Estimating the contribution of influenza, COVID-19 and extreme cold weather to excess mortality – a working paper

Winter 2022 to 2023, with backdated estimates to 2012 to 2013

Using an adapted FluMOMO model

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1. Introduction

The burden of influenza-related mortality has been estimated for many years based on assessing all-cause mortality and influenza incidence. Spikes of excess mortality are often seen when influenza circulation is at its peak or highest in a given winter period. This has led to regression models being developed that model a baseline mortality along with an attributable influenza component to estimate contribution of influenza. The baseline model is typically a Serfling (sine/cosine wave) with a trend.[1] More recently models have been extended to take into account extreme weather such as the FluMOMO model.[2]

The FluMOMO model has been used by the UK Health Security Agency (UKHSA) for many years to estimate influenza-related mortality and is published in annual reports.[3-6] However with the COVID-19 pandemic leading to very large mortality levels from late March 2020, and with very little influenza circulation in 2020 to 2021 and 2021 to 2022 winters, models were not run in those years. In 2022 to 2023, a large spike in influenza occurred in the winter, as well as a spike in all-cause mortality. Additionally, the circulation of the COVID-19 Omicron-variant and several periods of severe cold weather or cold snaps were also observed.[7] To estimate the contribution of these factors to the detected excess mortality, an adaption of FluMOMO was needed. This working paper presents results from adapting the model and includes estimates of the contributions of influenza, cold weather and COVID-19 to all-cause mortality. This is a complex task, and this paper is part of continued development and assessment of methods to assess the burden of these and other health risks. As such these results should be regarded as experimental statistics.

2. The original FluMOMO algorithm, as applied in England

Weekly mortality from data covering the current winter and previous 4 winters was used. Each time the model was run, influenza attributable excess mortality estimates were produced for the most recent winter and the prior 4 winters. Winter was taken as week 40 of one year to week 20 of the following year to cover a typical influenza season.

The algorithm used dates of death occurrences (not registrations). Recent deaths counts were uplifted to account for registration delay based on fitting the EuroMOMO model, which has a registration delay correction included.[8] It was set to run on all ages combined, as well as split by age group (under 5, 5 to 14, 15 to 64, and 65 and over).

The influenza indicator was derived by multiplying weekly Royal College of General Practitioners (RCGP) influenza-like illness (ILI) consultation rates by weekly influenza swab positivity rate using RCGP swabbing data. ILI rates were age specific, but influenza swab positivity for all ages was applied to all age groups due to small numbers.

Temperature data was taken from Eurostat but was UK-wide and averaged to give a UK mean temperature by day.[9] Low temperature was defined as when the weekly mean was lower than the sine/cosine wave modelled minimum mean daily temperature in that week of the year. For example, if the observed weekly mean was 2°C in a week when the estimated lowest mean temperature on any one day was 3°C then that week gets a parameter value of 1°C (2°C subtracted from 3°C). A similar approach was undertaken for high temperatures.

Weekly all-cause deaths were then modelled with components for:

- baseline – a trend and two sine and cosine Fourier elements with 52- and 26-week periods
- influenza activity – with the parameter allowed to change each season and with a lag up to 2 weeks
- extreme temperature – with lags of up to 2 weeks and with the same parameter for the whole time series

The model was fitted using Poisson regression with a rescaling of standard errors to allow for over-dispersion.

Contribution to excess mortality by influenza and extreme temperature was estimated by comparing the modelled estimates; from setting the parameters of extreme temperature and influenza to zero (baseline-only estimate), setting parameters of extreme temperature to zero (baseline plus influenza estimate), and setting parameters of influenza to zero (baseline and extreme temperature estimate). The influenza contribution was then derived by subtracting the baseline-only estimate from the baseline plus influenza estimate. The same method was used for extreme temperature.

Usually only overall deaths estimates were reported from modelling all ages combined. Since each age was modelled separately, the deaths from each age added up were likely not going to equal the deaths from modelling all ages.

3. Adaption to FluMOMO for winter 2022 to 2023

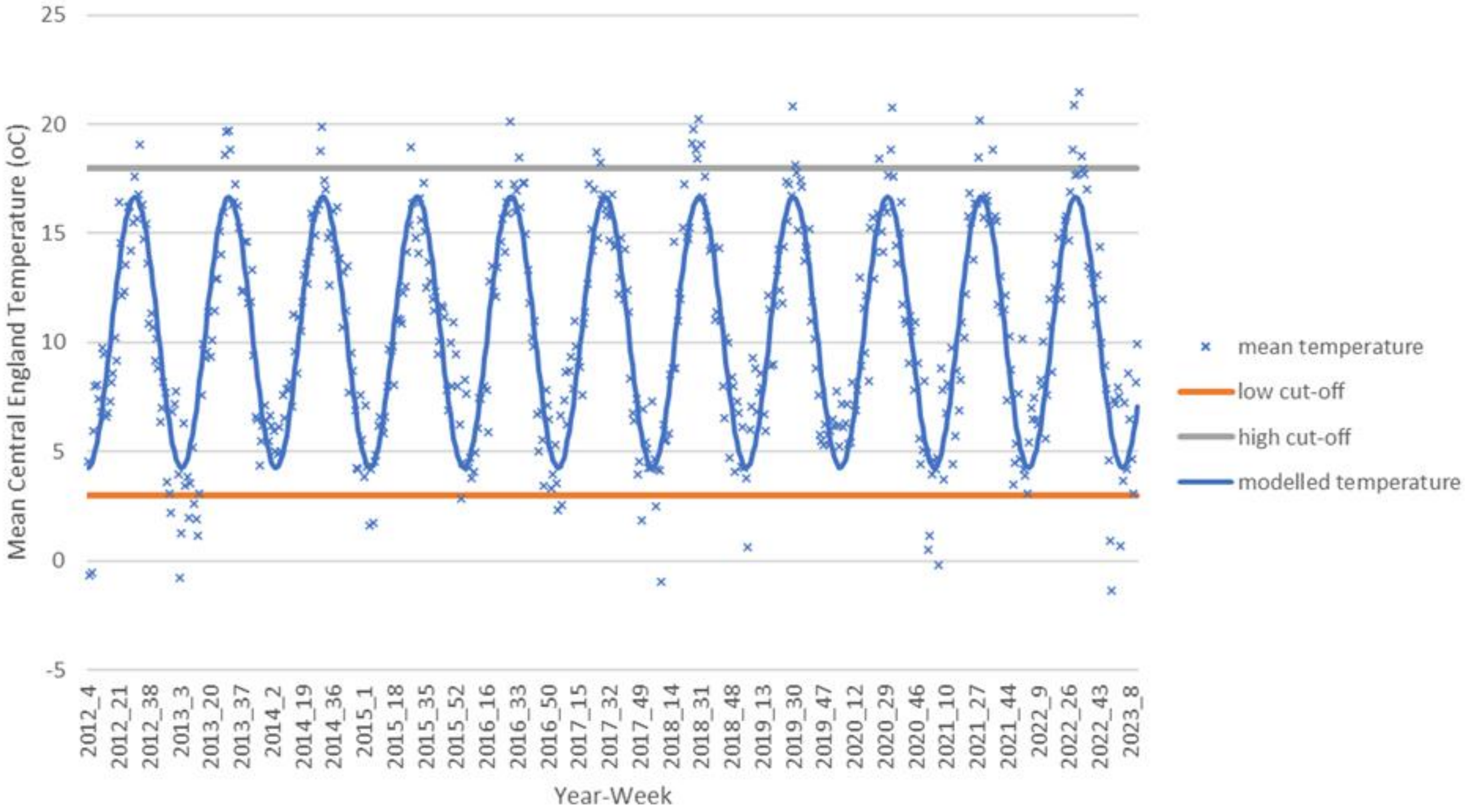
FluMOMO model was as described in Section 2, but with the following adaptions.

The time series used was extended to cover 2012/2013 to 2022/2023 (so 11 years rather than 5). This was done to improve the modelling of the baseline given that a period of time was excluded during the pandemic (see later). The longer time series also helped estimate the temperature effects better since a relatively small number of weeks have extreme temperature.

The temperature element was changed to use thresholds at 3°C (low) and 18°C (high), rather than comparing to the usual temperature for the time of year. For heat, no lag was allowed, whereas for cold, a 2-week lag was allowed. The Met Office Hadley Centre Central England Temperature (CET) dataset was used to create a weekly national mean temperature to measure against.[10] The difference from the threshold was calculated when temperatures went beyond them, so, for example, a weekly mean CET of 1°C was given a parameter value of 2 (3°C minus 1°C). This methodology change was done because having excess mortality from a cold day in the summer, or a warm day in the winter, is unlikely.

Figure 1 shows the temperature data, with thresholds just over 1°C above or below the modelled summer maximum and winter minimum temperature indicated. The thresholds identify several high weeks each summer and low weeks most winters to represent extreme weeks.

Figure 1. Mean Central England Temperature (with fitted line and the cut-offs used for extreme temperature)



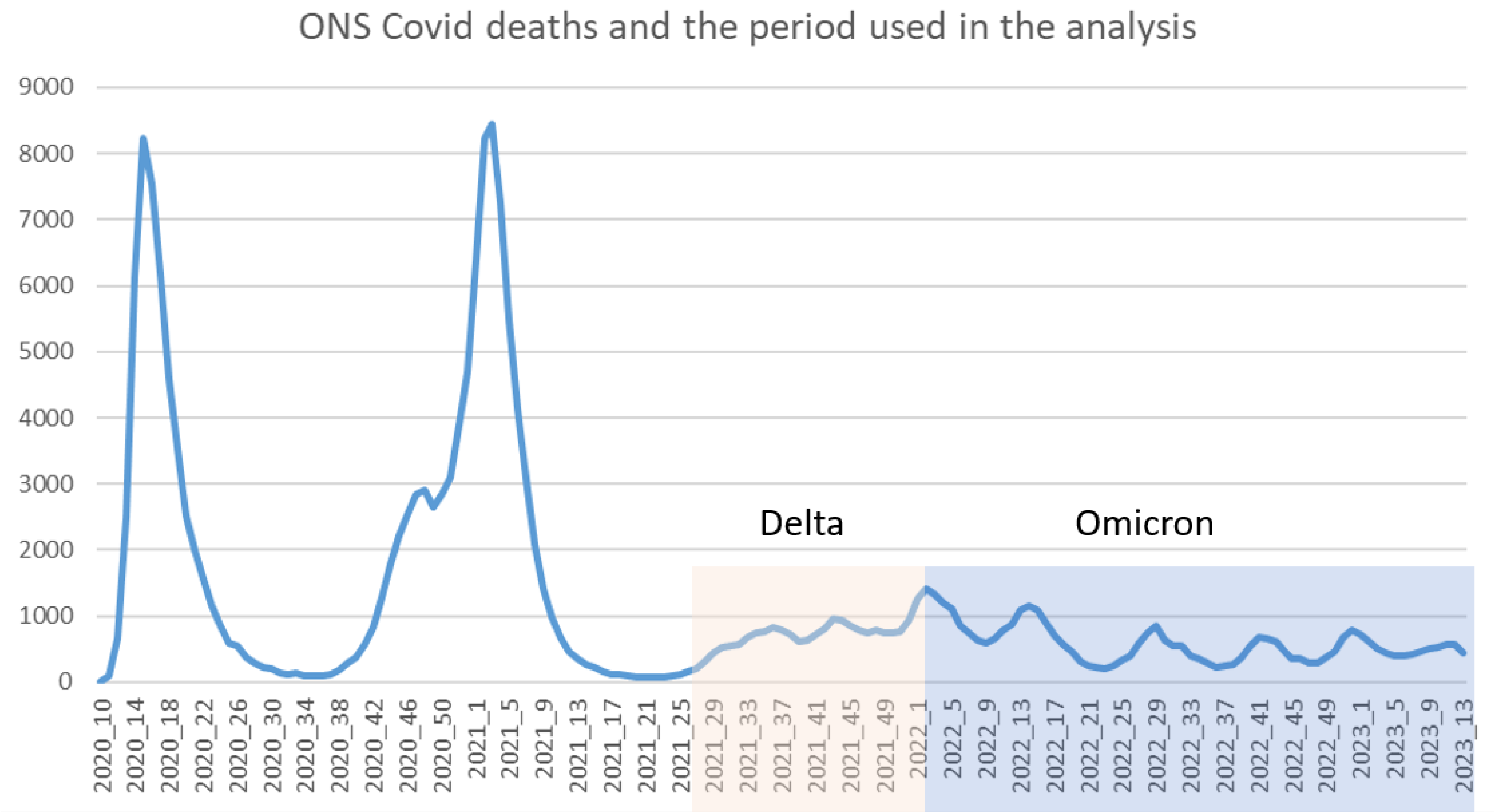
To address the initial two largest COVID-19-related spikes in number of deaths, and the low number in the weeks following the second spike, the period from week 13 2020 to week 26 2021 was given zero weight when fitting the models and excess mortality in the winter of 2020 to 2021 was not estimated. To further down-weight any remaining outliers, the model was re-weighted once with standardised residuals <-2 or >2 given a weight of 1/(residual^2).

To account for COVID-19 in the 2021 to 2022 and 2022 to 2023 analyses, weekly ONS COVID-19 death occurrences were included as an explanatory variable in the model. These were split into two series comprising deaths assumed to be due to the Delta variant from week 27 2021 to week 1 2022, and deaths assumed to be due to the Omicron variant from week 2 2022 onwards, meaning that two COVID-19 parameters for the contribution of Delta and Omicron to all-cause mortality were included in the model. Figure 2 shows the numbers of COVID-19 deaths with the Delta and Omicron periods that were included in the models highlighted.

The model therefore had explanatory variable for heat (1 parameter), cold (3 parameters to allow lags of up to 2 weeks), flu (33 parameters to cover 11 seasons and within each season lags of up to 2 weeks), COVID-19 (2 parameters to cover Delta and Omicron), and baseline (6 parameters to cover a constant, a trend and sine and cosine waves with periods 26 and 52).

Total deaths were calculated by summing across the 4 age groups. The 95% Confidence Interval (CI) for this was based on the standard errors of each of the estimates for each age group.

Figure 2. COVID-19-related deaths (ONS death certificate) week 10 2020 – week 13 2023



4. Sensitivity analyses

To assess robustness of estimates, particularly for 2022 to 2023, the following sensitivity analyses were done:

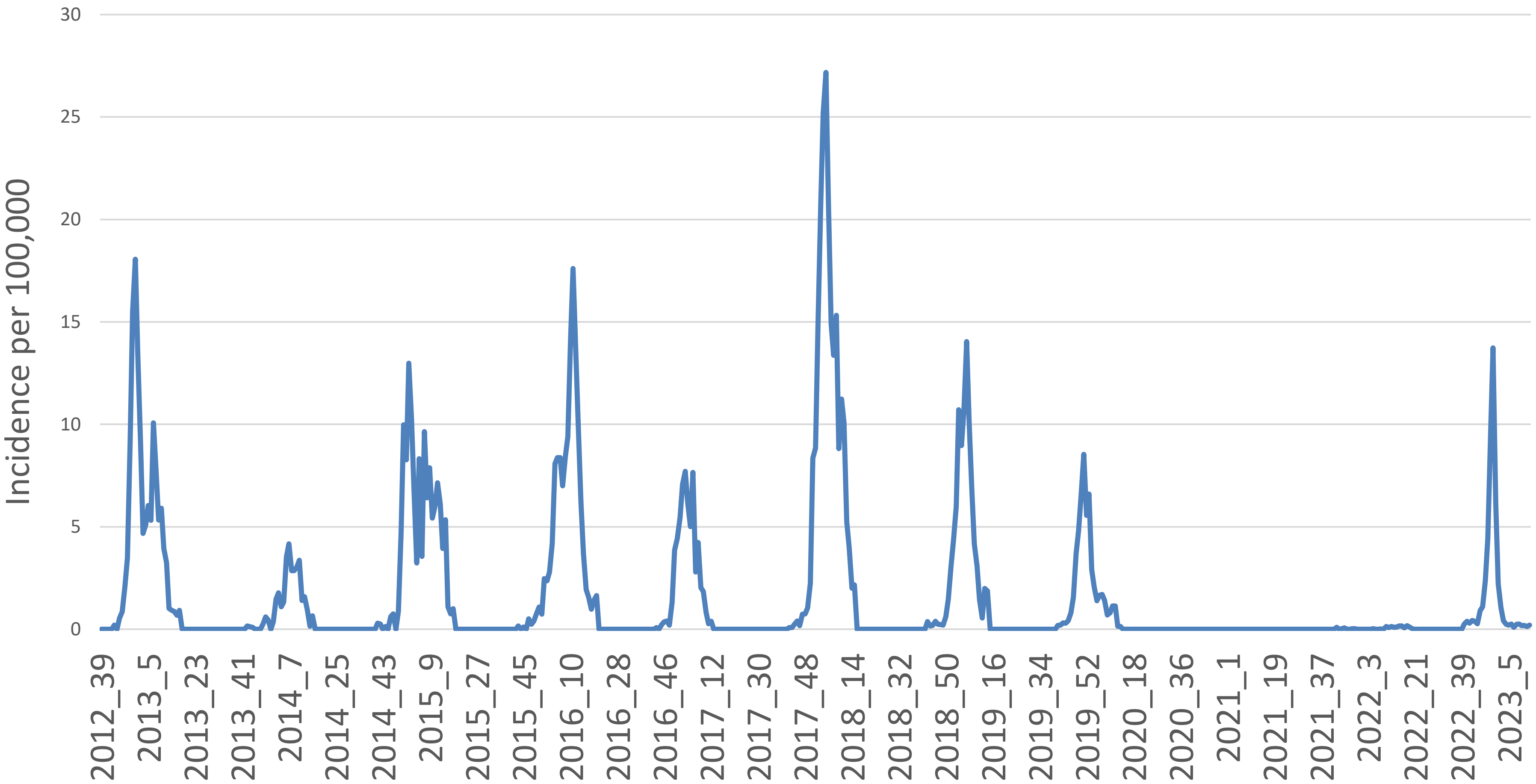
- temperature was also assessed as binary at the cut-offs (so 0 if not extreme and 1 if extreme) and semi-quantitative, with parameter values of 2 given for <1°C and >20°C and 1 given for 1°C to <3°C and 18°C to <20°C
- the model was run without including any of the parameters for COVID-19-related deaths
- the model was run after subtracting COVID-19-related deaths from all-cause deaths (and therefore also not including parameters for COVID-19-relatyed deaths)

5. Results

5.1. Descriptive

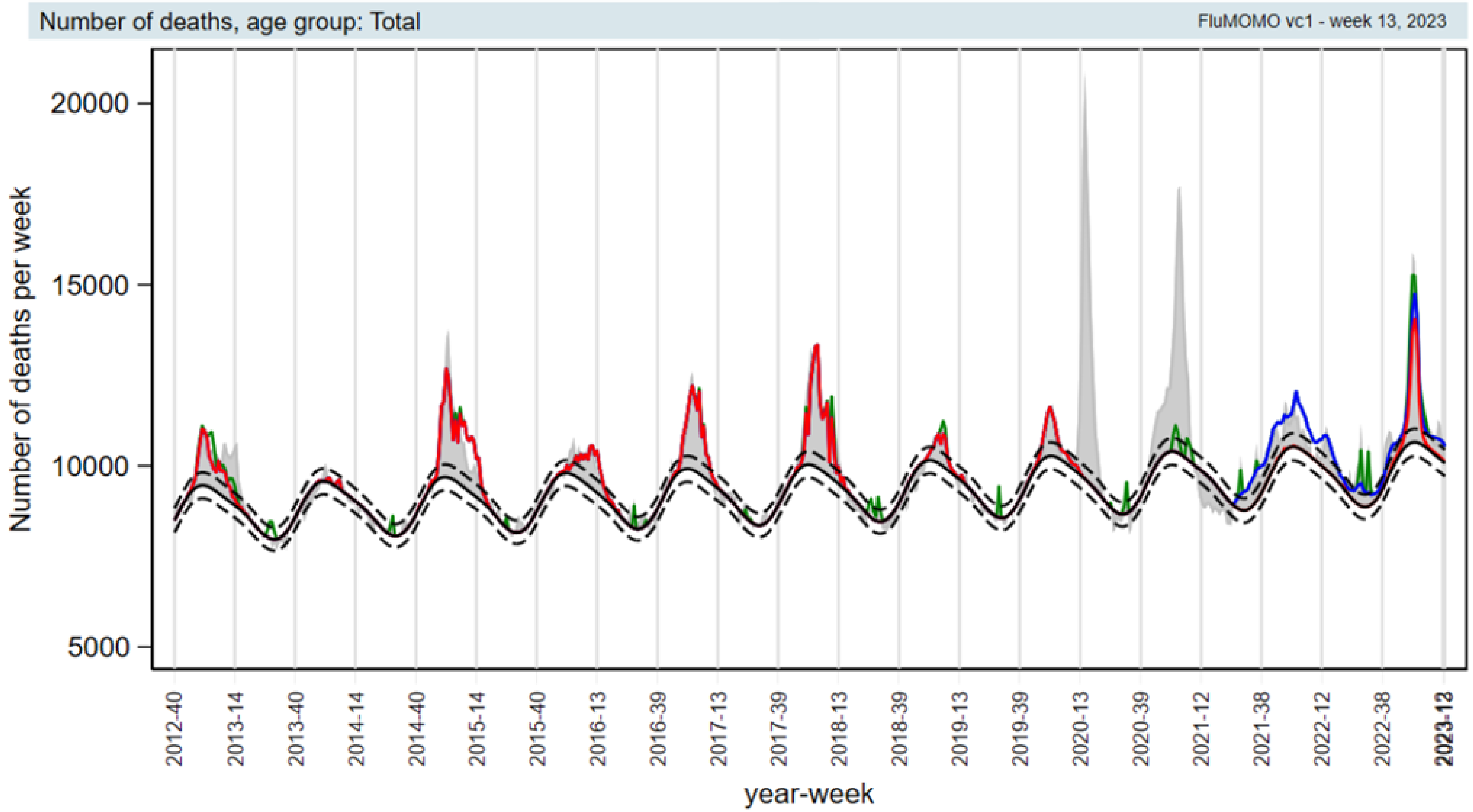
Results are based on deaths to week 13 2023, extracted in week 16 2023 to allow time for data to be more complete and less dependent on corrections for delayed death registration. The influenza indicator is shown in Figure 3 with almost no activity for two years prior to the 2022 to 2023 winter.

Figure 3: Influenza activity incidence by year 2012 to 2023



The modelled contribution of influenza, COVID-19 and temperature, when looking at the model with all ages combined, is shown in Figure 4. Note this is not the model used for all age estimates, as that combines across the individual ages. The model demonstrates the winter 2022 to 2023 spike in mortality is predominantly attributed to influenza (red), and partly attributed to cold weather (green) and COVID-19 (blue).

Figure 4: Modelled excess mortality



Black line: baseline, dotted black line: 95% confidence interval
Red: Effect of Influenza Activity (IA)
Blue: Effect of Covid (on top of IA)
Green: Effect of excess temperature (on top of IA & Covid)
Deaths week12 2020- week26 2021 excluded from modelling
Note: Negative effects of IA and COVID are not shown

5.2. Sensitivity analysis

The core model estimates for 2022 to 2023 are shown in Table 1 below with results from the sensitivity analysis. The results are quite robust to the temperature definition changes, and the different methods to account for COVID-19. It is interesting to note that while the model attributes 10,345 deaths to COVID-19, the actual number of ONS-coded deaths in the winter (weeks 20 to 40) was 13,180 so estimated excess deaths due to COVID-19 is 22% lower than ONS coded deaths. This analysis allows some additonal confidence in the results, but these types of models are sensitive to model specification, particularly for variables that are less prone to large spikes than influenza (that is COVID-19 and temperature).

Table 1: Attributed deaths for 2022 to 2023 for the core model and sensitivity analysis

Model	Influenza	COVID-19	Cold	Unexplained	Total
Core	14,623 (14,197-15,049)	10,345 (10,150-10,540)	5,533 (5,262-5,804)	3,029	33,528
Binary temperature	15,543 (15,227-15,859)	11,296 (11,100-11,492)	4,250 (4,086-4,414)	2,798	33,887
Semi-quantitative temperature	14,933 (14,579-15,287)	9,998 (9,803-10,193)	6,078 (5,838-6,318)	2,405	33,413
No COVID-19 parameter	15,563 (15,136-15,990)	-	5,675 (5,394-5,956)	1,488	22,726
Subtract COVID-19 deaths	14,913 (14,520-15,306)	-	5,622 (5,374-5,870)	546	21,081

5.3. Full results from the core model

The age split results and total are shown in Table 2 below for 2022 to 2023. Values in paratheses are 95% CI.

Table 2. Estimates of mortality by age 2022 to 2023

Age	Influenza	COVID-19	Cold	Unexplained	Total
0-4 years	9 (3-17)	0 (-1-1)	32 (24-42)	9	50
5-14 years	35 (26-45)	3 (1-4)	3 (1-5)	-27	13
15-64 years	2,033 (1,936-2,132)	522 (490-554)	362 (320-404)	73	2,989
65 years and over	12,546 (12,134-12,962)	9,820 (9,628-10,013)	5,136 (4,871-5,406)	2,974	30,476
Total	14,623 (14,197-15,049)	10,345 (10,150-10,540)	5,533 (5,262-5,804)	3,029	33,528

Note that estimates in children should be treated with caution, as the method is unlikely to be reliable enough to estimate such small excesses with accuracy.

The all-age estimates by year are shown in Table 3 below, including unexplained excess and total. Unexplained is negative if the estimated excess from influenza, COVID-19 and cold is more than the observed total excess above the baseline.

Table 3: Estimates of all age mortality by season (week 40 to week 20)

Year	Influenza	COVID-19	Cold	Unexplained	Total
2012/13	9,021 (8,643-9,399)	-	5,748 (5,541-5,955)	7,694	22,463
2013/14	167 (140-194)	-	0 (-10-10)	-4,824	-4,656
2014/15	29,965 (29,404-30,526)	-	1,452 (1,371-1,533)	-1,073	30,344
2015/16	12,223 (11,999-12,447)	-	88 (61-115)	320	12,630
2016/17	17,769 (17,533-18,005)	-	597 (545-649)	2,084	20,450
2017/18	22,419 (21,965-22,873)	-	3,215 (3,066-3,364)	6,580	32,212
2018/19	5,144 (4,966-5,322)	-	1391 (1,303-1,479)	-5,180	1,354

Year	Influenza	COVID-19	Cold	Unexplained	Total
2019/20	8,800 (8,608-8,992)	-	0 (-10-10)	52,456	61,256
2020/21	-	-	-	-	-
2021/22	104 (66-142)	25,971 (25,647-26,295)	0 (-14-14)	-5,269	20,806
2022/23 (to week 13)	14,623 (14,197-15,049)	10,345 (10,150-10,540)	5,533 (5,262-5,804)	3,029	33,528

6. Comment

Influenza-related mortality is estimated to be about 15,000 deaths for winter 2022 to 2023. This is higher than that seen in the previous 4 years, and a little lower than the average of the 2 seasons prior to that. It is lower than the biggest season in the past 11 years (2014 to 2015) where almost 30,000 deaths are estimated from an extended influenza season. The most striking observation of the 2022 to 2023 winter season was the big spike in mortality which rapidly declined. Because the effects of cold on mortality continue over a few weeks (hence the inclusion of lag terms) and because the Omicron COVID-19 waves have not shown large spikes, the method is less well suited to provide reliable estimates of the mortality contribution of these factors. The estimates mortality due to COVID-19 in 2022 to 2023 is somewhat less than the actual COVID-19 death numbers used in the model. This may be model misspecification, but equally could be because a proportion of deaths with COVID-19 on the death certificate were not due to COVID-19.[11] For temperature-related mortality, the 5,500 estimate is based on 3 cold weeks and is the highest since 2012 to 2013. This estimate is contingent on the definition of cold used. If thresholds were changed to assign more weeks to be cold weeks then it is likely more deaths would be attributed to severe cold weather, however the aim was to look at extreme cold weather only.

There are other factors not attributed that may contribute to winter mortality, such as increased pressures on acute health services and the circulation of other infections. The model methods assume these factors are captured in the seasonal component. The influenza estimates, in particular, are quite robust to other factors (unless those factors cause spikes at the same time as the influenza spike). Whilst further possible causes of winter mortality could be modelled the methodology is unlikely to give reliable estimates unless effects are large and occur in concentrated periods.

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