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EXCESS MORTALITY AMONG THE ELDERLY IN EUROPEAN COUNTRIES, DECEMBER 2014 TO FEBRUARY 2015

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Since December 2014 and up to February 2015, the weekly number of excess deaths from all-causes among individuals ≥ 65 years of age in 14 European countries have been significantly higher than in the four previous winter seasons. The rise in unspecified excess mortality coincides with increased proportion of influenza detection in the European influenza surveillance schemes with a main predominance of influenza A(H3N2) viruses seen throughout Europe in the current season, though cold snaps and other respiratory infections may also have had an effect.

In temperate countries in the northern hemisphere, the weekly number of deaths among the elderly (individuals aged ≥ 65 years) frequently exhibits sharp increases above normal expected levels of mortality during the winter season. The extent of this excess mortality varies considerably between years and between countries. This excess mortality in the elderly is often attributed to seasonal influenza, especially in seasons dominated by influenza A (H3N2), but factors other than influenza including other respiratory tract infections or environmental conditions (e.g. cold spells) can also play an important contributory role [1,2].

The European monitoring of excess mortality for public health action (EuroMOMO) network (www.euromomo.eu) monitors weekly 'real-time' all-cause age-specific excess mortality in countries in Europe through a standardised approach, allowing pooling of results. In the current winter of 2014/15, there has been an increased number of excess deaths observed among the elderly. We describe this observed excess mortality in Europe using all-cause mortality data up to and including week 9, 2015. The contributions of influenza and other factors to the excess mortality are also considered.

Analyses of all-cause mortality in Europe
Country level analyses

On a weekly basis, partners in EuroMOMO collect data on the number of deaths from all causes, and undertake timely data analyses by the use of a common algorithm. A time-series Poisson regression is used to predict the number of weekly deaths, adjusted for a linear trend and seasonal variation. The algorithm also corrects for any reporting delay, i.e. delays in the time between date of death and the date the death is registered, which can be lengthy [3].

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

For this study, sixteen European countries, namely, Belgium, Denmark, Estonia, Finland, France, Greece (municipalities of Athens, Keratsini-Drapetsona and Pireas and prefectures of Magnisia, Sporades, Kerkira, Achaia, Kavala and Thasos), Hungary, the Netherlands, Portugal, Spain, Sweden, Switzerland and the United Kingdom (UK: England, Northern Ireland, Wales, and Scotland) provided data for all-cause mortality analyses at country level.

Pooled country data analyses

Although sixteen countries submitted data to EuroMOMO, partners with marked delays in receiving data were not included in the pooled analyses. This resulted in data from 14 countries (Belgium, Denmark, Estonia, Finland, France, Hungary, the Netherlands, Portugal, Spain, Sweden, Switzerland and the UK (England, Wales, and Scotland)) being

included for such analyses. We used the stratified method as previously described [4]. The time-series in the pooled analysis included data from week 23, 2010 to week 9, 2015.

Comparison of mortality patterns

We used z-scores to standardise outputs enabling comparison of mortality patterns between different countries and between different time-periods. Excess mortality above two z-scores from the baseline in two consecutive weeks, was defined as above the normal level of the standard variation of data. The EuroMOMO hub, situated at Statens Serum Institut in Denmark, compiled the data outputs from individual partners.

Analyses in an epidemiological context

We collected information on influenza activity from influenza activity maps at the European Centre for Disease Prevention and Control (ECDC)'s website [5,6] and the joint ECDC/World Health Organization (WHO) Regional Office for Europe bulletin, FluNews Europe [7]. This included weekly indicators of intensity of transmission on influenza-like illness and proportion of positive influenza virus detections in the sentinel surveillance schemes in European countries. Finally, EuroMOMO network participants provided information on the epidemiological situation in the respective contributing countries, including temperature data.

Results

The country-specific analyses showed that in the present winter of 2014/15, all-cause excess mortality among the elderly has been above two z-scores from the baseline, for two consecutive weeks or more, in Belgium, France, Greece, Hungary, the Netherlands, Portugal, Spain, Switzerland, Sweden, England, Northern Ireland, Scotland and Wales. Mortality started to increase between week 50 and 52 of 2014, and an excess above baseline was first observed in England, the Netherlands and Portugal (week 50). As of week 9 2015, the mortality was still elevated in five of the 13 countries that were affected in consistent patterns of excess mortality in the elderly. Significant excess mortality was not yet observed in Estonia and Finland, and although excess mortality was recorded in Denmark this has, at present, only occurred over a single week. The Table describes the weekly patterns of excess mortality in relation to the assessment of intensity of influenza transmission as reported by ECDC.

Table. Excess mortality ≥ 2 z-scores over baseline among individuals aged ≥ 65 years and assessment of transmission intensity of influenza-like illness in EuroMOMO countries, by week, week 49, 2014–week 9, 2015^a (n=16 countries)



The pooled analysis, which shows excess mortality across 14 participating countries combined, revealed a sharp rise in mortality among individuals aged ≥ 65 years across Europe starting from week 49, 2014, crossing four z-scores above baseline in week 50, and reaching 21 z-scores in week 2 of 2015 (Figure 1). Some excess mortality was also observed in the age group 15–64 years, reaching four z-scores in week 51, 2014. In younger individuals, mortality has been within the expected range, although among children <5 years, z-scores slightly over 2 were reached in week 1 and 2, 2015.

Figure 1. Number of deaths by week and modelled baseline obtained from pooled analysis of data from EuroMOMO countries, week 23, 2010–week 9, 2015^a (n=14 countries)



Figure 2 shows the excess mortality among the elderly (estimated from the pooled model expressed as the number of z-scores above the baseline) in the 14 countries included and the proportion positive for influenza detections in the European sentinel surveillance schemes. By visual inspection, the increase in excess mortality follows the same pattern as the increase in per cent positive influenza virus detections. Both start to increase around week 49 of 2014 but influenza per cent-positive reaches a plateau around week 4 to 8 while excess mortality seems to peak in week 2, 2015, but remains elevated at least until week 8. Of note, the reduction of mortality after week 8 still does not represent a decrease below the 2 z-scores.

Figure 2. Excess mortality among those aged ≥ 65 years, expressed as the number of z-scores above the baseline (left axis) and the proportion positive for influenza detections in the European sentinel surveillance schemes (right axis), week 40, 2014–week 9, 2015^a



Discussion

We found evidence of a significant increase in excess all-cause mortality predominantly in the elderly in 13 of the 16 countries examined. The weekly patterns of excess mortality in relation to the intensity of influenza transmission show that in most weeks excess mortality coincides with medium or high influenza activity (78 of 97 weeks with excess mortality).

The current influenza season in the northern hemisphere has been predominated by influenza A(H3N2) virus [8], which according to FluNews Europe accounted for 56% of the detections across European Community (EC)/ European

Economic Area (EEA)/WHO European region countries [7]. It is expected that a winter season with predominance of influenza A(H3N2) has higher mortality impact on the elderly than a season with predominant influenza A(H1N1) or a season with low influenza A transmission [1,2]. Since its appearance in 2009, influenza A(H1N1)pdm09 has been a prevailing virus type, and this type is known to have less impact on the elderly [1,2,9-11]. Furthermore, in the present winter season 2014/15, most of the influenza A(H3N2) viruses characterised in Europe until week 9, 2015 exhibit antigenic differences from the virus included in the 2014/15 northern hemisphere influenza vaccine [5-8]. A reduction in the effectiveness of the A(H3N2) component of the influenza vaccine has been reported from several countries [12-15], which in consequence may lead to higher morbidity and mortality in vaccinated populations.

There are inconsistencies in the mortality findings, e.g. Finland and Sweden had several weeks of medium intensity of influenza transmission but until 1 March 2015 only two consecutive weeks with significant excess mortality were noted in Sweden and none in Finland. Furthermore, some countries see a pattern of an early rise in mortality whereas increases in influenza transmission (as assessed in the primary care sector) seems to appear later; this pattern, however is not unusual as will be discussed below.

There are several possible explanations for these observations. Firstly, an early rise in mortality may suggest that other factors, besides influenza, contribute to the occurrence of excess mortality. Temperature data from this winter indicate cold snaps in France, Greece, Spain and Switzerland (data not shown, available from the authors). Other infections, including respiratory syncytial virus (RSV)-associated disease might further add to excess mortality in some countries, but not in others. For example, the French syndromic surveillance systems noted intense activities for pneumonia and bronchitis starting from the end of 2014 (A. Fouillet, personal communication February 2015). Secondly, the assessment of influenza transmission intensity using primary care surveillance data is qualitative and is based on the available information and thus reflects the specific attributes of national surveillance systems, such as the population under surveillance. Influenza-like illness (ILI) consultations in primary care should be compared cautiously between countries, and although work has attempted to standardise this measure, ILI remains a concept to be treated with care, as it may not fully capture intensity of transmission [16,17]. Finally there may be a range of influenza-related factors such as differences in vaccination uptake; the effectiveness of the available vaccines against seasonal influenza or differences in circulating viruses and the extent of drift.

The pooled analyses of excess mortality result in a pattern that appears consistent with the European virological influenza data. The two time series follow a parallel increase, with an apparent stabilisation of the virological data from week 4, 2015. The interval from week 50, 2014, to week 3, 2015 when per cent-positive increases is likely to represent the time-period with most intense circulation of influenza virus, and it is at the end of this ascent that the impact on mortality is expected to be highest. The apparent decrease in excess mortality at the end of the observation period needs to be treated with caution as it may be affected by an uncertainty in the adjusted delays in reporting of deaths.

The similar temporal pattern between the increase in per cent positive influenza virus detections and excess mortality is not a proof of causality. Nonetheless, it indicates that it is likely that influenza is an important contributor to the observed excess mortality among the elderly given previous evidence of attribution [2,9,10,18,19]. Pooling of data, in this case both data on number of deaths and virological influenza data across Europe, provides more statistical power than country-specific analyses and may enhance patterns that are not apparent in individual countries or populations [4]. On the other hand, details may be lost when pooling data (e.g. excess in an individual country can be diluted when others experience no excess) and therefore the two approaches of data analysis and visualisation are complementary.

Studies have shown that multivariable regression models can be successfully used to estimate the impact of mortality risks from influenza viruses while adjusting for the impact of other determinants including extreme temperature [1,2,9,18,19]. In order to assess the public health impact of influenza at the population level, we are working to develop a common European approach to estimate the number of excess deaths associated with influenza adjusting for other such factors, as discussed previously [3].

The influenza season in 2014/15 differs from the two past seasons across Europe. The past seasons showed a mixed and heterogeneous pattern of influenza A(H1N1)pdm09, influenza A(H3N2) and influenza B with inter-country differences in the dominant circulating sub-type. Although the current season is not dominated entirely by influenza A(H3N2) across Europe, this influenza type is certainly more commonly detected compared with the previous two seasons. It is well recognised that A(H3N2) tends to particularly impact the elderly (as was seen in seasons before the 2009 pandemic). In the current winter, the effect of this virus may possibly be exacerbated by the emergence of a drift variant. Furthermore, the available vaccine may not effectively cover this subtype. We hypothesise that the observed excess mortality among the elderly is a result of this epidemiological situation, potentially aggravated by the added effects of cold snaps and other respiratory infections. Further work is planned at the end of the season to investigate this hypothesis.

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Conflict of interest

None declared.

Authors' contributions

KM designed and wrote the first version of the manuscript. LE did the analyses, graphs and figures. AM coordinated all correspondences between authors and implemented most comments. KM, JN and LE implemented additional comments from authors. All authors provided data and contributed in the writing of, and approved the final version of the manuscript.

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