Situation update in the European Region: overview of influenza surveillance data week 40/2009 to week 07/2010.

WHO/Europe publishes a weekly electronic bulletin on influenza activity in the Region[1] and performs periodic analysis of surveillance data provided by the 53 WHO European Member States.[2] A preliminary review of data submitted to EuroFlu between week 40/2009 and week 07/2010, compared with historical data where available, shows the following main developments:

- In most countries that reported data, levels of influenza activity are well below recent pandemic peak levels and across most of the European Region, the first wave of pandemic influenza activity is considered to be at an end.
- Countries in the European Region experienced an early start to the influenza season, and winter-time clinical activity also peaked earlier than it has in several years.
- The length of the winter pandemic (H1N1) 2009 wave was generally of similar length, compared with previous seasons.
- In 19 of 22 countries reporting five or more years of data, the peak clinical consultation rates that were observed during the 2009/2010 pandemic season did not exceed peak clinical consultation rates observed during the previous years. However in several countries, clinical consultation rates did exceed recent historical peaks within some younger age groups.
- Within the western part of the Region, the geographic progression of the pandemic occurred in a west to east direction.
- 49 out of 53 Member States reported laboratory-confirmed cases, the large majority of which occurred without complications.
- 4 572 laboratory-confirmed deaths associated with pandemic (H1N1) 2009 had been reported to WHO/Europe. Although these are underestimates of the actual number of deaths associated with pandemic H1N1 (2009) virus infections, these crude estimates of mortality suggest similar rates to those observed in countries during the winter season in the southern hemisphere.
- The vast majority of influenza virus detections were pandemic (H1N1) 2009 (99.74% of influenza A subtyped viruses from sentinel sources; N = 19 838). All pandemic (H1N1) 2009 viruses analysed antigenically (N = 1777) or genetically (N = 995) were similar to the vaccine strain and the majority were sensitive to both oseltamivir and zanamivir.

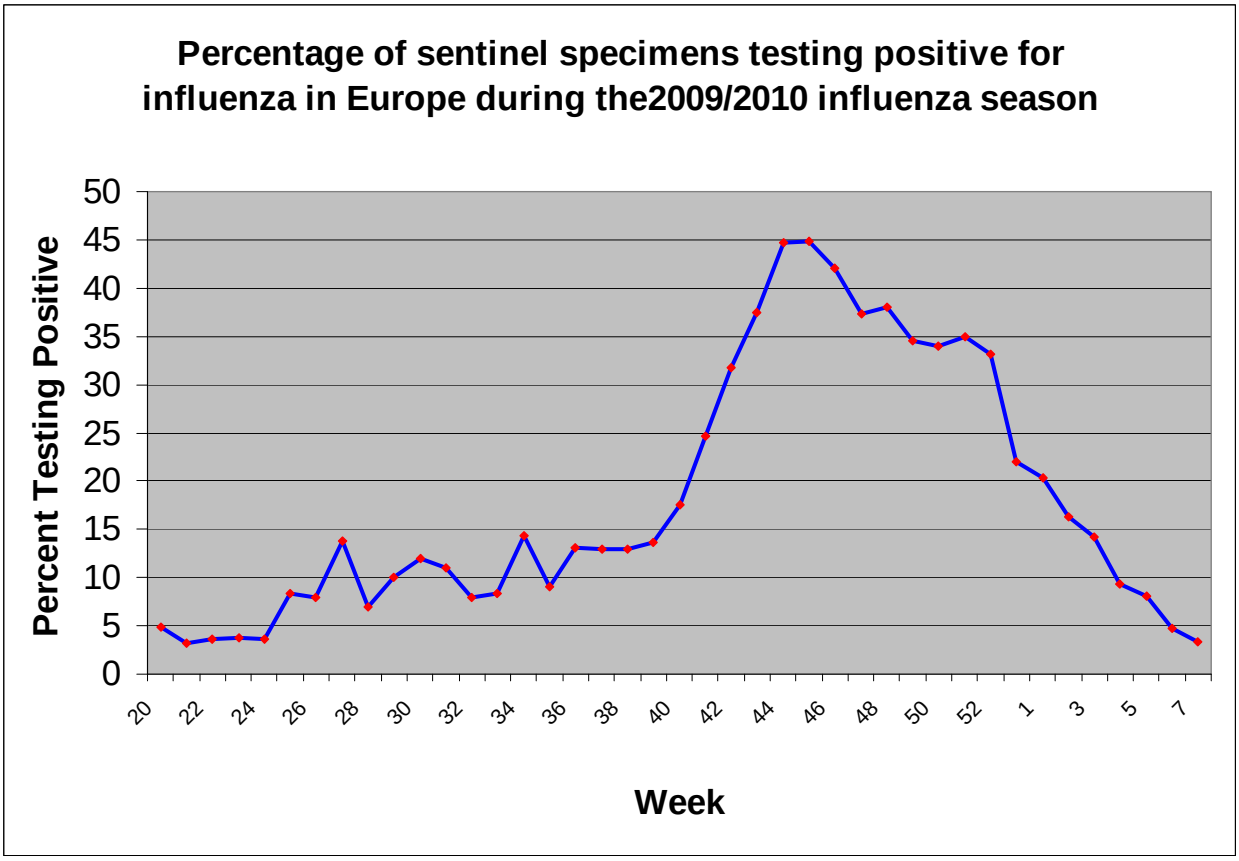
Is the current pandemic wave coming to an end in the European region?

- In most countries that reported data, levels of influenza activity are well below recent pandemic peak levels and across most of the European Region, the first wave of pandemic influenza activity is considered to be at an end.

During week 7/2010, the percentage of sentinel specimens testing positive for influenza in the region was 3.3%, down from a seasonal high of 45% during week 45/2009. In addition, no country that tested more than twenty sentinel specimens reported influenza positivity rates

[1] www.euroflu.org and http://www.euro.who.int/influenza/ah1n1
[2] http://www.euro.who.int/influenza/AH1N1/20091026_1 ; http://www.euro.who.int/influenza/AH1N1/20090523_1

greater than 20%. The viruses characterized to date correspond with the recommended viruses for influenza vaccines for use in the 2010–2011 northern hemisphere influenza season[3]. Pandemic influenza A(H1N1) 2009 remains the dominant influenza virus in circulation and in 40 of 42 reporting countries, over 98% of subtyped viruses are pandemic (H1N1) 2009 viruses. While these trends in clinical and virological data do suggest that this winter wave of pandemic influenza is coming to an end, surveillance will continue to monitor for any resurgence in pandemic or seasonal virus activity during the coming months. The recent decision by the WHO Director-General, Dr Margaret Chan, based on Emergency Committee discussions, to maintain pandemic alert level at phase six[4] underscores the need for countries to continue their routine surveillance of influenza without interruption.

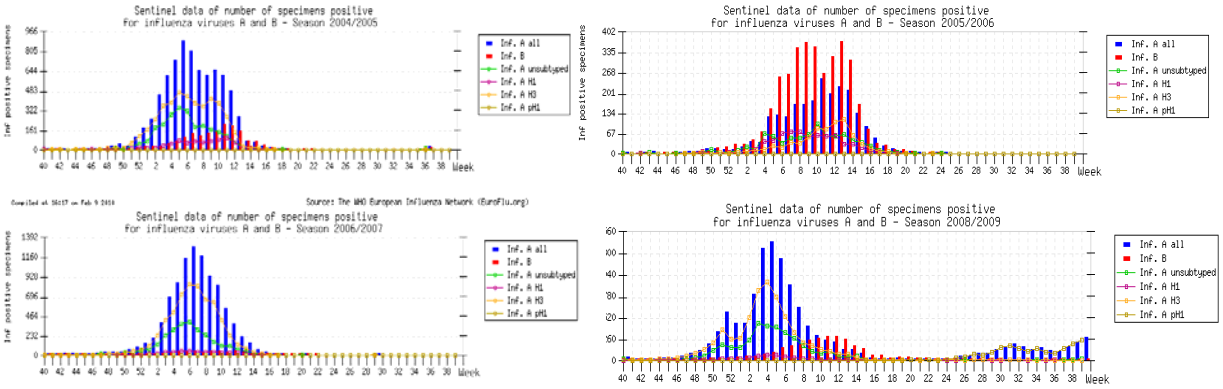


How does the overall timing and length of this season compare to previous seasons?

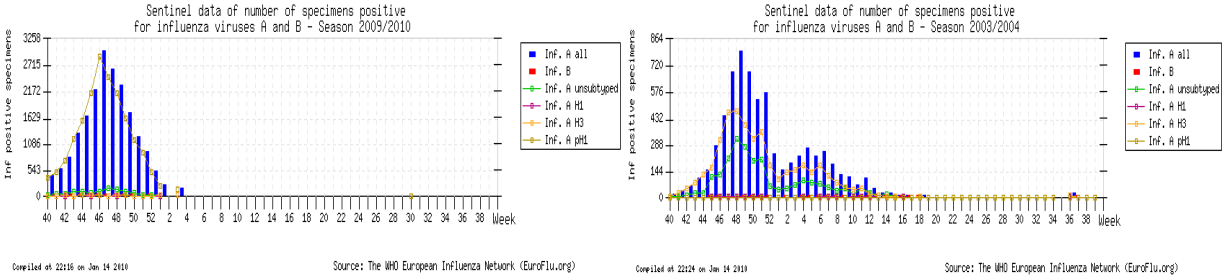
- Countries in the European Region experienced an early start to the influenza season, and winter-time clinical activity also peaked earlier than it has in several years.
- The length of the winter pandemic pandemic (H1N1) 2009 wave was generally of similar length, compared with previous seasons.

Data from the influenza seasons of 2004/2005 through 2008/2009 suggest that the peak of influenza activity has ranged between weeks 5 and 13 during recent years. This has included influenza seasons where seasonal influenza A(H1N1), A(H3N2) and influenza B have each been observed to be the dominant viruses in circulation, as shown in the examples below. Peaks in influenza B activity, whether as the dominant virus in 2005/2006 or as a co-dominant virus in 2004/2005 and 2008/2009, have tended to occur even later in the influenza season.

[3] http://www.who.int/csr/disease/influenza/vaccinerecommendations/en/index.html
[4] http://www.euro.who.int/influenza/AH1N1/20100224_2



As a result of the introduction of the pandemic (H1N1) 2009 influenza virus into circulation, the 2009/2010 winter influenza season in Europe arrived markedly early. During the pandemic wave of 2009/2010, 28 countries experienced a peak in clinical activity by week 51/2009, with the majority of peaks occurring around weeks 46-48/2009, possibly because the virus was able to spread with greater efficiency than normal in a population that was to a large extent immunologically naïve. However this early start to the influenza season is not unprecedented. A similar early peak was observed during week 48 of the 2003/2004 influenza season, a year when the influenza A(H3N2) "Fujian" drift variant emerged, also in a relatively naïve human population.



Regarding the length of the winter season during this pandemic, defined as the number of weeks between the first and last wintertime peaks in different countries +/- two weeks[5], it has been of approximately the same duration as previous seasons, namely 12 weeks. Data from the United Kingdom (England), which was the only European Member State to experience its pandemic peak before week 40, the start of traditional winter influenza season, is not included in this analysis[6].

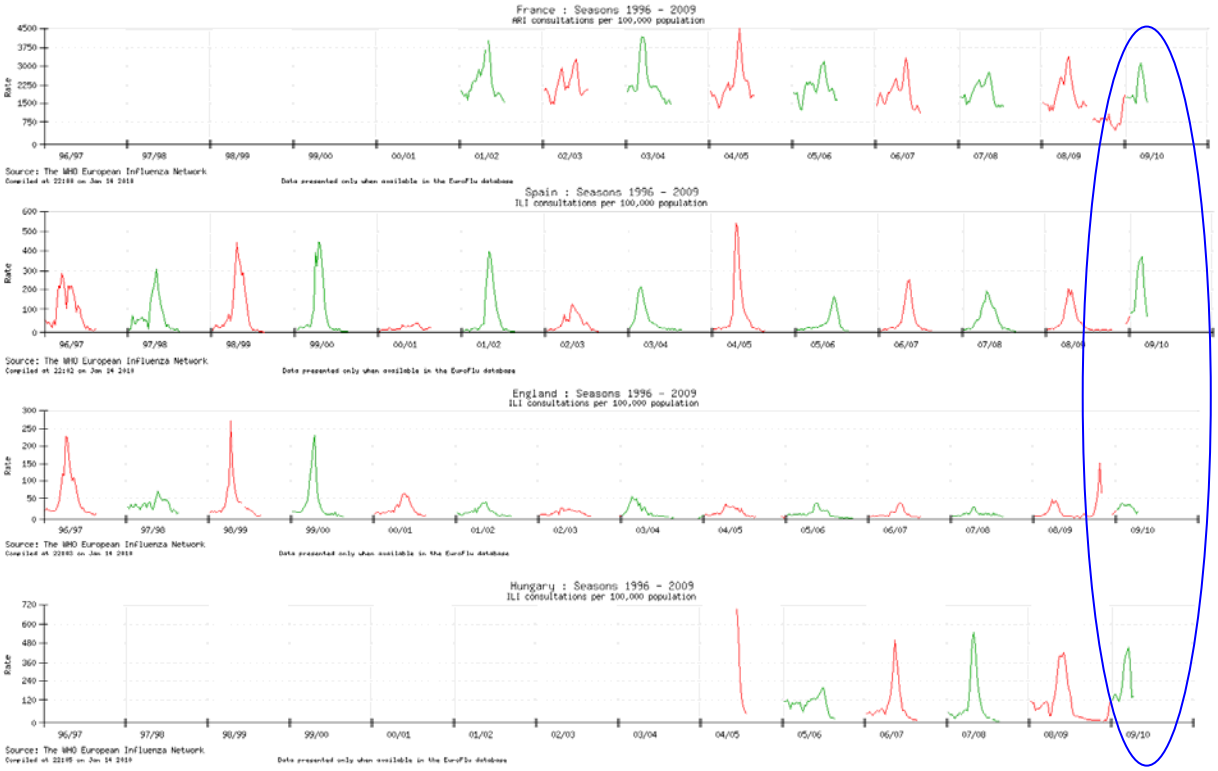
Have clinical consultation rates and influenza transmission intensity been higher than what has been observed during previous seasons?

- In 19 of 22 countries reporting five or more years of data, overall peak clinical consultation rates that were observed during the 2009/2010 pandemic season did not exceed peak clinical consultation rates observed during the previous years. However in several countries, clinical consultation rates did exceed recent historical peaks within some younger age groups.

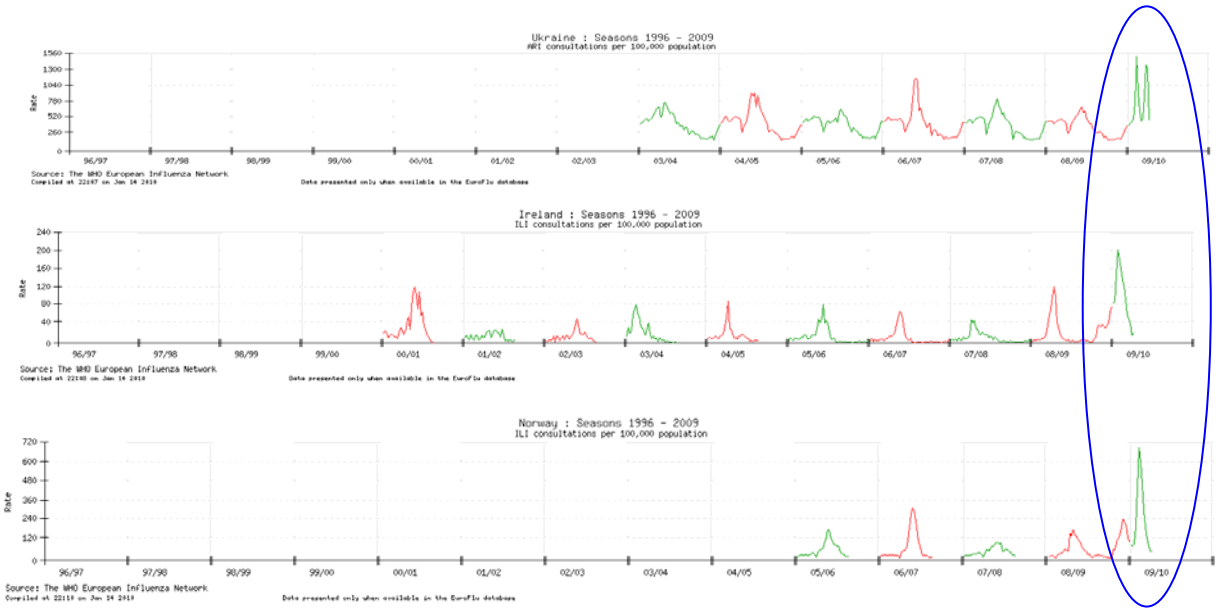
[5] http://www.biomedcentral.com/1471-2334/7/141

[6] http://www.euroflu.org/cgi-files/figures2002.cgi?year=2010&week=7&region=England&type=c

Twenty-two countries have provided five or more years of historical data (including the current year) on clinical consultation rates for ILI and/or ARI into the EuroFlu platform. In nineteen of these countries, the overall peak clinical consultation rates that were observed during the 2009/2010 pandemic season did not exceed clinical consultation rates observed in recent during recent years. Four examples are shown below.



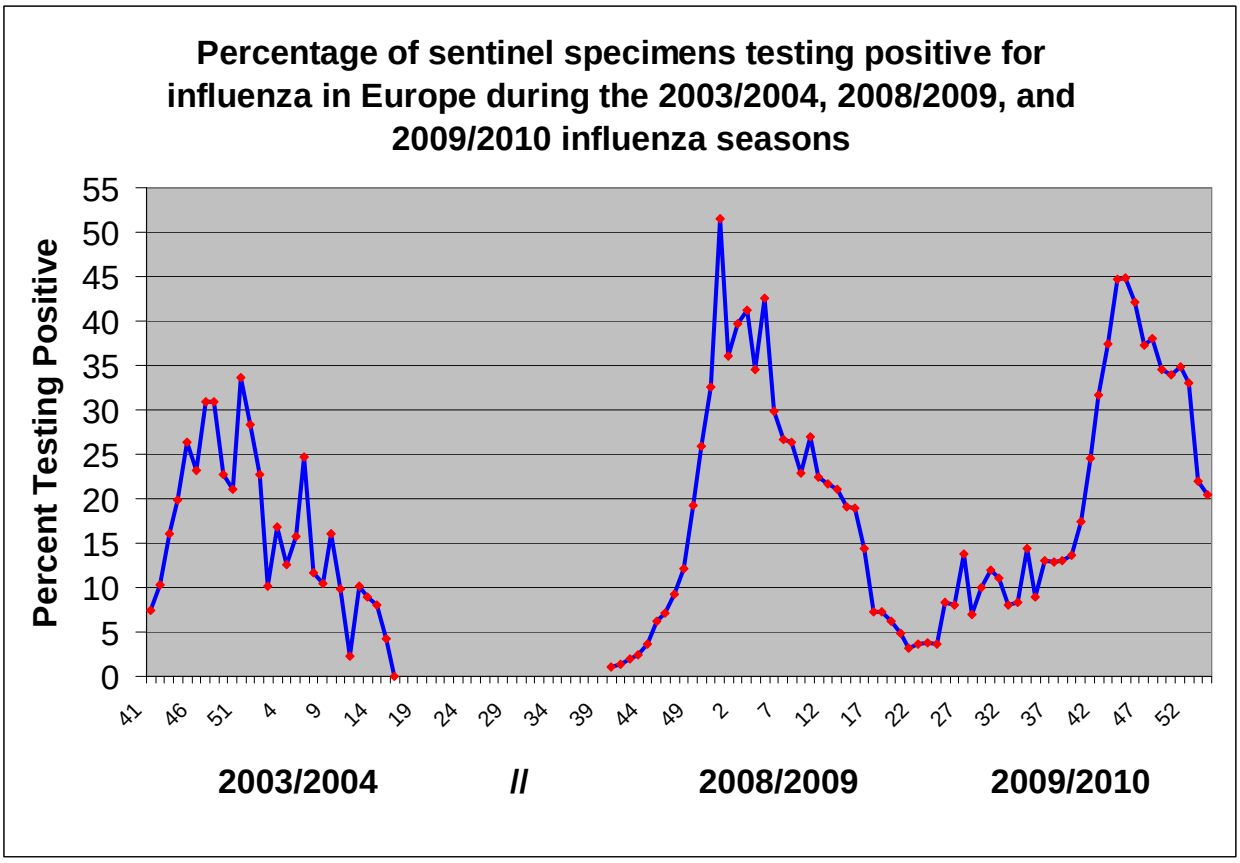
However in three other countries (Ireland, Norway and Ukraine) clinical consultation rates did exceed those that have been observed in recent history.



There is some age-specific variation in these findings. For example, overall peak consultation rates observed during the 2009/2010 pandemic were not higher than those observed during some recent years in Austria, Denmark, Germany, Italy, Latvia, Netherlands, Portugal, Slovenia,

Spain, Switzerland and Turkey. However in each of these countries, clinical consultation rates exceeded recent historical peaks within specific age groups. This was observed in the 0-4 age group (Denmark, Latvia, Netherlands), the 5-14 age group (Austria, Denmark, Italy, Netherlands, Portugal, Slovenia, Spain, Turkey, Latvia, Switzerland), and in the 15-64 age group (Germany, Latvia), reflecting the particular influence of the current pandemic on clinical consultation rates in younger age groups.

The intensity of influenza transmission as reflected in the percent of sentinel specimens testing positive for influenza during the pandemic season also has not exceeded what has been observed during recent years. During the current pandemic season of 2009/2010, the percent of sentinel specimens testing positive for influenza in the European Region peaked at 45% during week 45/2009. This can be compared to a peak positivity rate of 52% during week 52/2008. Both of these positivity rates are higher than during the 2003/2004 season involving the Fujian (H3) variant. However the expansion of molecular diagnostic methods in the region has also improved surveillance sensitivity since that time.



Has there been any detected west to east or south to north geographic progression of the pandemic?

- Within the western part of the Region, the geographic progression of the pandemic occurred in a west to east direction.

During several recent years the progression of influenza season among EU/EEA countries has followed significant eastward or northward patterns. This included significant west-to-east trends in 2001/02, 2002/03, 2003/04, 2004/05 and 2008/09; and significant south-to-north

trends in 2001/02, 2004/05, 2006/07, 2007/08. When looking at countries across the entire Region that had well-defined winter peaks in clinical consultation rates during 2009/10, and that also reported complete data into the EuroFlu platform, a pattern of geographic progression is not evident. However when countries are stratified by whether they are EU/EEA Member States or whether the midpoint of the country is located west or east of longitude 56E (the Ural mountains), a west-to-east pattern of pandemic progression emerged within the groupings of countries west of longitude 56E. These analyses are ongoing as we work to consider the pattern of introduction of viruses into the European Region from both the western and eastern hemispheres.

Results of directional correlation analyses (EU/EEA countries only)

Season	West-East R^2	p	South-North R^2	p	N	Dominant virus
2009-10	**0.201**	**<0.05**	0.047	-	22	H1N1
2008-09	**0.731**	**<0.01**	0.000	-	25	A(H3)
2007-08	0.057	-	**0.276**	**<0.01**	26	B
2006-07	0.073	-	**0.281**	**<0.01**	27	B
2005-06	0.032	-	0.002		17	B
2004-05	**0.679**	**<0.01**	**0.25**	**<0.05**	22	A(H3)
2003-04	**0.599**	**<0.01**	0.001		23	A(H3)
2002-03	**0.423**	**<0.01**	0.005		17	A(H3)
2001-02	**0.331**	**<0.05**	**0.482**	**<0.01**	17	A(H3)
2000-01	0.016		0.009		16	A(H1)
1999-00	0.069		0.058		14	A(H3)

Results of directional correlation analyses (53 country WHO/Euro Region)

Season	West-East R^2	p	South-North R^2	p	N	Dominant virus
2009-10	0.0001	-	0.006	-	35	H1N1
2008-09	**0.330**	**<0.01**	0.002	-	39	A(H3)

Results of correlation analyses (Countries west of longitude 56 degrees east)

Season	West-East R^2	p	South-North R^2	p	N	Dominant virus
2009-10	**0.15**	**<0.05**	0.0784	-	30	H1N1
2008-09	**0.852**	**<0.01**	0.020	-	34	A(H3)

Were indicators of severity and risk factors for severe outcomes different in Europe when compared to what was observed during the 2009 winter influenza season in the southern hemisphere?

- 49 out of 53 Member States had reported laboratory-confirmed cases, the large majority of which occurred without complications.
- 4 572 laboratory-confirmed deaths associated with pandemic (H1N1) 2009 had been reported to WHO/Europe. Although these are underestimates of the actual number of deaths associated with pandemic H1N1 (2009) virus infections, these crude estimates of mortality suggest similar rates to those observed in countries during the winter season in the southern hemisphere.

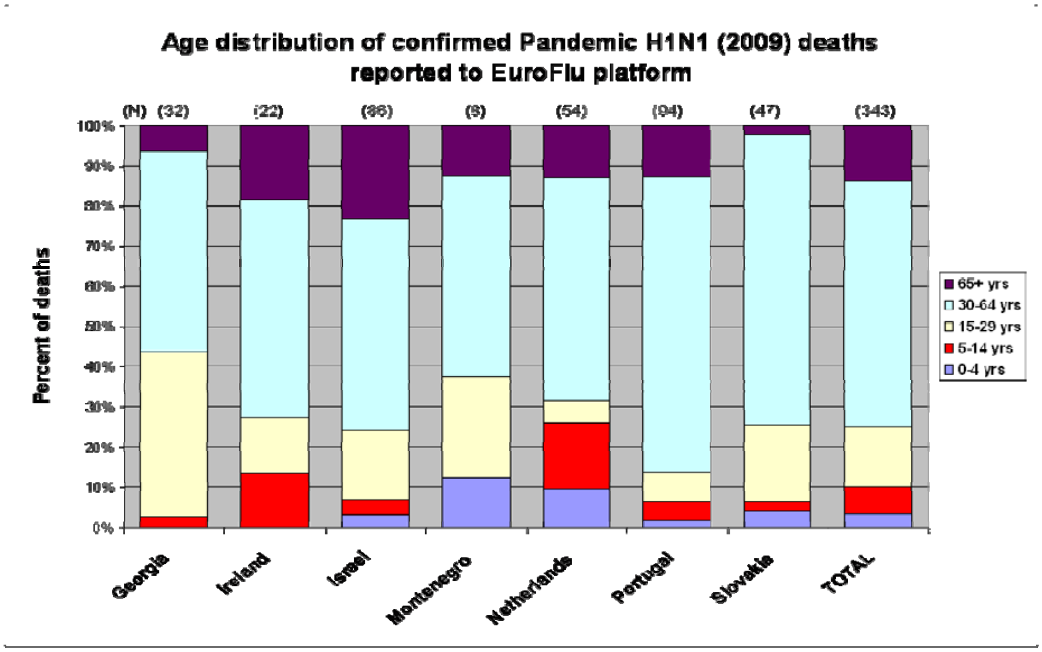
While overall clinical consultation and influenza positivity rates observed during the 2009/2010 pandemic have been comparable with recent influenza seasons, the age profile of persons at risk for severe outcomes has differed markedly. However a lack of standardization in epidemiologic investigation and pandemic surveillance activities between countries makes a concise summary of the findings in different countries difficult. As of 19 February 2010, 4572 laboratory-confirmed deaths associated with pandemic H1N1 (2009) virus infection had been reported in the European Region. This is, of course, an underestimate, as many additional deaths have been un-recognized or not tested in the laboratory. These limitations notwithstanding, the reports of laboratory-confirmed cases were used to calculate crude laboratory-confirmed pandemic H1N1 (2009) mortality rates (using 2009 country population estimates[7]) for each country in the Region.

[7] http://esa.un.org/unpp/

Country	Deaths as of February 19, 2010	2009 Population Estimate	Laboratory-confirmed pH1N1 (2009) Deaths/1,000,000 population
Andorra		86685	**n/a**
Azerbaijan		8933928	**n/a**
Belarus		9587940	**n/a**
Kazakhstan		15753460	**n/a**
Kyrgyzstan		5550239	**n/a**
Monaco		32904	**n/a**
San Marino		31537	**n/a**
Tajikistan		7074845	**n/a**
Turkmenistan		5176502	**n/a**
Uzbekistan		27794296	**n/a**
Bosnia & Herzegovina	2	3759633	**0.5**
Armenia	2	3090379	**0.6**
Belgium	19	10697588	**1.8**
Switzerland	18	7594561	**2.4**
Sweden	27	9293026	**2.9**
Germany	239	82056776	**2.9**
Albania	10	3169087	**3.2**
Austria	27	8387491	**3.2**
Netherlands	58	16653346	**3.5**
Russian Federation	521	140366560	**3.7**
Italy	235	60097564	**3.9**
Poland	149	38038096	**3.9**
Bulgaria	35	7497282	**4.7**
Ireland	22	4589002	**4.8**
France	302	62636580	**4.8**
Romania	122	21190154	**5.8**
Norway	29	4855315	**6.0**
Spain	271	45316584	**6.0**
Denmark	33	5481283	**6.0**
Iceland	2	329279	**6.1**
Luxembourg	3	491772	**6.1**
Croatia	29	4409659	**6.6**
Cyprus	6	879723	**6.8**
United Kingdom of Great Britain and Northern Ireland	423	61899272	**6.8**
The Former Yugoslav Republic of Macedonia	14	2043360	**6.9**
Lithuania	23	3255324	**7.1**
Georgia	33	4219191	**7.8**
Slovenia	16	2024912	**7.9**
Finland	43	5345826	**8.0**
Turkey	627	75705144	**8.3**
Serbia	83	9855857	**8.4**
Ukraine	429	45433416	**9.4**
Slovakia	52	5411640	**9.6**
Czech Republic	101	10410786	**9.7**
Portugal	106	10732357	**9.9**
Republic of Moldova	43	3575574	**12.0**
Malta	5	409999	**12.2**
Hungary	124	9973141	**12.4**
Israel	91	7285033	**12.5**
Greece	140	11183393	**12.5**
Montenegro	8	625516	**12.8**
Estonia	18	1339459	**13.4**
Latvia	31	2240265	**13.8**
international waters	1		**n/a**
European Region	**4572**	**893872541**	**5.1**

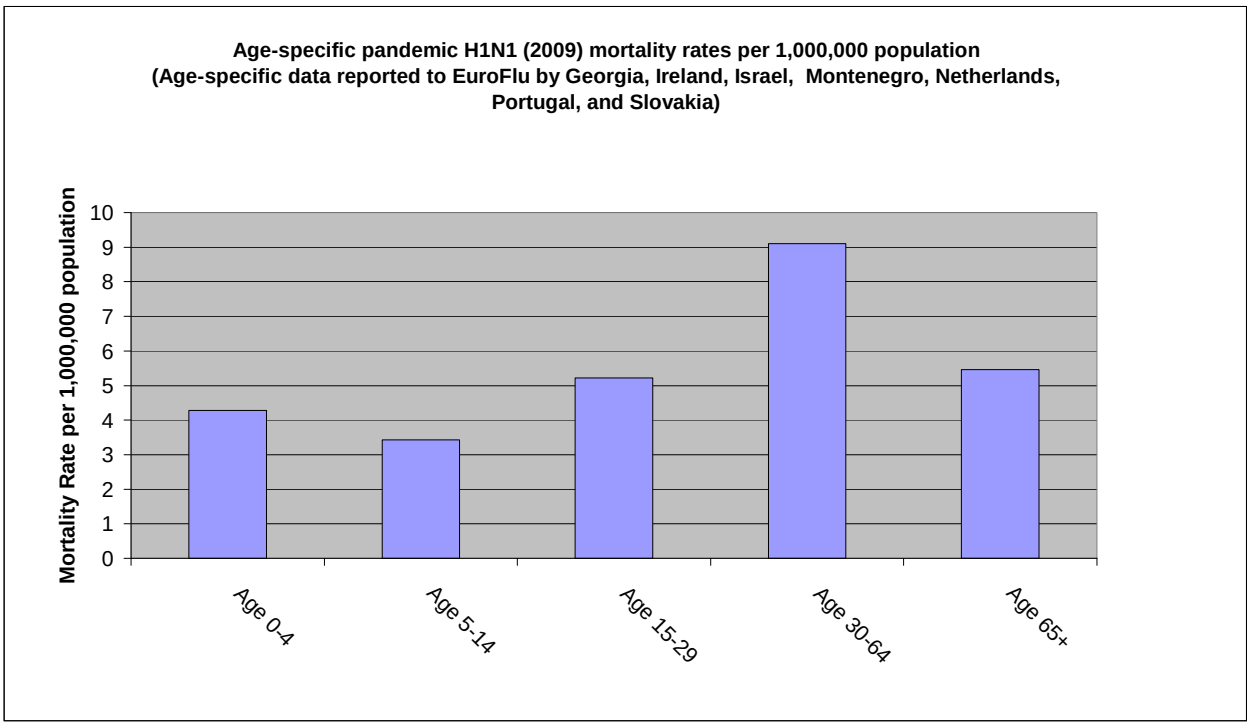
The overall crude mortality rate (CMR) for the European Region currently stands at 5.1 deaths per 1 000 000 population. Among 30 countries reporting 20 or more laboratory-confirmed pandemic H1N1 (2009) deaths, the CMR since the beginning of the pandemic currently ranges from 2.9 to 13.8 deaths per 1 000 000 population. It is important to state that this variation in estimates between countries likely reflects variation in the percent of populations exposed to the pandemic virus, the sensitivity of case detection and reporting, as well as possible differences in the actual rate of death among exposed persons. The range of country-specific estimates in the European Region appears similar to what was observed during the winter influenza season in the southern hemisphere, where reported CMRs for laboratory-confirmed pandemic H1N1 (2009) deaths ranged from 1.8 to 14.6 deaths per 1 000 000 population. More accurate assessments of mortality and mortality rates will likely be possible only one to two years after the pandemic has peaked and will rely on methods similar to those used to calculate excess mortality during seasonal influenza epidemics. Preliminary analyses of mortality data from the European Region have indeed suggested that higher all-cause mortality has been observed among children during the current pandemic than during previous influenza seasons.[8] However it must be emphasized that comparisons of the numbers of confirmed deaths with those estimated for seasonal influenza, either nationally or worldwide, are not reliable for several reasons and can be misleading.[9]

The severity of this pandemic is most clearly described in terms of specific age and risk-groups. Compared with seasonal influenza, the pandemic H1N1 (2009) has affected a much younger age group, in terms of those hospitalized, requiring intensive care, or dying.[10] While many countries reported laboratory-confirmed deaths and hospitalizations into the EuroFlu platform, an age distribution of laboratory-confirmed pandemic H1N1 (2009) deaths was only available for a subset of countries (representing both the eastern and western parts of the Region). Age-specific data on cumulative laboratory-confirmed pandemic H1N1 (2009) deaths are presented below for Georgia (as of week 7), Ireland (as of week 1), Israel (as of week 2), Montenegro (as of week 4), Netherlands (as of week 1), Portugal (as of week 2), and Slovakia (as of week 3). Most deaths have occurred in the 30-64 year age group in each of these countries.

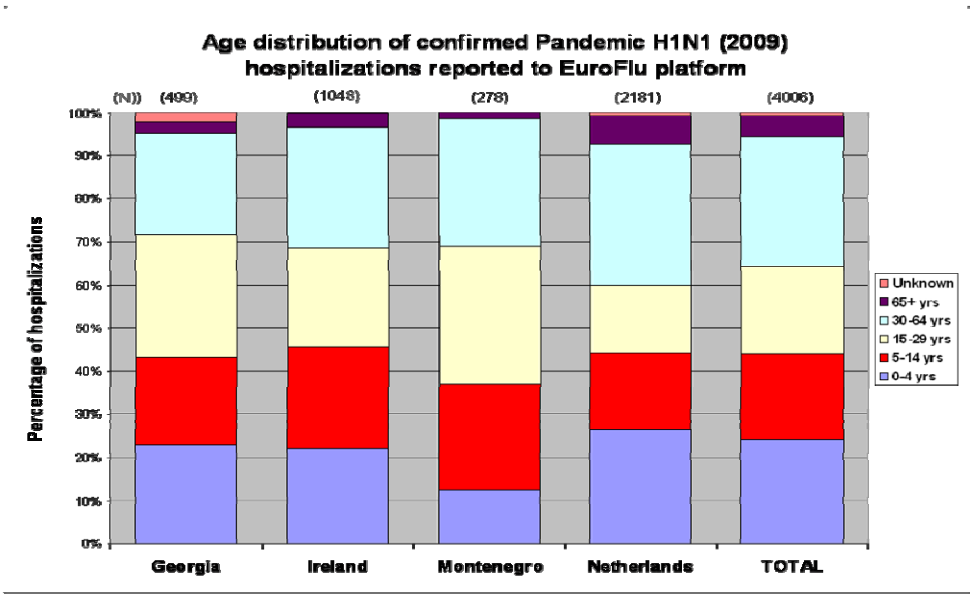


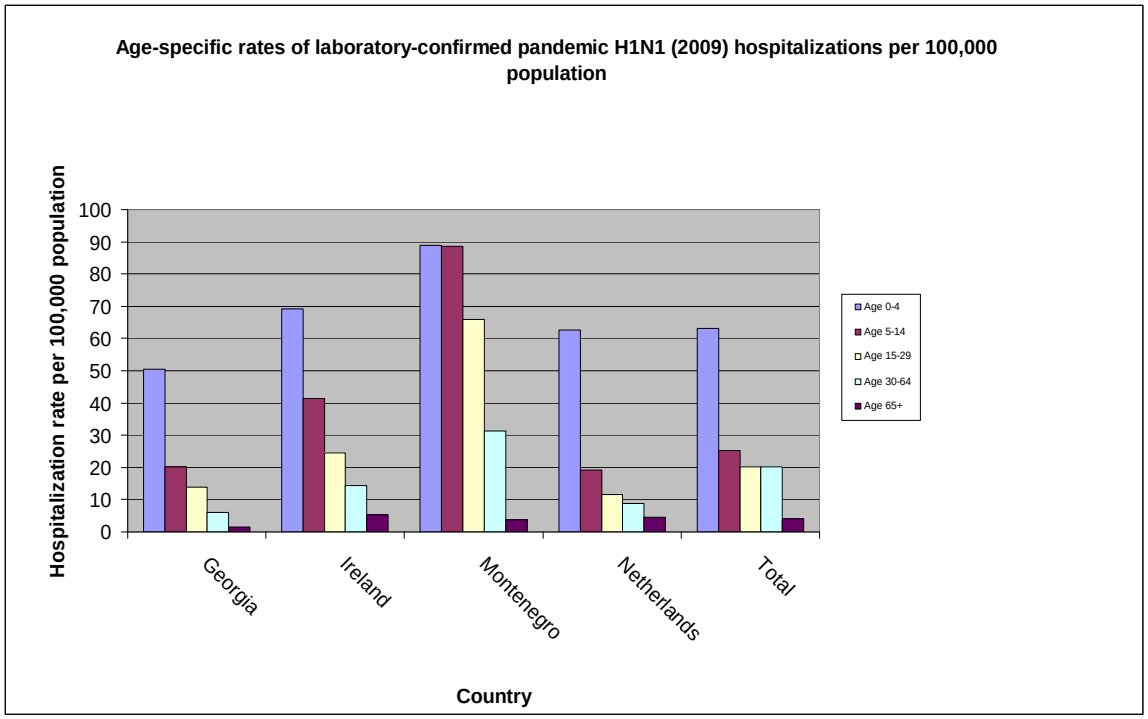
[8] Mazick et al., Eurosurveillance, Volume 15, Issue 5, 04 February 2010
[9] http://www.who.int/csr/disease/swineflu/notes/briefing_20091222/en/index.html
[10] http://www.who.int/csr/disease/swineflu/notes/briefing_20091222/en/index.html

Age-specific mortality rates associated with laboratory-confirmed pandemic H1N1 (2009) were also estimated using United Nations 2009 age-specific population estimates for these seven countries. These mortality rates are highest in the adult population, with the highest rates observed in the 30-64 year age group.



Four of these countries (Georgia, Ireland, Montenegro and Netherlands) additionally reported age-specific hospitalization data to EuroFlu. When compared to the age-distribution of laboratory-confirmed deaths, a notably larger fraction of laboratory-confirmed hospitalizations were reported in the 0-4 and 5-14 year age groups. Age-specific rates of hospitalizations also suggest declining rates of hospitalization with increasing age.





Taken together, these findings are also consistent with expectations following the winter pandemic wave in the southern hemisphere where hospitalization rates for children aged <5 years were consistently reported to be higher than those of other age groups. However age-specific mortality rates were observed to be highest in those aged 50–60 years.[11]

Publications of the results of epidemiologic analyses of severe cases also suggest a profile of underlying risk factors similar to what was observed in the southern hemisphere. When comparing the prevalence of conditions between more and less-severe cases of pandemic H1N1 (2009) virus infection, or between severe cases and estimated prevalence in the general population, chronic lung disease, asthma, diabetes and pregnancy have been observed to be risk factors for severe outcomes. Obesity has been suggested as a risk factor, although its independent contribution from underlying conditions such as diabetes is difficult to assess.[12,13,14]

Delays in treatment and care-seeking are also associated with increased risk of severe outcomes. A WHO-led rapid field investigation of severe cases early during the outbreak in western Ukraine (November, 2009) suggested that greater median days from illness onset to hospital admission, lower oxygen saturation on hospital admission and higher respiratory rates upon presentation to a hospital were all significantly associated with ICU admission or death. A complete overview of epidemiologic risk factors for severe outcomes is beyond the scope of this update but is ongoing. However, to facilitate a more rapid assessment during future influenza seasons, it remains an important priority to further strengthen the systematic reporting of severe influenza cases and the routine monitoring of hospitalized cases with severe acute respiratory illness in advance of the next winter influenza season.

[11] World Health Organization, Weekly Epidemiological Record, 13 NOVEMBER 2009, 84th YEAR / 13 NOVEMBRE 2009, 84e ANNÉE No. 46, 2009, 84, 477–484. http://www.who.int/wer
[12] Van Klooster et al., Eurosurveillance, Volume 15, Issue 2, 14 January 2010.
[13] Fuhrman et al., Eurosurveillance, Volume 15, Issue 2, 14 January 2010
[14] Rello J et al. Crit Care. 2009;13(5):R148.

What were the dominant viruses in circulation during the 2009/2010 season, and what percentage was resistant to the antiviral drugs oseltamivir or zanamivir?

- The vast majority of influenza virus detections were pandemic (H1N1) 2009 (99.74% of influenza A subtyped viruses from sentinel sources; N = 19 838). All pandemic (H1N1) 2009 viruses analysed antigenically (N = 1777) or genetically (N = 995) were similar to the vaccine strain and the majority were sensitive to both oseltamivir and zanamivir.

As shown in the table below for specimens collected as part of sentinel surveillance, the vast majority of influenza virus detections in the region from week 40/2009 up to week 07/2010 were pandemic (H1N1) 2009 and few seasonal influenza viruses were detected.

Sentinel virus detections, WHO European Region, Week 40, 2009 through Week 7, 2010.

sentinel specimens	**57 198**	%
sentinel virus detections	**19,890**	**34.77% positive**
Of these 19,890		
Influenza: A	**19,838**	**99.74%**
Influenza: B	**52**	**0.26%**
Of the 19,838 influenza A virus detections:	**19,838**	
subtyped	**18,948**	**95.51%**
Of these:· 18 948 subtyped:		
pandemic H1N1	**18,923**	**99.87%**
seasonal H1	**4**	**0.02%**
seasonal H3	**21**	**0.11%**

Eleven countries reported testing 1974 pandemic (H1N1) 2009 viruses for susceptibility to oseltamivir. Forty resistant viruses were detected, many of which were found in immunocompromised patients. No community spread of oseltamivir-resistant viruses has been reported. Of 1254 viruses that were tested for susceptibility to zanamivir, no resistant viruses were detected. Of the 140 viruses tested for susceptibility to amantadine, all were resistant.

All pandemic (H1N1) 2009 viruses analysed were antigenically (N = 1777) or genetically (N = 995) similar to the A/California/7/2009 (H1N1) virus, the recommended vaccine strain for the 2010 southern hemisphere influenza season and for the 2010/2011 northern hemisphere influenza season[15].

What can be expected during the upcoming season and during the next winter season?

[15] http://www.who.int/csr/disease/influenza/vaccinerecommendations/en/index.html

Surveillance systems that have been operating during the summer season in the temperate regions of the southern hemisphere are currently reporting few influenza detections.[16,17] As a result, there is no indication that abnormally high levels of summertime influenza activity are to be expected within the European Region. However influenza is unpredictable. The proportion of the population in many European countries that remains susceptible to pandemic H1N1 (2009) infection remains unclear, and this may influence the number of individuals who will become infected during the summer.

The extent to which circulating influenza A viruses remain antigenically similar to the A/California/7/2009 (H1N1) virus may influence the relative circulation of influenza A (H1N1) and influenza A (H3N2) during the next winter season and will also influence the anticipated burden of influenza in the European population. In this regard, the future burden of the pandemic H1N1 (2009) virus on populations over age 60, some of whom may have had a degree of immunity to the currently circulating virus, may in particular be influenced by any antigenic drift that occurs. While type B viruses have continued to circulate at low levels in Europe throughout the pandemic, as of Week 7/2010 there is no current evidence of any absolute increases in these virus detections across the European Region.

The results of serological studies are needed to better assess the extent of population immunity to pandemic (H1N1) 2009. Operation of sentinel surveillance systems through the summer remains very important in order to detect additional outbreaks, to monitor their epidemiology and to monitor currently circulating influenza strains.

What are the influenza surveillance priorities for the upcoming year?

Prior to the emergence of the pandemic H1N1 (2009) virus in human populations, the *WHO European Guidance for Influenza Surveillance in Humans* provided some suggestions to establish influenza surveillance to (i) establish seasonal baselines and circulation patterns; (ii) better manage their health resources through identification of priority groups for interventions; and (iii) to monitor trends and burden of severe disease caused by any influenza (seasonal or pandemic). The current experience with pandemic H1N1 (2009) further highlights the need for the establishment of efficiently functioning sentinel sites that can provide reliable, timely and high quality data on influenza circulation during times of increased burden on laboratory and epidemiological infrastructure. This surveillance should incorporate international standards that will facilitate the comparison of influenza and its circulation between European Member States and between Regions.

The most glaring gap to be addressed in influenza surveillance prior to the next winter season is the further strengthening of standard mechanisms for monitoring and reporting severe influenza.

Strong consideration should be given to establishing and strengthening sentinel surveillance for severe acute respiratory illness (SARI) to operate on a routine basis. This will allow trends in severe illness to be meaningfully monitored within countries and in the Region. This would include collection of a minimal amount of case-based data so the

[16] http://www.public.health.wa.gov.au/3/487/3/virus_watch_homepage.pm
[17] http://www.nicd.ac.za/

epidemiological profiles of severe influenza can also be reported in a standard manner. The EuroFlu platform is adapting to better manage and present SARI data as a routine component of its weekly bulletin.

This update also suggests that the reporting of aggregate and case-based data on severe cases of influenza to the EuroFlu platform can be useful to demonstrate the overall impact in the Region and to determine whether the epidemiologic profile of severe influenza is consistent across the Region. Emphasis will continue to be placed on the more efficient collection of a small amount of essential data from the WHO/Europe Member States in order to better monitor trends in influenza severity from the start of the next winter influenza season. This may include some stratification of aggregate data by gender in order to specifically assess the impact of influenza on women of childbearing age.

WHO/Europe is grateful for the enormous effort put forth by its Member States to maintain and strengthen influenza surveillance during this pandemic season. We welcome any further suggestions on the ways that the EuroFlu surveillance platform can assist with data presentation to inform policy decisions at the National level.