

Overrepresentation of influenza A(H1N1)pdm09 virus among severe influenza cases in the 2011/12 season in four European countries

J Beauté (Julien.Beaute@ecdc.europa.eu)¹, E Broberg¹, F Plata¹, I Bonmarin², J O'Donnell³, C Delgado⁴, N Boddington⁵, R Snacken¹

1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

2. Institut de Veille Sanitaire (InVS), Saint-Maurice, France

3. Health Protection Surveillance Centre, Dublin, Ireland

4. Centro Nacional de Epidemiología (National Centre of Epidemiology), Instituto de Salud Carlos III, Madrid, Spain

5. Respiratory Diseases Department, Health Protection Agency, London, United Kingdom

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In France, Ireland, Spain and the United Kingdom, the influenza season 2011/12 started in the final weeks of 2011 and has been dominated by influenza A(H3) viruses with minimal circulation of influenza A(H1N1)pdm09 and B viruses. A relatively greater proportion, however, of influenza A(H1N1)pdm09 viruses were reported in hospitalised laboratory-confirmed influenza cases in four countries. Compared to the season 2010/11, the proportion of subtype A(H3) among hospitalised cases has increased, associated with a larger proportion of cases in the youngest and oldest age groups.

The 2010/11 influenza season in Europe was dominated by influenza A(H1N1)pdm09 viruses, but influenza B viruses also circulated widely, being the dominant type in some countries such as Ireland [1]. In hospitalised cases, the A(H1N1)pdm09 virus was by far the most common virus reported. The 2011/12 influenza season started around week 52 when more than 10% of sentinel samples from the community tested positive for influenza virus [2]. In week 5 of 2012, as influenza activity was increasing throughout Europe, 42% of sentinel specimens tested positive for influenza virus, of which 89% were subtyped as A(H3) [3]. Here we report the distribution of virus strains in hospitalised cases for the 2011/12 season which differed markedly from those seen in primary care.

Influenza surveillance in the European Union

The sentinel surveillance of influenza-like illness (ILI) or acute respiratory infections (ARI) in Europe is carried out by the European Influenza Surveillance Network (EISN) under the coordination of the European Centre for Disease Prevention and Control (ECDC). This surveillance covers the 27 European Union (EU) Member States, Norway and Iceland. The surveillance season

lasts from week 40 to week 20 of the following year. On a weekly basis, cases meeting the European definition of ILI or ARI [4] are reported electronically to the European Surveillance System (TESSy) database held at ECDC.

Specimens from a subset of patients in the sentinel population have been collected since 1996 [5]. These specimens (nasal or pharyngeal swabs) are taken by general practitioners from patients with ILI, ARI or both and are sent to influenza-specific reference laboratories for virus detection. The selection of ILI patients to be swabbed is a systematic process that may differ across countries. During the 2009 pandemic, surveillance of hospitalised influenza cases was initiated, relying on the same network, and is still ongoing. Since admission to hospital is a medical decision, it is considered a good proxy for severity. Hence, a severe influenza case was defined as a person admitted to hospital with a laboratory-confirmed influenza infection. The criteria for laboratory confirmation were as described in the European case definition [4].

In the analysis presented here, we included those four EU countries which have been reporting laboratory-confirmed hospitalised influenza cases since the start of the 2011/12 influenza season: Reporting from France and the United Kingdom (UK) included only laboratory-confirmed influenza cases admitted to intensive care units (ICU), while Ireland and Spain reported all hospitalised laboratory-confirmed influenza cases.

We retrieved sentinel and severe influenza surveillance data for the seasons 2010/11 and 2011/12, restricting our analysis in the second season to the time period from week 40/2011 to week 5/2012 (week 3/2012 for the UK). Since the UK had not reported severe influenza in season 2010/11 to TESSy, we used data for that

season collected by the Health Protection Agency as reported by Bolotin et al. [6]. We compared influenza virus subtype distribution between sentinel specimens and specimens from hospitalised cases as well as the age distribution of hospitalised patients between seasons. Age distributions are presented with their medians and interquartile ranges (IQR) and compared by Mann-Whitney U test. Proportions were compared by chi-square or Fisher's exact tests and a significance level of less than 0.05.

Hospitalised and sentinel influenza cases

From week 40/2011 to week 5/2012, 1,432 sentinel and 199 hospitalised influenza cases were reported by the four countries included in the analysis, France, Ireland, Spain and the UK (Table 1). Of 118 hospitalised cases reported by Spain, 29 (25%) were admitted to ICU. One case of the three reported by Ireland was admitted to ICU. All cases from France and the UK were ICU cases as other cases were not monitored in these countries. In season 2010/11, 6,338 sentinels and 4,059 hospitalised influenza cases were reported by the same countries (Table 2).

TABLE 1

Distribution of influenza virus subtypes in sentinel specimens and specimens from hospitalised cases, France, Ireland, Spain, and United Kingdom, week 40/2011–week 5/2012 (n=1,631)

Influenza virus subtype	Surveillance level		p value
	Sentinel specimens n (%)	Hospitalised cases n (%)	
A(H1N1)pdm09	14 (1)	20 (10)	<0.01
A(H3)	1,219 (85)	108 (54)	<0.01
A (subtype unknown)	143 (12)	60 (30)	
B	56 (4)	11 (6)	0.28
Total	1,432 (100)	199 (100)	

TABLE 2

Distribution of influenza virus subtypes in sentinel specimens and specimens from hospitalised cases, France, Ireland, Spain, and United Kingdom, week 40/2010–week 20/2011 (n=10,397)

Influenza virus subtype	Surveillance level		p value
	Sentinel specimens n (%)	Hospitalised cases n (%)	
A(H1N1)pdm09	3,794 (59.9)	3,076 (75.8)	<0.01
A(H3)	182 (2.9)	24 (0.6)	<0.01
A (subtype unknown)	246 (3.9)	398 (9.8)	
B	2,116 (33.4)	561 (13.8)	<0.01
Total	6,338 (100)	4,059 (100)	

Virology

Of the 199 laboratory-confirmed hospitalised influenza cases in 2011/12, 20 (10%) were due to influenza A(H1N1)pdm09 virus, of which 19 had been admitted to ICU. Of 1,432 sentinel specimens that tested positive for influenza viruses during the same period, 14 (1.0%) were reported with this subtype ($p<0.01$) (Table 1). Conversely, 108 (54%) of the 199 hospitalised cases were due to influenza A(H3) virus, compared with 1,219 (85.1%) of the 1,432 sentinel cases ($p<0.01$). Of the 108 hospitalised influenza A(H3) cases, 33 (30%) had been admitted to ICU. Influenza B viruses were equally distributed between sentinel cases and hospitalised cases.

In season 2010/11, the proportion of influenza A(H1N1)pdm09 viruses was approximately 1.5 fold higher in reported hospitalised cases compared with sentinel cases, and the proportion of A(H3) viruses in reported hospitalised cases was approximately five times lower than in sentinel cases (Table 2). In 2010/11, the proportion of influenza B virus in hospitalised cases was smaller than in sentinel cases, while in season 2011/12, it was the same in sentinel and hospitalised cases.

Age and sex

Over the last two seasons, the median age of reported hospitalised cases in the four reporting countries was similar with 48 years (IQR 31–60) in season 2010/11 and 54 years (IQR 3–74) in season 2011/12. Nevertheless, the distribution across age groups was very different with young adults (15–44 years) and middle-aged adults (45–64 years) most affected during the 2010/11 season, and the youngest (0–4 years) and oldest (≥ 65 years) age groups most affected during the 2011/12 season.

Additional stratification by subtype seemed to suggest that changes in age distribution were related to the dominant subtype although this observation relied on small numbers. Thus, influenza A(H3), which is dominating the season 2011/12 seems to cause severe disease mainly in the age groups of 0–4 and ≥ 65 year-olds, while influenza A(H1N1)pdm09, which dominated the previous season caused severe disease mainly in the age groups of 15–44 and 45–64 year-olds (Figures 1 and 2). Influenza B viruses were more evenly distributed among age groups. The male:female ratio among the severe cases was 1.1 in season 2011/12 which was similar to previous seasons.

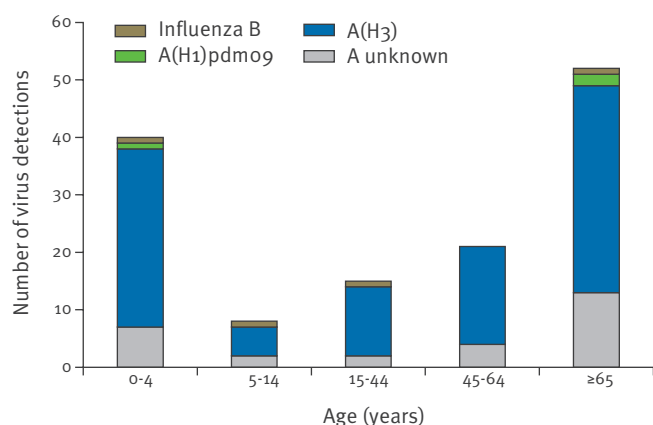
Because a relatively high proportion of influenza A viruses in hospitalised cases were not subtyped in the season 2011/12, we performed a sensitivity analysis in which we assumed that all influenza A viruses of unknown subtype were A(H3) viruses. The higher proportion of influenza A(H1N1)pdm09 in hospitalised cases as compared to sentinel cases remained statistically significant ($p<0.01$).

Mortality

Of the 97 hospitalised influenza cases with known outcome in season 2011/12, 11 died (11%). Seven of the 11 fatal cases were reported to have influenza A(H3), three with influenza A with unknown subtype and one with influenza B. In season 2010/11, 362 of 1,968 cases with known outcome were fatal (18.4%), which was not significantly higher than in 2011/12 ($p=0.08$). Of these 362 fatal cases, 286 (79%) were reported with influenza A(H1N1)pdm09, 53 (15%) with influenza A with unknown subtype, 21 (6%) with influenza B and two (1%) with A(H3).

FIGURE 1

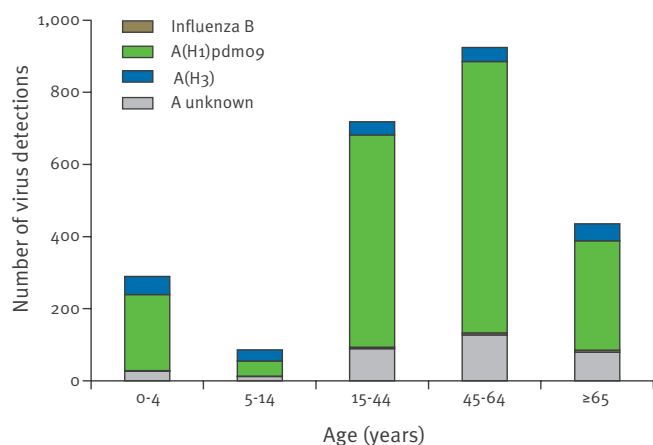
Influenza viruses detected in laboratory-confirmed hospitalised cases, by virus subtype and age group, France, Ireland, Spain and United Kingdom, week 40/2011–week 5/2012 ($n=136^a$)*



^a Cases for whom information on age was available.

FIGURE 2

Influenza viruses detected in laboratory-confirmed hospitalised cases, by virus subtype and age group, France, Ireland, Spain and United Kingdom, week 40/2010–week 20/2011 ($n=2,452^a$)*



^a Cases for whom information on age was available.

Discussion

The influenza season 2011/12 is the second season following the influenza A(H1N1)pdm09 pandemic. After the extinction of the former seasonal A(H1) influenza virus, A(H1N1)pdm09 appears to have been replaced by A(H3) viruses in sentinel respiratory specimens. Interestingly, this replacement was not as pronounced in severe cases, in whom A(H1N1)pdm09 influenza virus was found in a higher proportion than in sentinel cases (10% vs. 1%). The reason may be that A(H1N1)pdm09 influenza viruses could be more virulent than A(H3) viruses. The changes in influenza A virus distribution may have had an impact on the age distribution of hospitalised cases. Whilst young and middle-aged adults were more commonly affected during the 2009 influenza pandemic [7], the peaks observed in the youngest and oldest age groups before the 2009 pandemic were seen again in 2011/12. This age shift was also observed in the UK during the 2010–11 season [6]. To our knowledge, there are few publications on this topic because most surveillance systems collecting data on severe influenza cases have been implemented only recently. The main hypothesis explaining this shift assumes changes in demographic patterns and pre-existing immunity to A(H1N1)pdm09 influenza virus in older age groups conferred by prior exposure to viruses circulating in the 1950s [8,9].

This analysis has some limitations. Firstly, we cannot exclude a selection bias with two countries reporting all hospitalised cases and the other two only cases admitted to ICU. The high proportion (19/20) of A(H1N1)pdm09 influenza viruses reported in ICU cases also suggests that our results are biased towards the most severe cases. Secondly, a relatively high proportion of influenza A viruses in hospitalised cases were not subtyped in the season 2011/12 but results of the sensitivity analysis confirmed the observed trend.

Conclusion

The epidemiology of influenza virus types and subtypes may differ between mild and severe cases. Vaccine campaigns targeting populations at risk for severe disease should take this information into account. Our results demonstrate the potential value of collecting data on severe cases to better understand the epidemiology of influenza. Data collection should be harmonised and promoted in more EU countries. It may help to identify more clearly potential biases and to provide decisions makers with more accurate data on severe influenza cases.

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Conflict of interest

R. Snacken did some scientific work and organised meeting for the European Scientific Group on Influenza (ESWI) between 1992 and 2008. ESWI is funded by the pharmaceutical industry.

* Authors' correction:

The titles of Figures 1 and 2 were inverted. This was corrected at the request of the authors on 2 March 2012.

References

1. European Centre for Disease Prevention and Control. Influenza surveillance in Europe 2010–2011. Stockholm: ECDC; Dec 2011. Available from: http://ecdc.europa.eu/en/publications/Publications/111209_SUR_Influenza_surveillance_Europe%20_2010_2012.pdf
2. European Centre for Disease Prevention and Control. Weekly influenza surveillance overview – Week 1. Stockholm; 13 Jan 2012. Available from: http://www.ecdc.europa.eu/en/publications/Publications/120113_SUR_Weekly_Influenza_Surveillance_Overview.pdf
3. European Centre for Disease Prevention and Control. Weekly influenza surveillance overview – Week 5. Stockholm; 10 Feb 2012. Available from: http://ecdc.europa.eu/en/publications/Publications/120210_SUR_Weekly_Influenza_Surveillance_Overview.pdf.pdf
4. Commission Decision of 28 April 2008 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council. Notified under document number C(2008) 1589. 2008/427/EC. Luxembourg: Publications Office of the European Union. Official Journal. 18 Jun 2008; L 159. P. 0046–0090. Available from: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:159:0046:01:EN:HTML>
5. Paget J, Marquet R, Meijer A, van der Velden K. Influenza activity in Europe during eight seasons (1999–2007): an evaluation of the indicators used to measure activity and an assessment of the timing, length and course of peak activity (spread) across Europe. *BMC Infect Dis*. 2007;7:141.
6. Bolotin S, Pebody R, White PJ, McMenamin J, Perera L, Nguyen-Van-Tam JS, et al. A new sentinel surveillance system for severe influenza in England shows a shift in age distribution of hospitalised cases in the post-pandemic period. *PLoS One*. 2012;7(1):e30279.
7. Fuhrman C, Bonmarin I, Bitar D, Cardoso T, Duport N, Herida M, et al. Adult intensive-care patients with 2009 pandemic influenza A(H1N1) infection. *Epidemiol Infect*. 2011;139(8):1202–9.
8. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. *Lancet*. 2010;375(9720):1100–8.
9. Bansal S, Pourbohloul B, Hupert N, Grenfell B, Meyers LA. The shifting demographic landscape of pandemic influenza. *PLoS One*. 2010;5(2):e9360.