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European all-cause excess and influenza-attributable mortality in the 2017/18 season: should the burden of influenza B be reconsidered?

Jens Nielsen[1], Lasse S. Vestergaard[1], Lukas Richter[2], Daniela Schmid[2], Natalia Bustos[3], Tommi Asikainen[3] , Ramona Trebbien[1], Gleb Denissov[4], Kaire Innos[4], Mikko J. Virtanen[5], Anne Fouillet[6], Theodore Lytras[7], Kassiani Gkolfinopoulou[7], Matthias an der Heiden[8], Linus Grabenhenrich[8], Helmut Uphoff[9], Anna Paldy[10], Janos Bobvos[11], Lisa Domegan[12], Joan O'Donnell[12], Matteo Scortichini[13], Annamaria de Martino[14], Joël Mossong[15], Kathleen England[16], Jackie Melillo[17], Liselotte van Asten[18], Marit MA de Lange[18], Ragnhild Tønnessen[19], Richard A. White[19], Susana P. da Silva[20], Ana P. Rodrigues[20], Amparo Larrauri[21], Clara Mazagatos[21], Ahmed Farah[22], AnnaSara D Carnahan[22], Christoph Junker[23], Mary Sinnathamby[24], Richard G. Pebody[24], Nick Andrews[24], Arlene Reynolds[25], Jim McMenamin[25], Caroline S. Brown[26], Cornelia Adlhoch[27], Pasi Penttinen[27], Kåre Mølbak[1,28], Tyra G. Krause[1]

1. Statens Serum Institut, Copenhagen, Denmark
2. Austrian Agency for Health and Food Safety, Vienna, Austria
3. Sciensano, Brussels, Belgium
4. National Institute for Health Development, Tallinn, Estonia
5. Finnish National Institute for Health and Welfare, Helsinki, Finland
6. French Public Health Agency (Santé Publique France), Saint-Maurice, France
7. Hellenic Centre for Disease Control and Prevention, Athens, Greece
8. Robert Koch Institute, Berlin, Germany
9. Hessisches Landesprüfungs- und Untersuchungsamt im Gesundheitswesen, Dillenburg, Germany
10. National Public Health Institute, Budapest, Hungary
11. Ministry of Human Capacities, Budapest, Hungary
12. Health Service Executive - Health Protection Surveillance Centre, Dublin, Ireland
13. Dipartimento Epidemiologia del S.S.R., Lazio - ASL Roma 1, Rome, Italy
14. Ministero della Salute, Rome, Italy
15. Laboratoire National de Santé, Luxembourg
16. Directorate for Health Information and Research, Pieta, Malta

17. Department of Health Regulation, Pieta, Malta
18. National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands
19. Norwegian Institute of Public Health, Oslo, Norway.
20. Instituto Nacional de Saúde Doutor Ricardo Jorge, Lisbon, Portugal
21. National Centre of Epidemiology, CIBER Epidemiología y Salud Pública (CIBERESP), Carlos III Health Institute, Madrid, Spain
22. Public Health Agency of Sweden, Stockholm, Sweden
23. Federal Statistical Office, Neuchâtel, Switzerland
24. Public Health England, Colindale, United Kingdom
25. Health Protection Scotland, Glasgow, United Kingdom
26. World Health Organization, Regional Office for Europe, Copenhagen, Denmark
27. European Centre for Disease Prevention and Control, Solna, Sweden
28. Department of Veterinary and Animal Science, Faculty of Health and Medical Science, University of Copenhagen, Copenhagen, Denmark

Corresponding author:

Jens Nielsen

Infectious Disease Epidemiology and Prevention, Statens Serum Institut

Artillerivej 5, DK2300 Copenhagen, Denmark

Phone: +45 32683965, E-mail: nls@ssi.dk

Running heading: European mortality in the 2017/18 season

Keywords: Mortality, influenza, B/Yamagata, EuroMOMO, FluMOMO

Abstract

Objectives: Weekly monitoring of European all-cause excess mortality, the EuroMOMO network, observed high excess mortality during the influenza B/Yamagata dominated 2017/18 winter season, especially among elderly. We describe all-cause excess and influenza-attributable mortality during the season 2017/18 in Europe.

Methods: Based on weekly reporting of mortality from 24 European countries or sub-national regions, representing 60% of the European population excl. Russia and the Turkey part of European, we estimated age stratified all-cause excess morality using the EuroMOMO model. In addition, age stratified all-cause influenza-attributable mortality was estimated using the FluMOMO algorithm, incorporating influenza activity based on clinical and virological surveillance data, and adjusting for extreme temperatures.

Results: Excess mortality was mainly attributable to influenza activity from December 2017 to April 2018, but also due to exceptionally low temperatures in February-March 2018. The pattern and extent of mortality excess was similar to the previous A(H3N2) dominated seasons, 2014/15 and 2016/17. The 2017/18 overall all-cause influenza-attributable mortality was estimated to be 25.4 (95%CI 25.0-25.8) per 100,000 population; 118.2 (116.4-119.9) for persons aged 65. Extending to the European population this translates into over-all 152,000 deaths.

Conclusions: The high mortality among elderly was unexpected in an influenza B dominated season, which commonly are considered to cause mild illness, mainly among children. Even though A(H3N2) also circulated in the 2017/18 season and may have contributed to the excess mortality among the elderly, the common perception of influenza B only having a modest impact on excess mortality in the older population may need to be reconsidered.

Introduction

Mortality in temperate countries, in particular among senior citizens, exhibits a marked seasonality, with higher mortality in the winter period. Excess mortality may vary considerably between countries and from season to season (1-7). One of the main drivers of increased winter mortality is seasonal influenza, however seasonal transmission of other communicable diseases, such as RSV and enteric infections, as well as the effect of extreme ambient temperatures may also contribute (8,9).

Since 2009, the European network for monitoring of excess mortality for public health action, EuroMOMO (www.euromomo.eu), has monitored weekly all-cause, age-specific mortality in real-time in participating European countries and provided pooled estimates of excess mortality (observed minus expected), using the EuroMOMO model (10). These estimates are published on a weekly basis and included in the weekly FluNewsEurope bulletin (www.FluNewsEurope.org) to assess the influenza situation in Europe. Recently, the EuroMOMO model was supplemented with another time-series regression model, FluMOMO, which includes indicators of influenza activity and extreme temperatures (7). The aim of this model is to obtain timely estimates of influenza-attributable mortality adjusted for extreme temperatures.

From December 2017 a marked increase in all-cause excess mortality was observed within the participating countries, especially in western and southern European countries, and particularly among elderly (65 years or older). At the same time, most countries reported rates of Influenza Like Illness (ILI) reaching moderate levels, while only a few countries reported higher levels compared with recent seasons. However, in some countries number of influenza hospitalisations and intensive care admissions reached or exceeded peak levels of recent influenza seasons (11,12). Overall, the dominant influenza type was B/Yamagata followed by influenza A, with both A(H1N1)pdm09 and A(H3N2) circulating in varying patterns between countries (11,13). The WHO recommended vaccine components for the trivalent vaccine in the 2017/18 season on the Northern Hemisphere contained B/Victoria.

Knowledge about the burden of seasonal influenza is crucial to informing policies for prevention and control of influenza, in particular seasonal influenza vaccination programs. Hence, being able to quantify the mortality-burden of influenza, and associate it to circulating seasonal influenza viruses, adds valuable information.

The aim of the present study is to describe excess all-cause mortality and estimate all-cause mortality attributable to influenza during the season 2017/18 in Europe, using the EuroMOMO and FluMOMO models and available influenza surveillance and temperature data.

Methods

<u>All-cause excess mortality, the EuroMOMO model</u>

Countries participating in the EuroMOMO network collect data on number of all-cause deaths weekly, and undertake national analyses using the EuroMOMO model (4).

The EuroMOMO hub at Statens Serum Institut in Denmark receive mortality data aggregated by week and age group from the participating countries, and conducts country-stratified pooled analyses of these data (10). We estimated the pooled excess mortality for the winter season 2017/18 using all-cause mortality data from week 1/2014 to week 20/2018, from 24 participating national or sub-nation states (Austria, Belgium, Berlin (Germany), Denmark, England (UK), Estonia, Finland, France, Greece, Hesse (Germany), Hungary, Ireland, Italy, Luxembourg, Malta, Netherlands, Northern Ireland (UK), Norway, Portugal, Scotland (UK), Spain, Sweden, Switzerland, Wales (UK)), further on referred to as countries.

Mortality data reported to the EuroMOMO hub in week 27/2018 were used.

<u>Influenza-attributable mortality, the FluMOMO model</u>

The FluMOMO model is a multiplicative Poisson regression time-series model with overdispersion, ISO-week as time unit and a post-estimation correction for skewness of the residuals by applying a 2/3-power correction, and have been described in detail elsewhere (7).

To estimate influenza-attributable mortality for each country we used the all-cause mortality data from EuroMOMO, aggregated by week and age group, combined with weekly influenza activity (IA) and temperature data. As IA indicator, we used the Goldstein index (14), defined as the ILI rate multiplied by the Positive Percentage (PP), i.e. proportion of sentinel influenza-positive specimens among all sentinel specimens tested for influenza. This indicator combines the clinical measure of influenza circulating in the population (ILI) with PP to take into account that not all ILI cases are due to influenza. In countries or seasons, where ILI data were unavailable, Acute Respiratory Infection (ARI) rates or alternatively the indicator Intensity (Low, Medium, High or Very High; a qualitative measure, recommended to be based on the Moving Epidemic Method (18)) was used.

ILI/ARI/Intensity data as well as virology data were downloaded from the TESSy database at the European Centre for Disease Prevention and Control (ECDC) (15). Virological data registered in TESSy are not age differentiated, therefore the same all-ages virological data had to be used in each age group. Ambient daily temperature data from weather stations in each of the participating countries was captured from the National Oceanic and Atmospheric Administration (NOAA) (16). Weekly extreme temperatures were defined as degrees of temperature above the expected weekly average maximum temperatures or below the weekly average minimum temperature (7).

We estimated the pooled mortality attributable to influenza and extreme temperatures for the winter seasons 2012/13 to 2017/18 using country-stratified pooled analyses, thus adjusting for differences in baselines between countries. The analyses were conducted for each season using data from the five preceding seasons.

Clinical and virological influenza data were downloaded in week 27/2018, as was ambient temperatures.

Mortality rates, background populations

Based on the estimated number of deaths, mortality rates were calculated using national or sub-national population data as of January 1st every year, downloaded from EuroSTAT (17) in week 27/2018, and linearly interpolated through the year.

Results

Overall, the European 2017/18 influenza season was dominated by influenza B (Figure 1). The weekly influenza PP was nearly two times higher for influenza B than influenza A, however with some variation between the participating countries.

All-cause mortality for all ages exceeded threshold levels (> +2 z-scores) in all participating countries except in Greece. Excess mortality was first observed in Spain in week 46/2017 (Table 1), followed by Scotland in week 47; England, Northern Ireland, and Portugal in week 49; France, Ireland, and Italy in week 50; Norway, Switzerland, and Wales in week 51; Denmark in week 52; Austria and Netherlands in week 1/2018. Belgium and Hungary had two weeks periods around New Year. Mortality in France, Norway, and Switzerland returned to expected levels at the end of January and in Scotland in February. For the other countries, the excess continued, and from February-March 2018 Belgium, Estonia, Finland, France, Hesse, Berlin, Luxembourg, Norway, Malta, and Sweden had mortality exceeding expected levels. Countries in the southwestern part of Europe and Scotland experienced particularly high all-cause excess mortality during the 2017/18 influenza season (high z-score value in table 1).

The pooled estimates of excess all-cause mortality of the 24 participating countries rose sharply for the age groups 15-64 years and 65 years or older in week 48/2017, exceeding 4 z-scores above baseline in week 49/2017 (Figure 2). Over the season, there were two waves of excess mortality, the first peak in the beginning of 2018 and a second less pronounced peak in February-March 2018.

Previously published pooled estimates of excess mortality according to the EuroMOMO algorithm for the 2012/13 to 2016/17 seasons (19) and the estimates for the 2017/18 season are shown in table 2. The excess all-cause mortality rate, i.e. the deviation from the estimated baseline, for the 2017/18 season was 33.8 (95%CI 32.8-34.9) per 100,000 population across all ages, which approximated the high mortality rates observed in the two A(H3N2) dominated seasons 2014/15 and 2016/17 (Figure 3). Mortality rates were highest among those aged 65 years and older, whereas the mortality rate among children < 15 years was lower than the previous seasons.

According to the FluMOMO model, excess mortality in the 2017/18 season could largely be attributed to seasonal variation in influenza activity (Figure 4). Furthermore, the FluMOMO model indicated that the second late peak in mortality to some extent could be attributed to the exceptionally cold temperatures in February-March 2018 in addition to a declining, but still prominent excess mortality attributable to influenza.

The pooled 2017/18 mortality attributable to influenza was estimated to be 25.4 (25.0-25.8) per 100,000 population for all ages, slightly below the 2014/15 and 2016/17 seasons (Table 2) but following the pattern of these seasons (Figure 5). In the age group 15 to 64 years, the influenza-attributable mortality was estimated to be 3.1 (3.1-3.2) per 100,000 population, which was significantly higher than the five previous seasons.

With the participation of 24 European countries corresponding to a population of 361 million inhabitants (Tables 2 and 3), the pooled analyses cover 60% (361/599) of the European population excl. Russia and the Turkey part of Europe of 599 million (20). If we extend our results to this European population, excess number of deaths in Europe during the 2017/18 season would be 202 (196-209) thousand, and number of deaths attributable to influenza 152 (150-155) thousand.

Discussion

Seasonal influenza causes a major health burden (21), especially for the elderly and persons with underlying health conditions. In addition to the direct effects of influenza infection, underlying health conditions may be exacerbated leading to poor health outcomes and even premature death. In this situation, influenza or respiratory tract infection may not be registered as cause of death. Hence, estimates of influenza-attributable mortality based on all-cause rather than cause-specific mortality e.g. respiratory deaths including influenza and pneumonia, is expected to be higher. Influenza-attributable deaths coded as non-respiratory deaths have been found to be at the same magnitude as for respiratory influenza mortality (22,23). Therefore, all-cause mortality attributable to influenza may be expected to be around the double of influenza mortality based on respiratory cause of death alone.

Recently, a global study estimated average annual influenza-associated respiratory mortality rates in Europe from 1999 to 2015 to be 3.1 to 8.0 per 100,000 population (24). As expected, these estimates are lower than the median of the all-cause estimates of influenza-attributable mortality of 13.3 per 100,000 population (Table 3). However, considering, as mentioned, that influenza-associated deaths from respiratory deaths may represent only half of all influenza-attributable deaths, corresponding to all-cause mortality rates of roughly 6 to 16, the estimated rates from the two studies are consistent.

The EuroMOMO pooled analyses showed that the 2017/18 seasonal excess mortality started on the Iberian Peninsula and spread across the southern and western parts of Europe, while mortality tended to be within normal levels in the northern, eastern, and central parts of Europe until February-March 2018, where Europe experienced a period with exceptionally cold temperatures. The FluMOMO pooled estimates of mortality attributable to influenza activity adjusted for extreme temperatures showed a similar pattern, including a marked elevated mortality attributable to influenza among adults (15 to 64 years old). High numbers of hospital and ICU admissions were reported among elderly (11), supporting increased disease impact especially among adults and elderly. In contrast, the influenza-attributable mortality among children <15 years of age was at the same level or lower than previous seasons.

During the 2017/18 season, influenza B/Yamagata circulated widely and dominated over mixed influenza A subtypes. Many European countries experienced a marked excess mortality among the elderly similar to that observed during the A(H3N2) dominated seasons 2014/15 and 2016/17. This observation challenges the common perception that influenza B has only a modest impact on severe illness and mortality in the elderly population (25,26). Published data on burden of influenza B in Europe is scarce (27). However, a global review found that influenza B can pose a significant burden (28). A Canadian study reported that the age distribution differ between the two B lineages, with a substantially higher median age for B/Yamagata (29). This may explain the pattern in mortality observed during the B/Yamagata dominated 2017/18 season. However, A(H3N2) circulated too, and may also have contributed to the excess mortality among elderly. It is also possible that the European population was more susceptible to B/Yamagata infection as B/Victoria has been the main circulating lineage since the 2014/15 season and before that 2012/13 (11). Though B/Yamagata was included in the WHO recommended vaccines from 2012/13 to 2015/16, the immunity in the population may be limited due to low coverage, as influenza vaccination programmes in most European countries target only risk groups in order to minimise severe outcomes, and do not consider indirect protection and herd immunity. However, even though influenza B/Yamagata was not included in the 2017/18 season's trivalent influenza vaccine, which was most widely used in European countries, the vaccine effectiveness against influenza B has been estimated to 36-54% (30), maybe due to preserved immunity from previous immunisation (infection or vaccination) (31) or cross protection.

<u>Limitations</u>

Pooled estimates can both mask and accentuate differences between countries in excess and influenza-attributable mortality. Therefore, an important component in the EuroMOMO procedures is the initial national analyses to reveal excess mortality at country level, while the pooled analyses may reveal small increases in mortality not immediately recognisable locally. For example, an excess mortality among adults aged 15-64 years was detected in the pooled analyses in the current season, but only in few of the countries' national analyses.

All analyses of influenza-attributable mortality were performed at the EuroMOMO hub, using IA data from TESSy. This has the advantage of using common, standardised IA data, but also has limitations e.g. missing a local review and validation process.

The Goldstein Index: ILI x PP, represents the most conservative indicator of influenza activity and was the IA indicator used in the FluMOMO model (7,14). However, not all countries report ILI, and we used ARI or Intensity, where ILI was unavailable. Further, virology data from TESSy were not age-stratified; hence, the same all-ages-PP was used in each of the age groups, which may have masked differences between age groups. The impact of these limitations in IA should be investigated.

Mortality attributable to influenza differentiated by type/sub-type may provide an improved understanding of the burden attributable to each type/sub-type. However, the nearly equal pattern in the circulation of influenza A and B in the 2017/18 season (Figure 1) introduced collinearity between the influenza types i.e. making the effects difficult to separate. Further, splitting the IA parameter into type/sub-type substantially reduced the statistical power making the model unstable. Therefore, it was not feasible to make type/sub-type differentiated estimates.

Heterogeneity in mortality patterns between countries may reflect some real differences, possibly related to differences in influenza circulation by type/sub-type, country-specific population susceptibility, differences in influenza vaccine uptake, varying from 5 to 75% coverage among elderly (32), or vaccine effectiveness. Therefore, regional analyses have the potential to provide added value. However, with few participating countries in some regions of Europe, this was not explored further.

We extended the estimated excess mortality in the participating countries to the European population, this extension is uncertain as potential differences in climate, influenza transmission, underlying immunity and access to health care between the participating and non-participating European countries were not taken into account.

Conclusion

Using the existing EuroMOMO and FluMOMO models and available influenza and temperature data, we have shown that during the 2017/18 season, dominated by influenza B/Yamagata, Europe experienced a marked excess mortality among adults and elderly attributable to influenza. The impact of the 2017/18 influenza epidemic on mortality was similar to that of the previous influenza A(H3N2) dominated seasons in 2014/15 and 2016/17. The European number of deaths attributable to influenza was estimated to be 152 thousand persons. We found a lower influenza-attributable mortality compared to excess mortality, which may indicated that other circulating pathogens might also have contributed to the all-cause excess mortality.

A non-negligible circulation of A(H3N2) may have contributed to the high excess mortality among elderly. However, the large influenza-attributable mortality burden in elderly during an influenza B dominated season challenge the common perception of influenza B primarily affecting children and young adults and having limited impact in the elderly population.

Finally, our findings suggest that the overall influenza-related mortality is significantly higher than influenza mortality based on respiratory causes of deaths alone. However, as data on mortality are crucial to informing policies pertaining prevention and control of influenza, in particular seasonal influenza vaccination programs, further studies are needed to fully assess the burden of all-cause and cause-specific influenza mortality.

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Authors' contributions

Jens Nielsen drafted the manuscript and performed all analyses, graphs, and tables. Lasse S Vestergaard, Kåre Mølbak, and Tyra G Krause wrote parts of the manuscript. Authors from the participating countries provided data and contributed to drafting the manuscript. All authors reviewed and approved the final version.

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Declaration of interests:

All authors declare no competing interests.

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Table 1. Weekly all-cause mortality for all ages exceeding the threshold level (+2 z-scores) during the 2017/18 winter season by country, based on the EuroMOMO algorithm.

Year	2017													2018																			
Week	40	41	42	43	44	45	46	47	48	49	50	51	52	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Country																																	
Austria	0	1	0	0	1	0	0	0	0	1	0	1	1	2	3	3	1	4	0	3	5	6	6	5	1	3	1	0	1	0	0	0	0
Belgium	0	0	0	0	0	0	0	0	0	1	1	1	2	2	1	1	0	1	1	3	4	8	8	5	4	3	0	0	0	0	0	0	0
Denmark	0	0	0	0	0	0	2	0	0	1	1	0	2	2	1	2	1	2	3	5	4	6	6	4	5	3	3	3	0	0	0	0	0
England[a]	0	0	0	0	0	0	0	1	0	2	3	5	6	8	7	7	5	4	3	3	3	4	5	2	1	0	0	0	0	0	0	0	0
Estonia	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	3	3	3	3	2	1	1	1	1	0	0	0	0
Finland	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	2	2	1	3	0	0	0	0	0	0
France	0	0	0	0	0	0	0	0	0	1	2	2	4	5	4	3	1	1	2	2	3	6	7	4	3	2	2	1	1	0	0	0	0
Berlin[b]	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3	3	5	4	3	2	1	1	0	0	0	0	0
Hessen[b]	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	4	6	8	6	4	2	2	0	0	0	0	0	0
Greece	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	0	1	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0
Hungary	0	0	0	0	0	0	0	0	0	0	1	4	2	0	0	0	0	0	1	2	3	4	4	3	2	1	0	0	0	0	0	0	0
Ireland	0	0	0	1	0	0	1	0	0	0	2	1	4	5	5	5	2	3	1	1	0	2	2	0	0	0	0	0	1	0	0	0	0
Italy	1	0	0	0	0	0	0	0	0	1	2	2	3	7	5	4	3	2	1	1	2	3	3	1	0	0	0	0	0	0	0	0	0
Luxembourg	0	2	0	0	0	0	0	1	0	1	0	0	0	0	1	0	0	0	2	2	2	2	4	0	1	0	0	0	0	0	0	0	0
Malta	0	0	0	0	1	0	1	0	0	1	1	1	2	4	1	2	1	1	2	3	4	2	2	1	1	0	1	0	0	0	1	0	0
Netherlands	0	0	0	0	0	0	0	0	0	0	2	1	1	3	3	3	2	3	4	5	6	8	10	7	4	3	1	0	0	0	0	0	0
N. Ireland[a]	0	0	0	1	0	0	0	2	1	2	1	3	3	5	7	4	4	3	1	3	1	1	0	1	0	0	0	0	0	0	0	0	0
Norway	0	0	0	1	0	0	0	0	0	1	0	2	1	3	1	3	0	1	2	2	2	2	3	2	3	0	1	1	0	0	0	0	0
Portugal	1	0	1	0	0	0	2	1	1	4	4	4	6	7	7	6	5	5	6	6	6	5	2	2	1	2	3	2	1	0	0	0	0
Scotland	1	2	0	0	0	0	1	2	1	4	5	5	10	11	10	7	5	2	2	1	1	3	1	1	0	0	1	0	0	0	0	0	0
Spain	1	0	0	0	0	0	2	2	2	3	5	5	7	12	11	10	8	7	7	7	5	5	4	3	1	1	2	1	0	0	0	0	0
Sweden	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	3	4	5	3	2	2	3	0	0	0	0	0	0
Switzerland	1	0	0	0	0	0	0	0	2	1	1	2	1	4	4	3	1	1	2	3	3	6	5	4	2	1	1	1	0	0	0	0	0
Wales[a]	1	1	0	0	0	0	0	0	0	0	1	2	3	2	4	3	2	2	2	3	1	3	4	1	0	0	0	0	0	0	0	0	0

a) United Kingdom b) Germany

Values = z-score above 0. Red = above +2 z-scores. Yellow = weeks considered as above +2 z-scores i.e. included in periods with excess.

Table 2. Cumulated pooled all-cause excess mortality during the winter season based on the EuroMOMO algorithm, by season (week 40 to week 20) 2012/13 to 2017/18.

Season	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18
Circulating types of influenza[1]	A(H1N1)pdm09 (47%) B/Yamagata (53%)	Mixed A (98%) B/Yamagata (2%)	A(H3N2) (67%) B/Yamagata (33%)	A(H1N1)pdm09 (56%) B/Victoria (44%)	A(H3N2) (89%) Mixed B (11%)	Mixed A (33%) B/Yamagata (67%)
WHO recommended vaccine strains	A(H3N2) A(H1N1)pdm09 B/Yamagata	A(H3N2) A(H1N1)pdm09 B/Yamagata	A(H3N2) A(H1N1)pdm09 B/Yamagata	A(H3N2) A(H1N1)pdm09 B/Yamagata	A(H3N2) A(H1N1)pdm09 B/Victoria	A(H3N2) A(H1N1)pdm09 B/Victoria
Age groups	**Excess all-cause mortality per 100,000 population (95% CI)**					
0-4	1.14 (0.36;1.92)	1.76 (1.00;2.52)	1.38 (0.62;2.14)	2.42 (1.70;3.14)	0.88 (0.15;1.60)	-1.07 (-1.72;-0.41)
5-14	0.49 (0.31;0.67)	0.18 (0.02;0.35)	0.51 (0.35;0.67)	0.50 (0.34;0.66)	0.18 (0.03;0.34)	0.13 (-0.01;0,27)
15-64	2.09 (1.66;2.53)	1.67 (1.22;2.12)	5.94 (5.53;6.35)	4,85 (4.47;5.23)	3.49 (3.13;3.86)	5.03 (4.71;5.35)
≥65	88.20 (81.42;94.99)	-12.46 (-20.11;-4.79)	214.17 (207.60;220.74)	14.71 (8.82;20.60)	152.79 (146.43;159.16)	154.12 (149.35;158.89)
Total	17.25 (15.96;18.55)	-1.39 (-2.96;0.18)	43.63 (42.30;44.96)	5.37 (4.15;6.58)	29.21 (27.97;30.45)	33.81 (32.76;34.85)
Number of countries participating	14	17	18	19	21	24
Population covered (millions)	268	275	279	340	345	361

1) For 2012/13 and 2013/14 all EU/EEA sentinel samples reported to ECDC (https://ecdc.europa.eu/en/seasonal-influenza/surveillance-and-disease-data/aer). From 2014/15 and onward, all European sentinel samples reported to WHO/ECDC (http://flunewseurope.org/Archives)

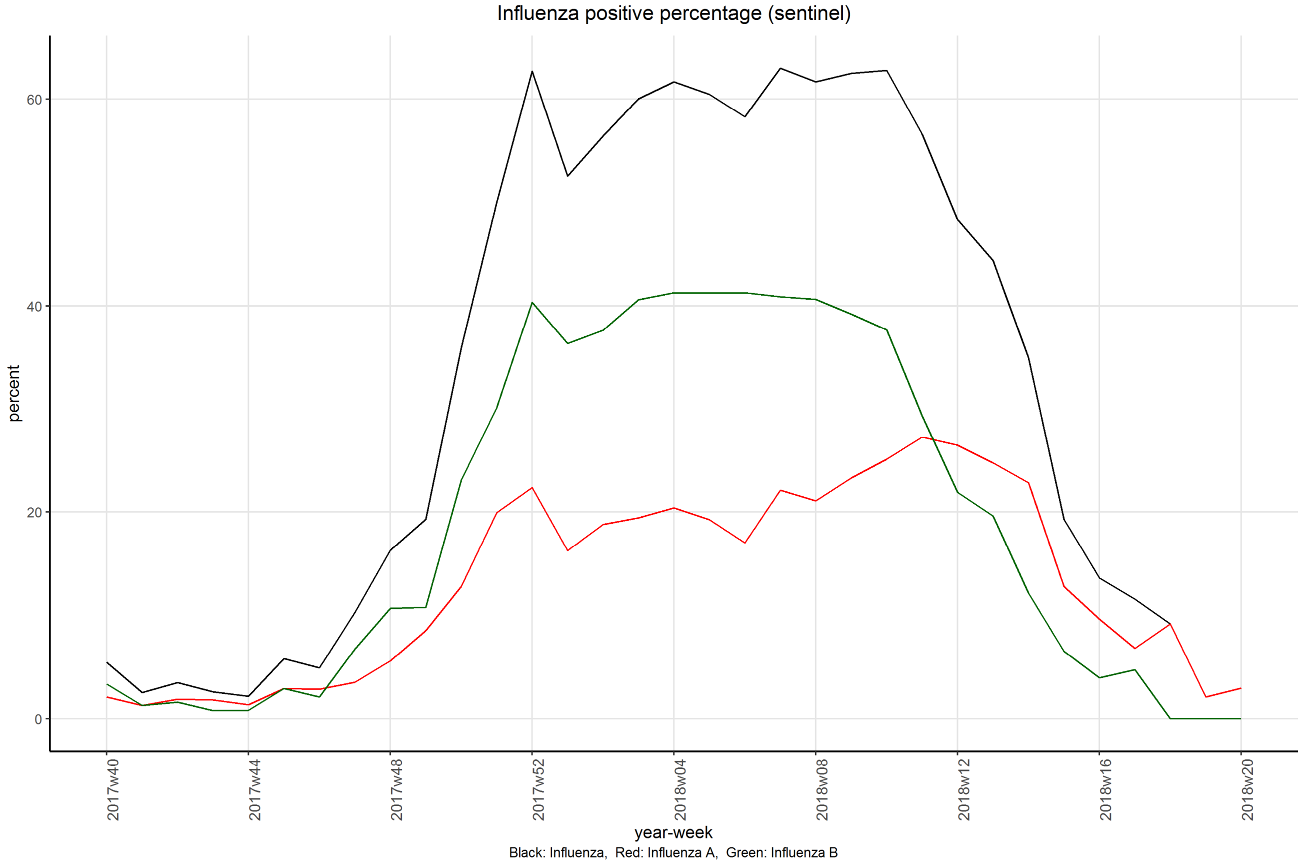
Note: Excess mortality is defined as observed mortality minus baseline

Table 3. Cumulated pooled estimates of mortality attributable to influenza during the winter season based on the FluMOMO algorithm, by season (week 40 to week 20) 2012/13 to 2017/18

Season	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18
Circulating types of influenza[1]	A(H1N1)pdm09 (47%) B/Yamagata (53%)	Mixed A (98%) B/Yamagata (2%)	A(H3N2) (67%) B/Yamagata (33%)	A(H1N1)pdm09 (56%) B/Victoria (44%)	A(H3N2) (89%) Mixed B (11%)	Mixed A (33%) B/Yamagata (67%)
WHO recommended vaccine strains	A(H3N2) A(H1N1)pdm09 B/Yamagata	A(H3N2) A(H1N1)pdm09 B/Yamagata	A(H3N2) A(H1N1)pdm09 B/Yamagata	A(H3N2) A(H1N1)pdm09 B/Yamagata	A(H3N2) A(H1N1)pdm09 B/Victoria	A(H3N2) A(H1N1)pdm09 B/Victoria
Age groups	**Influenza-attributable mortality per 100,000 population (95% CI)**					
0-4	0.39 (0.30-0.48)	1.09 (0.94-1.24)	0.88 (0.75-1.01)	0.69 (0.57-0.81)	1.05 (0.91-1.20)	0.14 (0.08-0.19)
5-14	0.25 (-0.03-0.82)	0.03 (0.01-0.05)	0.08 (-0.41-0.89))	0.22 (0.17-0.27)	0.11 (0.07-0.14)	0.11 (0.08-0.15)
15-64	2.14 (2.06-2.22)	0.55 (0.50-0.60)	2.41 (2.33-2.49)	2.40 (2.32-2.49)	1.43 (1.37-1.50)	3.14 (3.05-3.22)
≥65	64.46 (62.72-66.21)	0.61 (0.52-0.71)	147.41 (145.39-149.44)	15.95 (15.00-16.91)	129.90 (127.92-131.88)	118.17 (116.42-119.93)
Total	13.34 (13.02-13.66)	0.31 (0.24-0.38)	28.58 (28.22-28.95)	3.05 (2.87-3.23)	25.65 (25.26-26.05)	25.41 (25.03-25.80)
Number of countries participating	14	17	18	19	21	24
Population covered (millions)	268	275	279	340	345	361

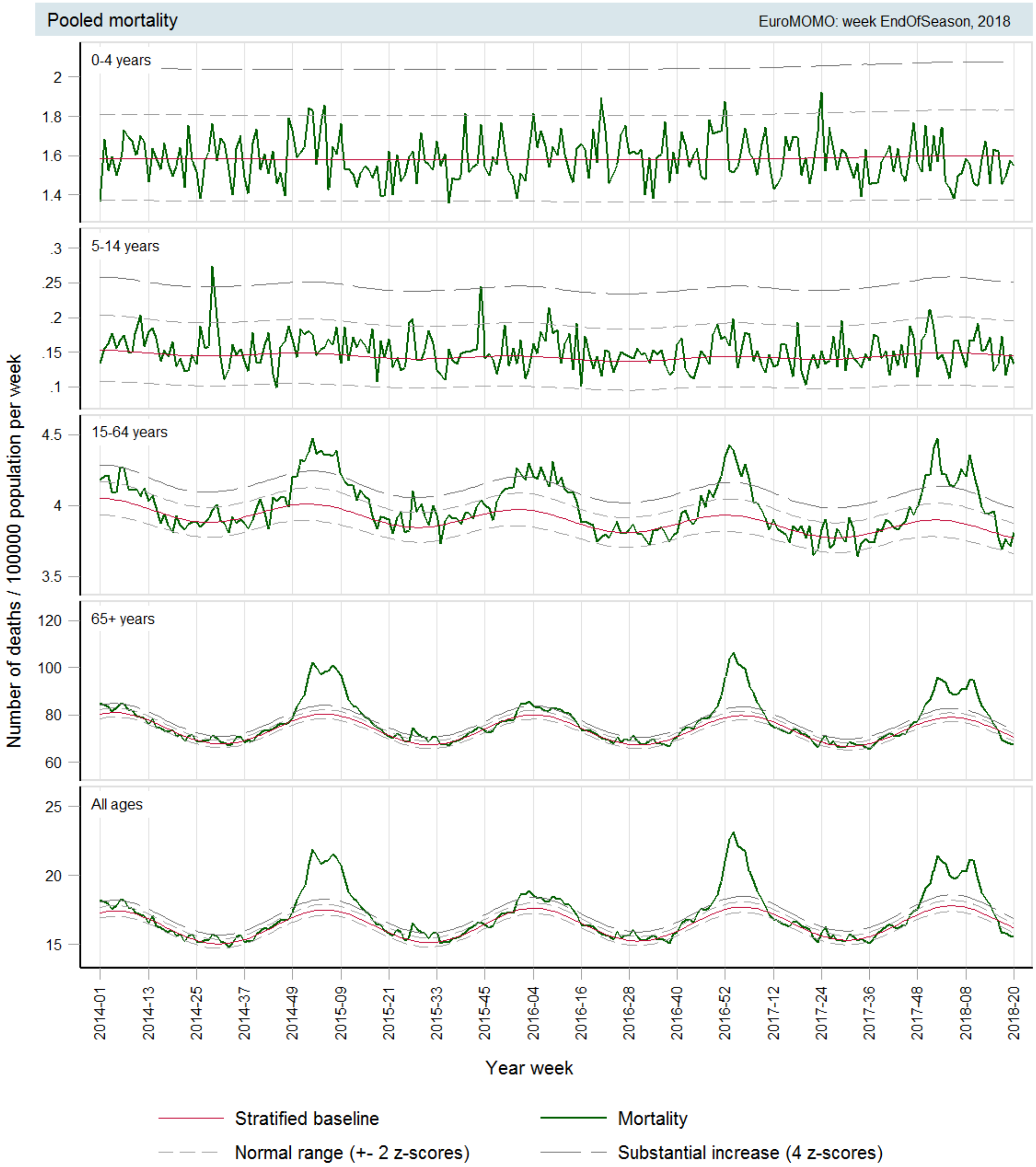
1) For 2012/13 and 2013/14 all EU/EEA sentinel samples reported to ECDC (https://ecdc.europa.eu/en/seasonal-influenza/surveillance-and-disease-data/aer). From 2014/15 and onward, all European sentinel samples reported to WHO/ECDC (http://flunewseurope.org/Archives)

Figure 1: Percentage influenza positive sentinel specimens, pooled from 24 European countries* by week of reporting and influenza virus type, week 40/2017 to week 20/2018.



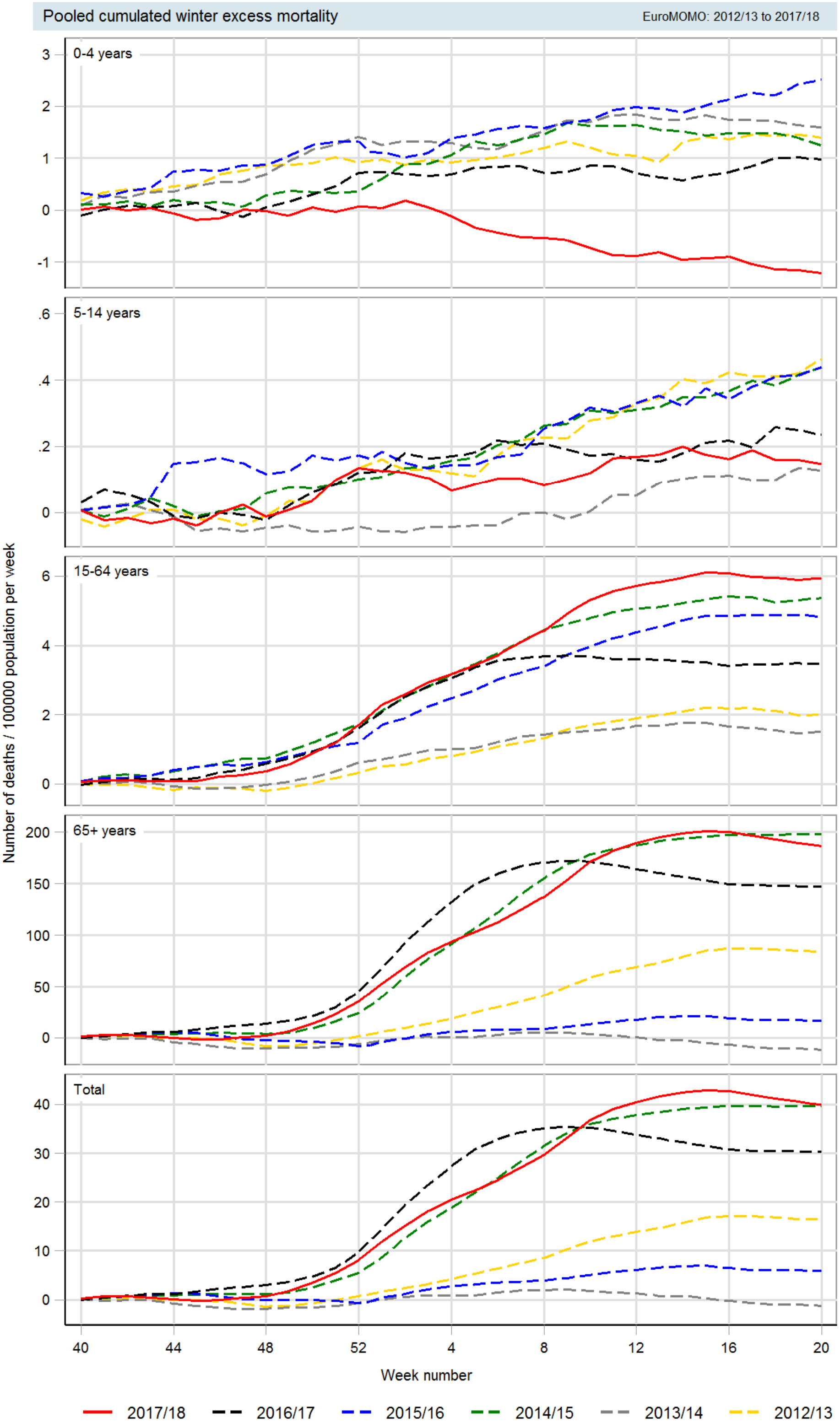
* Participating countries: Austria, Belgium, Berlin (Germany), Denmark, England (UK), Estonia, Finland, France, Greece, Hesse (Germany), Hungary, Ireland, Italy, Luxembourg, Malta, Netherlands, Northern Ireland (UK), Norway, Portugal, Scotland (UK), Spain, Sweden, Switzerland, Wales (UK)

Figure 2: All-cause mortality pooled from 24 European countries based on the EuroMOMO algorithm, by age group, week 01/2014 to week 20/2018



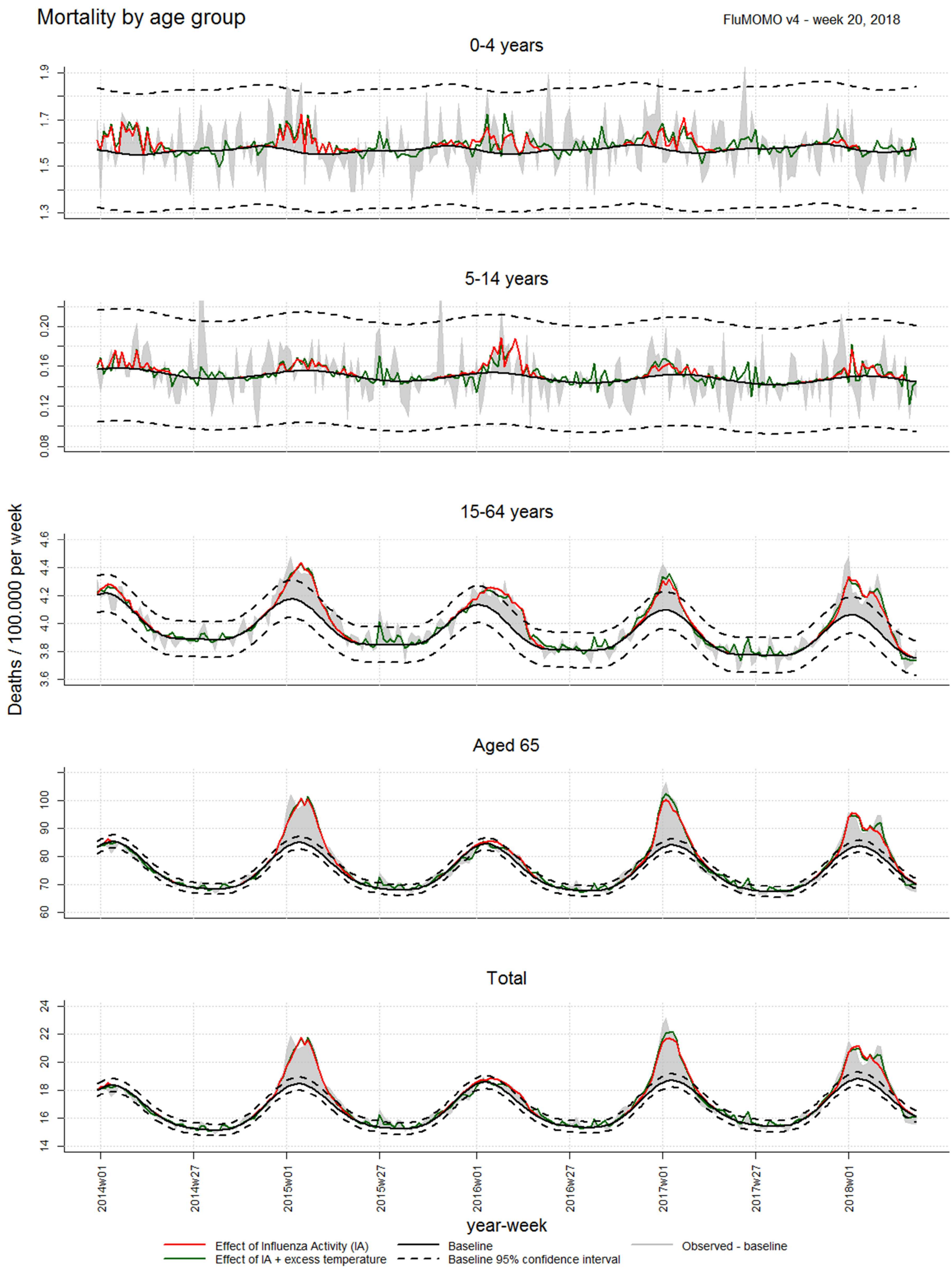
Participating countries:
Austria, Belgium, Denmark, Estonia, Finland, France, Germany (Berlin), Germany (Hesse), Greece, Hungary, Ireland, Italy, Luxembourg Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, UK (England), UK (Northern Ireland), UK (Scotland), UK (Wales)

Figure 3: Cumulated excess mortality pooled from 24 European countries based on the EuroMOMO algorithm, by age group and week, for the influenza seasons 2012/13 to



2017/18

Figure 4: All-cause mortality pooled from 24 European countries based on the FluMOMO algorithm, by age group, week 01/2014 to week 20/2018



Participating countries: Austria, Belgium, Berlin (Germany), Denmark, England (UK), Estonia, Finland, Franc, Greece, Hesse (Germany), Hungary, Ireland, Italy, Luxembourg, Malta, Netherlands, Northern Ireland (UK), Norway, Portugal, Scotland (UK), Spain, Sweden, Switzerland, Wales (UK)

Figure 5: Cumulated influenza attributable mortality pooled from 24 European countries based on the FluMOMO algorithm, by age group and week, for the influenza seasons 2012/13 to 2017/18