

# Early and unexpectedly severe start of influenza epidemic in the Czech Republic during influenza season 2012–13

J Kyncl (jkyncl@szu.cz)<sup>1,2</sup>, M Havlickova<sup>3</sup>, A Nagy<sup>3</sup>, H Jirincova<sup>3</sup>, I Piskova<sup>4</sup>

1. Department of Infectious Diseases Epidemiology, National Institute of Public Health, Prague, Czech Republic

2. Department of Epidemiology, Third Faculty of Medicine, Charles University in Prague, Czech Republic

3. National Reference Laboratory for Influenza, National Institute of Public Health, Prague, Czech Republic

4. Epidemiology Division, Department of Public Health Protection, Ministry of Health of the Czech Republic, Prague, Czech Republic

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**A sudden increase in severe influenza has been registered in the Czech Republic since the end of 2012, with 264 cases requiring intensive care, including 51 deaths. Most patients had at least one risk factor. Severe influenza in patients with obesity, smoking and/or haematological disorders including haematological cancers was more frequent than in the pre-pandemic period. The seasonal influenza vaccination status of the cases indicates indirect efficiency of the current vaccine in preventing severe influenza.**

Influenza virus activity in Europe is detected each season, yet the precise timing and magnitude of this activity remain highly unpredictable. There was increased media attention regarding the re-occurrence of severe influenza A(H1N1)pdm09 cases at the beginning of 2013 in the Czech Republic. This led to a higher demand of antiviral drugs. In order to clarify the current influenza situation, we provide here representative data from the case-based reports of severe influenza cases and combine them with the data received from routine surveillance.

## Influenza surveillance in the Czech Republic

Epidemiological and virological surveillance of influenza and other viral acute respiratory infections (ARI) is well established in the Czech Republic (population: 10.5 million) [1]. The surveillance system is active throughout the year and uses the European Union case definition for influenza [2]. Data are collected weekly and analysed at national level. The information is provided to the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO), where it is analysed together with the data from other countries of the European Union and the WHO European Region, respectively [3,4]. There is no routine reporting of severe acute respiratory infection (SARI) from hospitals. Nevertheless, due to the occurrence of increased numbers of severe influenza cases during the pandemic in 2009, the Regional Public Health Authorities started, on request of the Ministry of Health of the Czech Republic to provide case-based

information about hospitalised patients with influenza illness who require treatment at intensive or resuscitation care units.

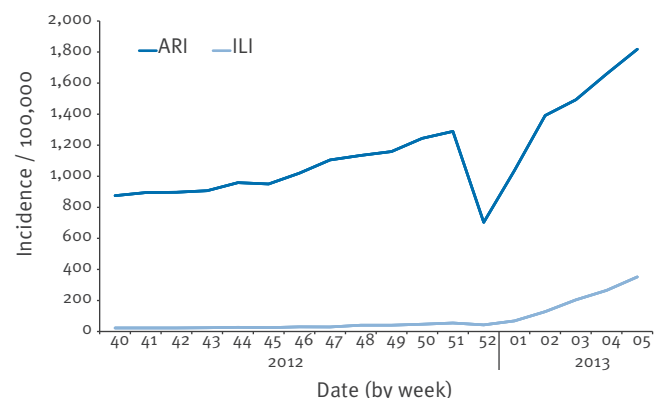
To gain insight into the genetic characteristics of the influenza A viruses circulating in the Czech Republic, the National Influenza Reference Laboratory in Prague sequences the full coding region of the genome from selected isolates or positive clinical specimens and subsequently performs phylogenetic analysis of representative A(H1N1)pdm09 influenza virus strains.

## Influenza season 2012/13

Since mid-November 2012, the incidence of ARI and influenza-like illness (ILI) has been increasing in all monitored age groups (0–5, 6–14, 15–24, 25–59, ≥60 years and total population). There was an artificial decrease in reporting during the Christmas and New Year holidays that is seen every year. Since the beginning of January 2013, the reported ARI and ILI rates have not been unusual, and the influenza epidemic threshold of 1,600 ARI cases per 100,000 population

**FIGURE 1**

Weekly morbidity from acute respiratory infection and influenza-like illness, Czech Republic, influenza season 2012/13



Rates per 100,000 population; data up to 1 February 2013.

per week was reached as late as during week 4 of 2013 (week ending 25 January 2013) (Figure 1).

Nevertheless, two other indicators signalled significant influenza activity in the Czech Republic. Firstly, the absolute numbers as well as the percentage of influenza-positive samples among the tested specimens (sentinel sampling consists of two swabs, one child and one adult, collected per week from each of the 14 regions in the Czech Republic) has been considerably higher after week 51, 2012 (Table 1).

Secondly, hospital surveillance has noted a clear increase of very severe influenza illness since the beginning of the year 2013, compared to non-epidemic period. By 1 February 2013, a total of 264 hospitalised patients (159 male and 105 female) with severe influenza illness that required treatment at intensive or resuscitation care units (ICU) have been reported to public health authorities (Table 2). Among those were 51 deaths (34 men and 17 women).

Of the 264 ICU patients, 174 (66%) were positive for influenza A(H1N1)pdm09 virus, 76 (29%) were positive for influenza A(unknown sub-type), six were positive for influenza A(H3N2) virus, one for influenza B virus, and seven cases remained unconfirmed by virology (determined by clinical diagnosis only). The virological results for influenza ICU patients were similar to the data from combined sentinel and non-sentinel surveillance.

The mean age of the influenza ICU patients was 56 years (min: one month; max: 92 years; median: 59 years). The mean age of the fatal influenza ICU cases was 64 years (min: 27 years; max: 92 years; median: 67 years). The main risk factors included: obesity with body mass index above 30 (79/264), smoking (65/264), chronic cardiovascular (77/264), respiratory (46/264) or haematological illness (21/264), often in combination. Only seven patients were vaccinated against seasonal influenza during autumn 2012.

Phylogenetic analysis of the haemagglutinin (HA) gene of the first three strains in the 2012/13 season, representing the influenza A(H1N1)pdm09 viruses currently circulating the Czech Republic, indicate that they cluster

within the H1N1pdm09 group 6. This group, along with H1N1pdm09 group 7, represents the currently predominating phylogenetic lineages of this influenza virus strain in Europe (Figure 2; Table 3). Comparing our HA sequences with the A/California/7/2009(H1N1) strain revealed up to 12/549 amino acid changes (A/Czech Republic/140/2012(H1N1); 97.8% identity), three of which were localised within the known antigenic sites (in H3 numbering): Ca2 (H141R), Sb (S188T) and Ca1 (S206T).

## Discussion and conclusions

Influenza A(H1N1)pdm09 and untyped influenza A viruses were found in almost all cases of influenza ICU patients. Since the A(H1N1)pdm09 virus was the predominant strain we suppose that the majority of untyped influenza A viruses also belonged to this subtype. The majority of deaths were linked primarily to rapidly developing respiratory failure as already described [5]. In particular, progressive pneumonitis caused by A(H1N1)pdm09 virus is difficult to explain since the virus is neither shown to have markedly increased virulence over other seasonal influenza viruses, nor it is a particularly strong cytokine inducer in vitro [6]. The potential for increased pathogenicity could be a result of the combination of other genetic markers [7].

The current influenza situation in the Czech Republic is not exceptional as such. It is relatively similar to the season 2010/11 when the influenza A(H1N1)pdm09 virus dominated the epidemic. However, other European

**TABLE 2**

Number of severe influenza patients at intensive care units and deaths by week, Czech Republic, 22 December 2012–1 February 2013 (n=264)

	Number of new cases	Of which deaths
week 52, 2012	12	3
week 1, 2013	28	3
week 2, 2013	40	5
week 3, 2013	60	13
week 4, 2013	56	16
week 5, 2013	68	11
<b>Total</b>	<b>264</b>	<b>51</b>

**TABLE 1**

Sentinel and non-sentinel influenza virus detections, Czech Republic, influenza season 2012/13 (n=994)

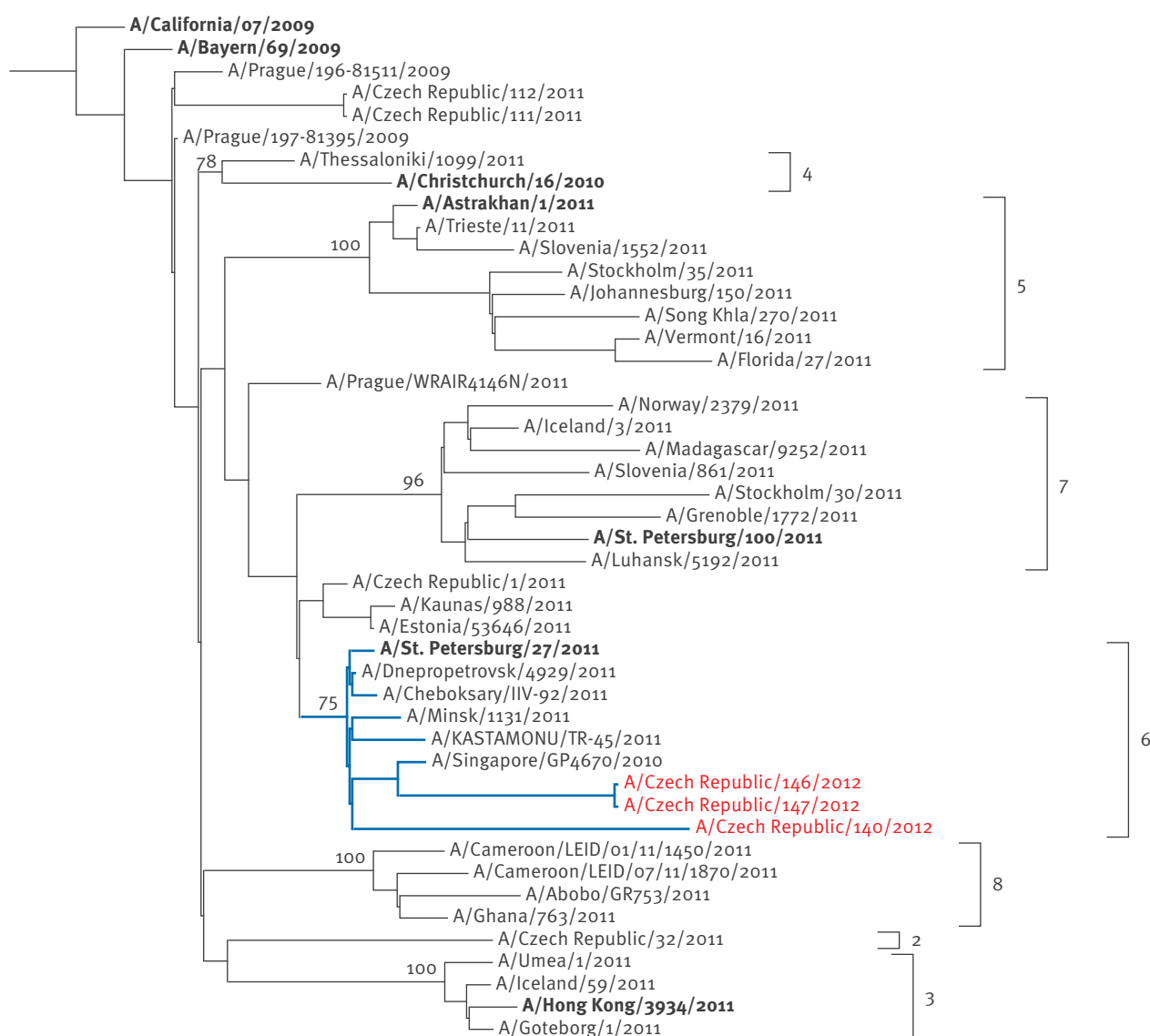
Week	40	41	42	43	44	45	46	47	48	49	50	51	52	1	2	3	4
Influenza A		1				3	1	1	2		5	16	35	59	61	117	129
Influenza A(H1N1)pdm09							2			1	5	10	10	67	133	95	164
Influenza A(H3N2)		1	1									4	3		12	10	16
Influenza B		1		2			1				1	2	1	3	6	5	8
<b>Total influenza-positive</b>	<b>0</b>	<b>3</b>	<b>1</b>	<b>2</b>	<b>0</b>	<b>3</b>	<b>4</b>	<b>1</b>	<b>2</b>	<b>1</b>	<b>11</b>	<b>32</b>	<b>49</b>	<b>129</b>	<b>212</b>	<b>227</b>	<b>317</b>
<b>Samples tested</b>	<b>15</b>	<b>32</b>	<b>37</b>	<b>40</b>	<b>40</b>	<b>37</b>	<b>35</b>	<b>33</b>	<b>61</b>	<b>58</b>	<b>81</b>	<b>82</b>	<b>75</b>	<b>260</b>	<b>529</b>	<b>681</b>	<b>697</b>
Positivity in %	0	9	3	5	0	8	11	3	3	2	14	39	65	50	40	33	45

countries do not report such high numbers of severe influenza this year [3,4]. So far during this season, only 14 fatalities have been reported from EU countries in which hospital surveillance of severe influenza disease is established, 12 of these occurred in France [3]. With regards to circulation of influenza viruses in Europe, the situation is varied. For example, influenza B virus is dominant mainly in the United Kingdom (UK), influenza A(H3N2) in Denmark and A(H1N1)pdm09 in Austria, Lithuania and Norway [3]. This report may serve as an alert that a sudden increase in severe influenza cases may soon be seen also in other, especially Eastern European, countries this season.

The observations presented here prompted us to build up the following hypothesis: the proportion of people vaccinated against influenza in the Czech Republic is small, only approx. 5% of the whole population. As this year's seasonal vaccine is matching the circulating viruses well, which resulted in a vaccine effectiveness of 62% in the United States [8], the proportion of people protected against influenza in other countries should be higher than in the Czech Republic, especially in Western Europe where the influenza epidemic started earlier.

In addition, we have to consider that the effectiveness of the trivalent vaccine may well be different for the different components. If the virus mix circulating in one country was considerably different from what is

**FIGURE 2**  
Phylogenetic tree of influenza A(H1N1) haemagglutinin gene



The H1 tree was constructed from representative sequences collected from 2009 to 2012 and obtained from the Global Initiative on Sharing All Influenza Data (GISAID) and the Influenza Virus Resource databases. The tree was generated with the maximum-likelihood algorithm in the PHYLIP programme (Felsenstein, 2004) [9] on the basis of 1,650 nt sequences and rooted to the A/California/7/2009(H1N1) influenza strain. Bootstrap values (100 re-samplings) in percentages are indicated at key nodes. The viruses sequenced in this report are highlighted in red and the reference strains in bold. The cluster representing the influenza A(H1N1)pdm09 group 6 is coloured blue.

TABLE 3

Origin of the haemagglutinin sequences of pandemic influenza A(H1N1) isolates included in the phylogenetic analysis

Isolate name	Collection date	Isolate ID		Originating laboratory
		IVR	GISAID	
A/Prague/197-81395/2009(H1N1)	2009-06-27	GU290047		National Institute of Public Health, Prague, Czech Republic
A/Prague/196-81511/2009(H1N1)	2009-07-15	GU290055		
A/Czech Republic/32/2011(H1N1)	2011-01-18		EPI_ISL_90718	
A/Czech Republic/1/2011(H1N1)	2011-01-25	JF682629		
A/Czech Republic/111/2011(H1N1)	2011-10-25	JQ693484		
A/Czech Republic/112/2011(H1N1)	2011-10-25	JQ693492		
A/Czech Republic/140/2012(H1N1)	2012-11-16		EPI_ISL_133958	
A/Czech Republic/146/2012(H1N1)	2012-12-27		EPI_ISL_133959	
A/Czech Republic/147/2012(H1N1)	2012-12-24		EPI_ISL_133960	
A/Prague/WRAIR4146N/2011(H1N1)	2011-01-18	CY098004		Walter Reed Army Institute of Research, Maryland, United States
A/California/07/2009(H1N1)	2009 (month and day unknown)	CY121680		New York Medical College/NCBI, NIH, Bethesda, United States
A/Thessaloniki/1099/2011(H1N1)	2011-03-08		EPI_ISL_90764	Institut Pasteur Hellenique, Athens, Greece
A/Bayern/69/2009(H1N1)	2009 (month and day unknown)		EPI_ISL_73686	Robert Koch-Institute, Berlin, Germany
A/Cheboksary/IIV-92/2011(H1N1)	2011-02-22	JN704791		The D.I.Ivanovsky Institute of Virology, Moscow, Russian Federation
A/St. Petersburg/27/2011(H1N1)	2011-02-14		EPI_ISL_90760	WHO National Influenza Centre, St. Petersburg, Russian Federation
A/Astrakhan/1/2011(H1N1)	2011-02-28		EPI_ISL_90787	
A/St. Petersburg/100/2011(H1N1)	2011-03-14		EPI_ISL_90954	Russian Academy of Medical Sciences, St. Petersburg, Russian Federation
A/Dnepropetrovsk/4929/2011(H1N1)	2011-03-10		EPI_ISL_99894	Institute of Epidemiology and Infectious Diseases AMS of Ukraine, Kiev, Ukraine
A/Luhansk/5192/2011(H1N1)	2011-03-07		EPI_ISL_99895	
A/Minsk/1131/2011(H1N1)	2011-02-15		EPI_ISL_94707	Laboratory of Influenza and ILI, Minsk, Belarus
A/Estonia/53646/2011(H1N1)	2011-02-01		EPI_ISL_94695	Health Protection Inspectorate, Tallin, Estonia
A/Kaunas/988/2011(H1N1)	2011-02-15		EPI_ISL_99909	Lithuanian AIDS Center Laboratory, Vilnius, Lithuania
A/Stockholm/35/2011(H1N1)	2011-11-22		EPI_ISL_100460	Swedish Institute for Infectious Disease Control, Solna, Sweden
A/Stockholm/30/2011(H1N1)	2011-11-09		EPI_ISL_99784	
A/Goteborg/1/2011(H1N1)	2011-04-12		EPI_ISL_93766	
A/Umea/1/2011(H1N1)	2011-01-28		EPI_ISL_90424	
A/Norway/2379/2011(H1N1)	2011-12-08		EPI_ISL_100455	St. Olavs Hospital HF, Trondheim, Norway
A/Slovenia/861/2011(H1N1)	2011-02-05		EPI_ISL_95550	National Institute of Public Health, Ljubljana, Slovenia
A/Slovenia/1552/2011(H1N1)	2011-04-30		EPI_ISL_95564	
A/Kastamonu/TR-45/2011(H1N1)	2011-02-12		EPI_ISL_95555	Refik Saydam National Public Health Agency, Ankara, Turkey
A/Iceland/3/2011(H1N1)	2011-01-10		EPI_ISL_99914	Landspítali - University Hospital, Reykjavik, Iceland
A/Iceland/59/2011(H1N1)	2011-03-24		EPI_ISL_99924	
A/Trieste/11/2011(H1N1)	2011-01-11		EPI_ISL_90758	Istituto Superiore di Sanità, Rome, Italy
A/Grenoble/1772/2011(H1N1)	2011-09-21		EPI_ISL_103048	CRR virus Influenza region Sud, Cedex, France
A/Vermont/16/2011(H1N1)	2011-12-22		EPI_ISL_103212	Vermont Department of Health Laboratory, Burlington, United States
A/Florida/27/2011(H1N1)	2011-10-30		EPI_ISL_99811	Florida Department of Health-Tampa Bureau of Laboratories, Tampa, United States
A/Christchurch/16/2010(H1N1)	2010-07-12		EPI_ISL_79722	WHO Collaborating Centre for Reference and Research on Influenza, Victoria, Australia
A/Singapore/GP4670/2010(H1N1)	2010-12-30	CY091676		National Public Health Laboratory, Singapore,
A/Song Khla/270/2011(H1N1)	2011-09-12		EPI_ISL_99814	WHO National Influenza Centre, National Institute of Medical Research (NIMR), Nonthaburi, Thailand
A/Hong Kong/3934/2011(H1N1)	2011-03-29		EPI_ISL_93746	Government Virus Unit, Kowloon, Hong Kong
A/Johannesburg/150/2011(H1N1)	2011-07-10		EPI_ISL_99903	National Institute for Communicable Disease, Sandringham-Johannesburg, South Africa
A/Ghana/763/2011(H1N1)	2011-05-13		EPI_ISL_94709	University of Ghana, Accra, Ghana
A/Cameroon/LEID/07/11/1870/2011(H1N1)	2011-07-07		EPI_ISL_99899	Centre Pasteur du Cameroun, Yaoundé, Cameroon
A/Cameroon/LEID/01/11/1450/2011(H1N1)	2011-01-19		EPI_ISL_99900	Centre Pasteur du Cameroun, Yaoundé, Cameroon
A/Abobo/GR753/2011(H1N1)	2011-09-12		EPI_ISL_103049	Pasteur Institut of Côte d'Ivoire, Abidjan, Cote d'Ivoire
A/Madagascar/9252/2011(H1N1)	2011-08-10		EPI_ISL_99934	Institut Pasteur de Madagascar, Antananarivo, Madagascar

circulating in another country, that could affect severity of disease in these countries. Regardless of the reasons behind the current situation, early admission, prompt diagnosis and early antiviral treatment improve the outcome of patients infected with influenza A(H1N1) pdm09.

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## Conflict of interest

None declared.

## Authors' contributions

JK wrote the manuscript and is responsible for analysis of data from epidemiological surveillance. MH and HJ are responsible for analysis of data from virological surveillance, both contributed to the manuscript. AN did the genome sequencing and phylogenetic analysis and contributed to the manuscript. IP run the hospital ICU database and contributed to the manuscript.

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