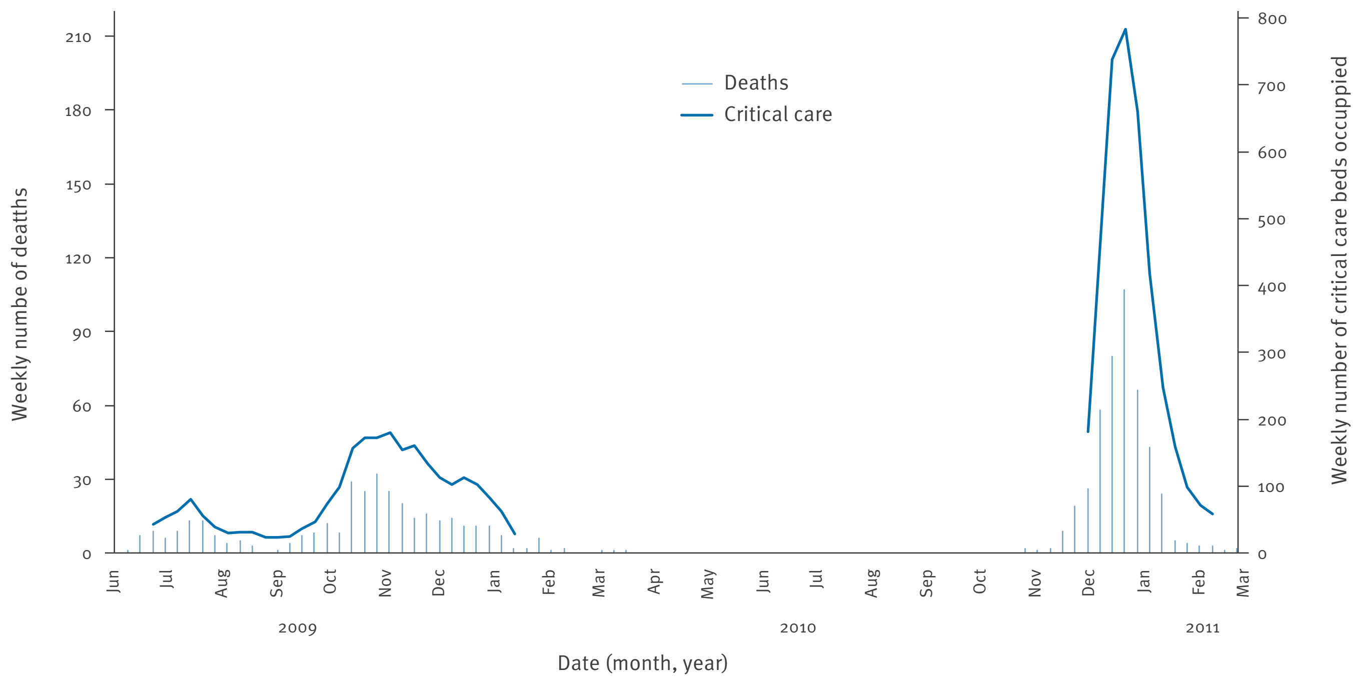
Influenza-related general practice consultations and hospital admissions, England, 5 January 2009–13 March 2011




GP: general practice.

**Figure 2**

Influenza-related critical care admissions and deaths, England, 15 June 2009–13 March 2011



The first wave occurred in July and August 2009, peaking 12 weeks after the first case of influenza A(H1N1) pdm09 was reported in England. This wave was characterised by a short sharp rise and fall in influenza activity, as assessed both by general practice consultations and hospital admissions.

The second wave occurred in autumn 2009. There was a gradual and prolonged rise in influenza activity that lasted for several weeks. Assessed by general practice consultations, the incidence of influenza in the community was lower than in the first wave. However, rates of influenza activity in hospital were much greater than those in the first wave.

**Table 1**

Influenza-related general practice consultations, hospital admissions, critical care admissions and deaths, England, pandemic year 2009/10 and second year 2010/11[a]

| Type of influenza-related event | Number of events | |
|---|---|---|
| | Pandemic year 2009/10[a] | Second year 2010/11[a] |
| Number of general practice consultations | 580,000 | 370,000 |
| Number of hospital admissions | 7,879 | 8,797 |
| Number of critical care admissions | 1,700 | 2,200 |
| Number of deaths | 361 | 474[b] (436) |

[a] Pandemic year: 29 June 2009 to 28 February 2010. Second year: 4 October 2010 to 27 February 2011.

[b] Deaths reported by the Health Protection Agency from 4 October 2010 to 4 May 2011. The number in parentheses is the estimated number of deaths due to influenza A(H1N1), based on 91.9% of all influenza-related deaths in the United Kingdom being attributable to influenza A(H1N1) [21].

The third wave occurred in December 2010 and January 2011 and was characterised by a short sharp rise and fall in influenza activity. This wave was associated with greater peaks in hospital and critical care admissions than either of the previous two waves.

Overall, the burden of severe illness caused by influenza (deaths, critical care and hospital admissions) was greater in the second year than the pandemic year (Table 1). There were approximately 10% more hospital admissions, 30% more deaths and 30% more critical care admissions in the second year than in both waves of the pandemic year combined. The reverse was true for general practice consultations: there were approximately 35% fewer of these in the second year than in the pandemic year.

Influenza activity in the second year was concentrated far more intensively than in the pandemic year. Most of the activity was concentrated in an eight-week period. The busiest four weeks in the second year involved three times as many hospital admissions as the busiest four weeks in the pandemic year (20 December 2010 to 16 January 2011: 1,643 admissions per week; 2 November 2009 to 30 November 2009: 510 admissions per week). Similarly, there were over three times as many critical care admissions per week over the same periods (mean critical care bed occupancy: 661 vs 170). The peak weekly hospital admission rate in the second year was more than three times that of the pandemic year (week ending 2 January 2011: 2,334 admissions; week ending 3 October 2009: 604 admissions). The peak critical care bed occupancy in the second year was four times that of the pandemic year (851 beds on 4 January 2011, compared with a peak of 196 in November 2009).

**Table 2**

The age distribution of influenza-related general practice consultations, hospital admissions, critical care admissions and deaths, England, pandemic 2009/10 and second year 2010/11[a]

| Type of influenza-related event | Number of events (%) by age group | | | | Chi-square test p value |
|---|---|---|---|---|---|
| | 0–4 years | 5–14 years | 15–64 years | ≥65 years | |
| **Number of general practice consultations** | | | | | |
| Pandemic year[a] | 61,000 (11) | 94,000 (16) | 390,000 (67) | 34,000 (6) | <0.001 |
| Second year[a] | 25,000 (7) | 42,000 (11) | 280,000 (74) | 27,000 (7) | |
| **Number of hospital admissions** | | | | | |
| Pandemic year | 1,790 (27) | 1,182 (15) | 4,429 (56) | 478 (6) | <0.001 |
| Second year | 1,551 (18) | 461 (5) | 5,797 (66) | 988 (11) | |
| **Mean number of critical care beds occupied[b]** | | | | | |
| Pandemic year | 7.8 (10) | 4.9 (5) | 59 (73) | 8.7 (11) | 0.067 |
| Second year | 15.8 (4) | 7.9 (2) | 280 (80) | 47 (13) | |
| **Number of deaths** | | | | | |
| Pandemic year (England only) | 22 (6) | 35 (10) | 240 (66) | 64 (18) | 0.004 |
| Second year (United Kingdom)[c] | 25 (4) | 25 (4) | 415 (71) | 122 (21) | |
| Population in England (millions) | 3.2 (6) | 5.9 (11) | 34.3 (66) | 8.4 (16) | |

[a] Pandemic year: 29 June 2009 to 28 February 2010. Second year: 4 October 2010 to 27 February 2011.

[b] Counted at 8 a.m. on Wednesdays.

[c] Only includes those for whom age at death was known.

For every 10,000 general practice consultations in 2009/10 there were 136 hospital admissions, 29 critical care admissions and six deaths. The respective numbers for 2010/11 were approximately twice as great, being 238 hospital admissions, 59 critical care admissions and 13 deaths. In contrast, measures of severe illness had similar ratios between the two seasons. For every 1,000 hospital admissions in 2009/10 there were 215 critical care admissions and 45 deaths. In 2010/11, the respective numbers were 250 critical care admissions and 53 deaths.

In the second year, the younger age groups (0–4 years, 5–15 years) were less prominently affected than in the pandemic year. The burden shifted towards working-age people (16–64 years) and the elderly (Table 2, chi-square $p<0.001$ for general practice consultations and hospital admissions). This shift was seen consistently across all measures of influenza activity.

Public interest in influenza, indicated by volume of Internet searches, showed four peaks of activity (Figure 3). The first occurred in April 2009, when the new strain of the virus was first widely publicised, leading to worldwide concern about an imminent pandemic. The second peak in interest occurred in July 2009, coinciding with the first wave of influenza activity in England. Two further, smaller peaks coincided with the second and third waves of influenza activity in England. Public interest relative to the burden of influenza (as measured by number of hospital admissions per week) was relatively high during the first wave of activity, lower during the second wave of activity and very low in the third wave. Public interest in influenza was four times as great in July 2009 as in January 2011, whereas the rate of hospital admission was four times as great in January 2011 as in July 2009.

During the pandemic year, the National Pandemic Flu Service operated from 23 July 2009 to 11 February 2010. It dispensed 1,161,157 courses of antiviral medication during this time. Community pharmacists dispensed fewer courses: 10,610 in the pandemic year (June to February) and 38,692 in the second year (October to February). Overall, 30 times more courses of antiviral medication were dispensed in the pandemic year than in the following year (1,171,767 vs 38,692 courses).

## Discussion

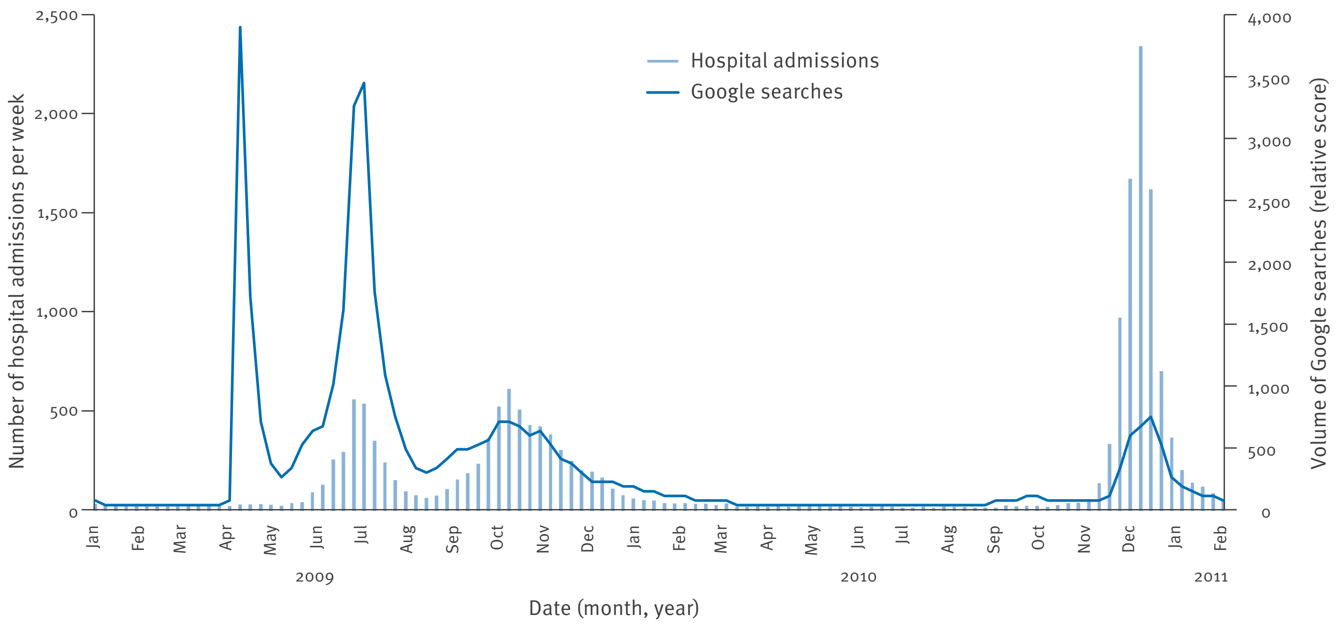
In England, influenza A(H1N1)pdm09 caused more hospital admissions, more critical care admissions and more deaths in its second year of circulation than in the pandemic year itself. There were fewer general practice consultations and there was less public interest in influenza in the second year than in the pandemic year. This is a worrying finding given that an effective vaccine was available for the duration of the influenza season following the pandemic year.

## Ascertainment bias is unlikely

We looked at whether systematic differences in the methods of ascertainment or changes to the definitions of any of the measures analysed between the two years could explain this difference. The case definition of a death was actually narrower in the second year than in the pandemic year. For hospital and critical care admissions, the case definitions and ascertainment methods were the same in both years. However, the system for reporting critical care admissions in the second year was not established until mid-December,

**Figure 3**

Hospital admissions for influenza and Google searches for ‘flu’, England, 19 January 2009–27 February 2011



after many admissions are likely to have occurred. For all these reasons, both deaths and critical care admissions are likely to have been underestimated in the second year relative to the pandemic year. It therefore seems unlikely that systematic differences in ascertainment can explain the principal finding of our study.

Could ascertainment of deaths, critical care and hospital admissions have been increased by enhanced clinical awareness of influenza, leading to greater testing for, and diagnosis of, the disease? This seems highly implausible. Public awareness and clinical awareness of influenza was markedly lower in the second year. Why would England be alone among western countries in experiencing a phenomenon of increased clinical diagnosis and reporting of influenza in the second year relative to the pandemic year? No such effect was found in the United States, Canada, Australia or New Zealand. If anything, clinical ascertainment of cases in England is likely to have been greater in the pandemic year, when there was huge media interest in this novel event and clinicians' awareness of the circulation of the virus was high. Moreover, there was a great deal of communication between the government and front-line clinicians. This would all suggest that the true difference between the two years was in fact greater than that reported here.

The methods of influenza surveillance in general practice in England are long established and unchanged in recent years. The existence of the National Pandemic Flu Service from July 2009 until February 2010 was intended to reduce the burden on general practice. No equivalent system existed in the second year. General practice consultation rates are therefore likely to be relatively suppressed in the pandemic year compared with the second. Again, this suggests that the difference between the two years reported here is a highly conservative estimate.

Finally, all three measures of severe illness showed similar changes. We have also heard anecdotal accounts from intensive care physicians that the 2010/11 influenza season brought with it serious cases of influenza in previously healthy young individuals on a scale that appeared worse than in the pandemic itself. Taken together, this leaves little room for doubt that there was a genuine increase in hospital and critical care admissions and in deaths between the two years.

## Most countries did not suffer a worse second year

International comparisons are somewhat difficult because of uncertainty about the quality of surveillance across the two years. Those comparisons that can be made suggest that England's experience is unusual. In the second year, the United States experienced lower peak ILI consultations (4.6% vs 7.7% of weekly outpatient visits), fewer paediatric deaths (105 vs 282) and a lower hospitalisation rate (19.1 per 100,000 population vs 29.0 per 100,000 population) than in the pandemic year [24]. New Zealand reported a lower peak ILI rate (150 per 100,000 in 2010 vs 275 per 100,000 in 2009), fewer hospital admissions (998 vs 1,517) and fewer deaths (16 vs 35) [25]. Similar patterns were seen in Canada and Australia [26-28].

The European picture is less clear [29], but many European countries have reported fewer cases of severe illness and fewer deaths in the second year [30,31]. Only the experience of Ireland, Greece and the other UK nations looks similar to that of England. Ireland had small increases in the numbers hospitalised, treated in critical care and dying [32,33]. Greece experienced more intensive care admissions and fatal cases in the post-pandemic season than in the pandemic season (368 vs 294 and 180 vs 149 respectively), although the magnitude was not on the same scale as in England [34]. Broadly, the English pattern was replicated in the other UK nations, with higher peak levels of influenza activity in 2010/11 and similar or slightly more deaths (69 deaths in Scotland in 2009/10 vs 63 in 2010/11, Wales 28 vs 34, Northern Ireland 18 vs 31) [9,21].

## Government response was the major difference between the two years

What could explain the greater burden of severe illness in the second year? The virus has been closely observed. Its genetic composition had not changed [21]. Influenza B virus was more evident in the second year than in the pandemic year. It was the causative agent detected in 24.1% of positive influenza specimens (compared with just 0.3% in the pandemic year) but accounted for just 6.6% of deaths [21]. There were anecdotal reports of serious illness caused by coinfection in the second year, but the total number of these reports is not great [2,35,36]. While the small shift in age distribution towards older age groups, who are more prone to the severe effects of influenza, will have contributed to the greater burden of severe illness [34], similar shifts have been seen elsewhere but not resulted in a greater burden of severe illness [28]. Peak transmission in the second year occurred later in the year, when the weather in England was colder and drier. This may have had a role in facilitating greater transmission of the virus in the second year [37-39].

However, the most notable difference between the two years was the government response. The public health response in the pandemic year was highly assertive. Strong public awareness and education campaigns were run. Extensive and rolling media coverage throughout the duration of the emergency is likely to have enhanced public understanding. Antiviral drugs were widely used for symptomatic individuals and (in the early phase) their contacts. Schools were closed, with antiviral treatment of cases and contacts. Unlike previous influenza pandemics, a vaccine was made available and used before the end of the pandemic year.

In contrast, in the influenza season that followed the pandemic year, the approach was laissez-faire. The traditional influenza public awareness campaign was cancelled. There was no attempt to warn about the likelihood that the pandemic virus would be circulating (thus affecting younger age groups). There was no drive to vaccinate children, although it is unclear to what extent this was influenced by emerging concerns about pandemic vaccine safety in children and adolescents [40,41]. The National Pandemic Flu Service was not activated and antivirals were not used extensively.

The 30-fold difference in antiviral usage between the two years is profound. The widespread use of antiviral medication in the community combined with public awareness during the pandemic year is likely to have led to early treatment. This is likely to be important in preventing adverse outcomes, such as hospitalisation, critical care admission and death [42,43]. A reduction in virus transmission, particularly among children [43-45], from widespread antiviral use may also have contributed to the reduced burden of severe illness in the pandemic year. Other public health measures may also have had an important impact on the emerging disease [46,47].

Some countries took a very proactive approach to immunisation in the second year. New Zealand achieved record levels of immunisation [25]. In the United States, the Centers for Disease Control and Prevention emphasised the special importance of vaccination, extending its availability to all healthy adults [48].

In England, when the virus began to circulate in early December 2010, uptake of vaccine among the eligible groups aged six months to 65 years was only about 40% [49]. The final uptake figures, at around 50%, were comparable to the pandemic year [50]. Given that this group was at increased risk of severe complications in comparison with a typical influenza season, it is disappointing that higher levels of immunisation were not achieved, particularly as influenza causes more deaths among those aged under 65 years than any other vaccine-preventable disease [19,51,52].

## Reduction in general practice consultation rates

What might account for the reduction in general practice consultation rates between the two years? These rates are driven by the incidence of influenza and by the proportion of those affected who seek care. Given the greater burden of severe illness in the second year without any change in the virus itself, it seems unlikely that the incidence of influenza was lower in the second year than in the pandemic year. Consistent with the demonstrated lower level of public interest, it seems likely that the public were less likely to consult when symptomatic in the second year.

A lower rate of general practice consultations might itself have contributed to higher rates of severe illness. It is likely to have contributed to delayed and lower use of antivirals. It is also possible that the detection of superimposed bacterial illness or other severe illness may have been delayed.

## Predictable age distribution: younger than those with typical seasonal influenza

Both years saw a high ratio of young to elderly influenza deaths in comparison with that seen in a typical influenza season. The second year saw a small shift away from the younger age groups towards adults of working age. This is consistent with past influenza behaviour. Analysing historical influenza mortality data from the United States, Simonsen et al. have shown that a marked shift in mortality away from the elderly to the young has occurred in the first year of previous pandemics [53]. This shift persists, slowly drifting back towards the elderly over a period of 10 to 20 years. Influenza A(H1N1)pdm09 is so far behaving similarly. This shows the importance not only of remaining vigilant after the first passing of the pandemic wave, but also of maintaining heightened vigilance for several years after.

## Conclusion

England experienced a greater burden of severe illness due to influenza A(H1N1)pdm09 in the second year of its circulation than in the pandemic year. The difference appears to be real rather than fallacious. By the time of the second influenza season, much had been learnt about the potential impact of the virus and an effective vaccine developed. Despite this, a large number of deaths, critical care and hospital admissions occurred, many of these in otherwise healthy people of working age. The differences in the government response over the two years were striking and likely to have contributed to the increased impact of the disease in the second year.

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News

# European Food Safety Authority publishes its second report on the Schmallenberg virus

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On 2 April 2012 the European Food Safety Authority (EFSA) published its second report on the Schmallenberg virus (SBV), to date identified in animals in eight European Union (EU) Member States (MS) [1]. In this report, EFSA compiled and analysed data on PCR or serologically confirmed cases in the MS and these data show that the proportion of infected ruminants is low even if the figures need to be looked at with caution. The report contains maps showing the distribution of the animal cases.

The Schmallenberg virus can affect both wild and domestic ruminants, but there is currently no evidence that it can cause illness in humans.

The SBV is a newly recognised *Orthobunyavirus* that was first detected in November 2011 in cattle in the Netherlands and Germany. Since then, the SBV has been reported in ruminants from Belgium, Germany, France, Italy, Luxembourg, the Netherlands, Spain, and the United Kingdom.

The disease causes transient clinical signs in adult cattle (fever, diarrhoea, reduced milk yield, etc.), abortions and congenital malformation in newborn animals. The virus is assumed to be primarily transmitted via biting midges.

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