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The Public Health England report on 'Excess Winter Mortality 2012-13'

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Abstract

In February of 2012 deaths in England and Wales showed a semi-permanent and unexpected increase which endured to around mid-2013. This increase appears to be linked to an increase in A&E attendance and emergency medical admissions. In August of 2013 Public Health England published a report designed to assure everyone that the excess deaths were merely confined to a few weeks during the winter of 2012/2013. However this report which relies on output from the EuroMOMO methodology can be shown to contain methodological limitations. The case for a genuine infectious outbreak is investigated.

Key Words: Deaths, EuroMOMO, medical admissions, emergency department attendance, infectious outbreak, cytomegalovirus

Introduction

Most will be aware of the media attention regarding a period of excess mortality which commenced in early 2012 and extended into 2013 (Telegraph & Argus 2013) and has been linked to increased emergency department attendance and emergency medical admissions (Jones 2013b,d). Previous occurrences of this event have been documented in 1993, 1996, 1999, 2002, 2007 (Jones 2012a,b) and have been linked to a curious cycle in the gender ratio at birth (Jones 2013c). On the 15th August, 2013 Public Health England (PHE) responded with a definitive report designed to end all speculation regarding the higher deaths in 2012/2013 (Public Health England 2013) and thereby assure us that the excess deaths are simply restricted to a smaller number of weeks in the winter of 2012/2013. Or have they?

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The accompanying letter to this report lets us know that the work that led to the whole controversy had potential 'methodological weaknesses'. A strange conclusion since the methods used appear to be fairly standard and the conclusions highly informative. Have they been labeled 'dubious' simply because they disagree with the EuroMOMO agreed standard methodology?

Euro-MOMO (**Euro**pean **mo**nitoring of excess **mo**rtality for public health action) is an EU-wide project which aims is to develop and strengthen real-time mortality monitoring across Europe. It is intended enhance the management of serious public health risks such as pandemic influenza, heat waves and cold snaps (see www.euromomo.eu). The key issue is that the EuroMOMO methodology is very much focused on the identification of large infectious outbreaks (such as influenza epidemics) or periods of high excess death arising from extreme temperatures.

However, I suspect that it will only be the very eagle-eyed among you that spotted the obvious flaw in the whole PHE argument. Namely in Figure 3 of the PHE report the baseline (blue line), against which excess deaths are determined, trends upward over time.

Trend in Deaths

This is a direct contradiction to the expected trends in the number of deaths produced by the Government Actuary. For example, in the 1999-based forecast of total deaths for the whole of the UK deaths were expected to reach a minimum around 2009 – 2012 (see Figure 1). Since that time life expectancy has increased faster than was expected and hence the 2008-based forecasts for England reach a minimum around 2016 - 2017. At regional level the minimum varies for the South West (2014-2016), South East (2015), London (2022), North East (2017-2019), and the earliest expected minimum was 2012 for the East of England. The latest 2012-based forecasts (incorporating the 2011 census data) are not due until later this year and will presumably be very close to the 2008-based forecasts or if anything will slightly extend the point at which the minimum is reached.

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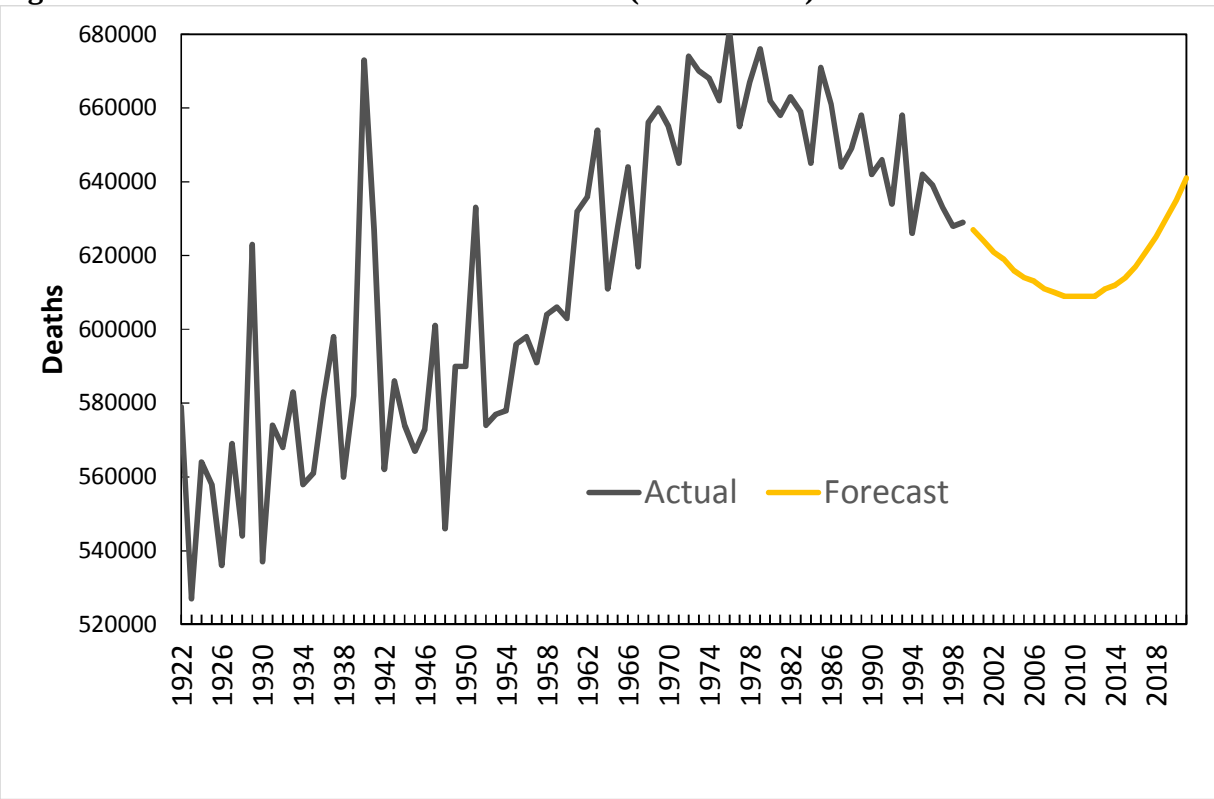
Hence between 2008 and 2013 the baseline should be trending slightly downward at around 500 fewer deaths per month, although the actual time-curve is non-linear. Were PHE inadvertently led astray by the application of a standard methodology?

Figure 1: Actual and forecast deaths in the UK (1922 to 2020)



Footnote: All data used in the following figures is from Office of National Statistics.

EuroMOMO explained

To get to the bottom of the matter I asked PHE to specify the exact date range that was used to calculate the baseline in their report. In answer to my question (by email) I received the following two answers (by return email). Answer 2 was in response to my request to 'specify the exact dates that went into the baseline'.

Answer 1

"I understand that the EuroMOMO baseline is modelled using a *generalised linear model* (GLM) Poisson distribution corrected for over dispersion. The model is fitted on a historical dataset of 5 years, excluding a period to correct for reporting delay (the most recent 50 weeks). Spring and

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summer weeks are used to fit the baseline when it is assumed that additional processes leading to excess deaths are not likely to happen. These parameters are standard across all European participating countries." *Italics added*

Answer 2

"The baseline shown in the figure in the PHE report was produced with data up to week 24 2013. The model is fitted on a historical dataset of five years (back to week 25 2008), excluding the most recent 50 weeks to correct for reporting delay, so week 25 2008 – week 26 2013. Out of this times series, spring and summer weeks are used to fit the baseline. For exact details and clarification on the spring and summer weeks, you will need to contact the European team to check."

Which in plain English means that data from the summer months of 2008 through to 2012 was used to calculate the baseline. Please note that the following explanation is not designed to replicate EuroMOMO but to illustrate the principles.

Figure 2: Ratio of daily maximum to median deaths (1989 to 2000) in England & Wales

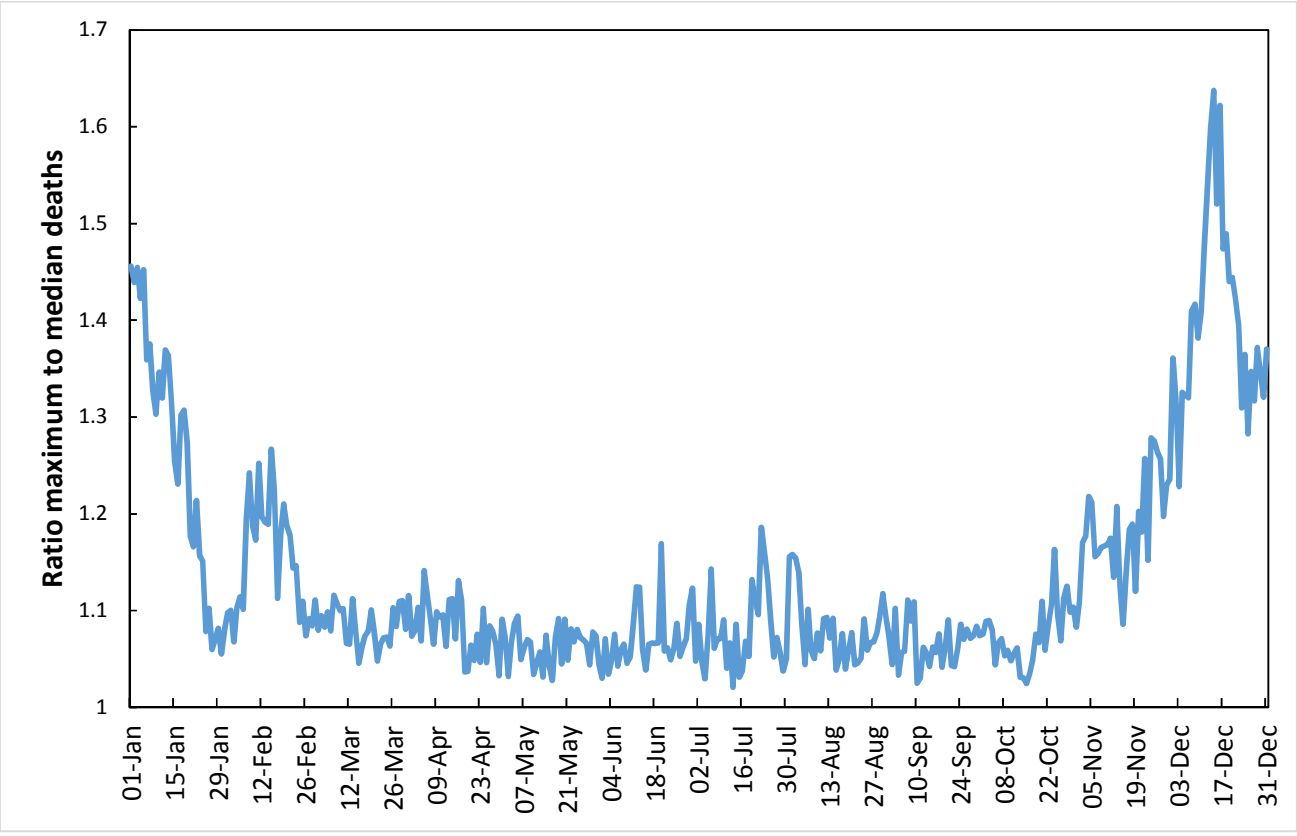

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Figure 2 shows why the use of the summer months may be desirable, namely, the variability in deaths around the median value was lowest from 26th February to 12th October (at least between 1989 and 2000) and corresponds to the summer months plus some extra leeway. The baseline therefore seeks to exclude the more volatile deaths during the winter months. However the six summer months (May to September) only account for 45% of the total deaths and it goes without saying that you can only die once. So if you die this year you cannot die in the next and vice versa. Hence there is a strong argument for using the total deaths in favor of just the summer deaths despite the higher volatility, i.e. you trade off higher accuracy of the known total against the lower volatility of an estimate.

Figure 3: Hypothetical baseline using 'whole year' or 'summer' deaths in England & Wales

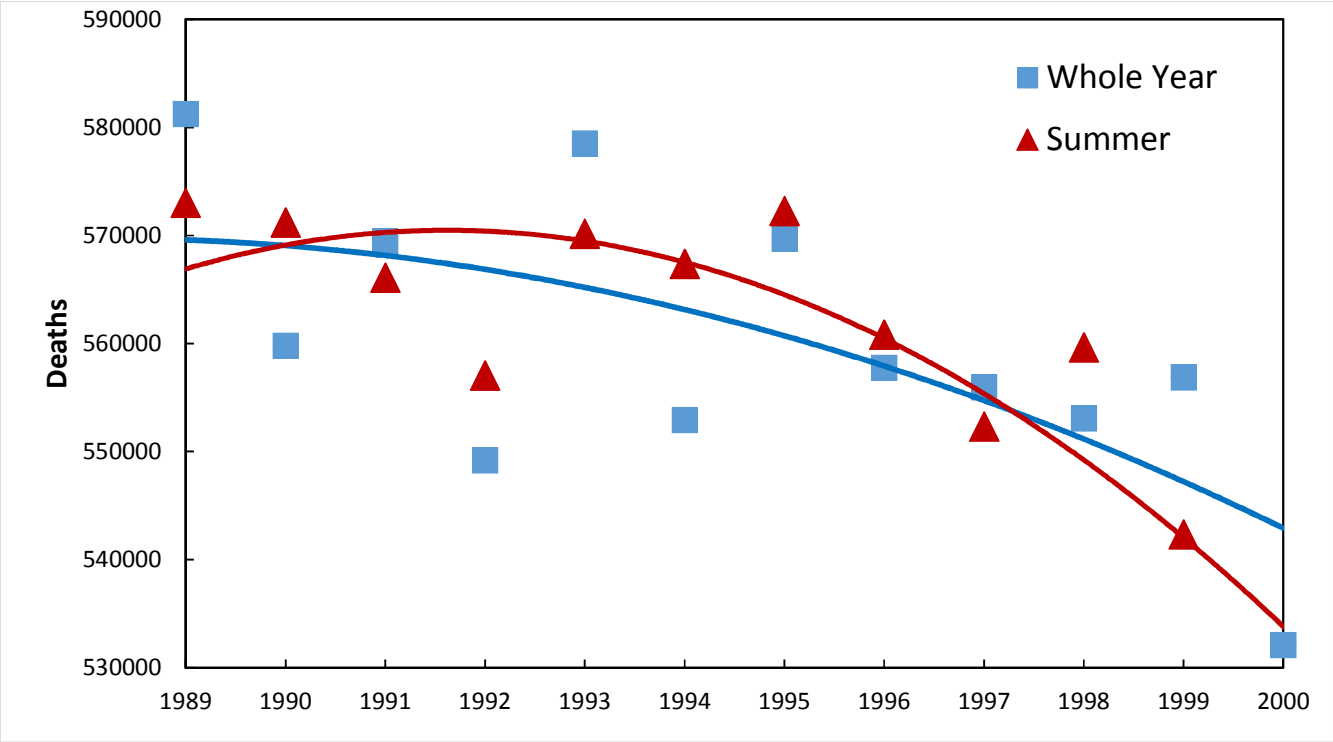

Figure 3 attempts to illustrate how this could affect the calculation of a hypothetical baseline by taking the trend in whole year deaths and comparing this to the trend in summer deaths (on this occasion May to September deaths multiplied by 2.64 to give a full year total).

In England & Wales the peak which occurs around 1980 for the whole of the UK (Figure 1) occurs later at around 1993 and is somewhat flatter, however, it does continue to decline beyond 2000 as is the case for the UK.

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Which hypothetical baseline in Figure 3 is correct? The trend line using 'summer deaths' has less scatter due to the fact that the highest variation in deaths occurs in the winter but the 'whole year' trend encompasses all the deaths (nearly twice as many). The answer is probably neither is 'correct' but is a reflection of two different approaches.

However, using the 'summer' method in Figure 3 leads to the conclusion that 1993 is not a high year but using the 'whole year' method it is high. Using a daily series of deaths Figure 5 however clearly shows that 1993 is indeed a high year during which one of the outbreaks of the new type of infection occurred early in the year (as was the case in early 2012). See later discussion.

There are two fundamental reasons that the use of deaths in the summer months between 2008 and 2012 would give an incorrectly upward sloping baseline:

1. Although total deaths between 2008 and 2011 were decreasing the majority of the decrease was in the winter months and is therefore (wrongly) excluded from the EuroMOMO baseline calculation. This would tend to give a flat baseline rather than a declining one.
2. The large step-like increase in deaths which commenced in February 2012 continued through the summer of 2012 and was therefore part of the baseline. Add this to an already apparently flat baseline from 2008 to 2011 and this will largely be responsible for tilting the trend upward.

To include a period of very high deaths at the end of a time series is in itself not good practice because you have assumed that the high deaths are 'normal' behavior. Hence, at the very least the PHE report should be re-calculated excluding the summer of 2012. We are only left to surmise that the period of high deaths was seen as 'embarrassing' because no one at the DH/PHE/NHS England had any real answers and EuroMOMO gave a convenient 'official' escape clause.

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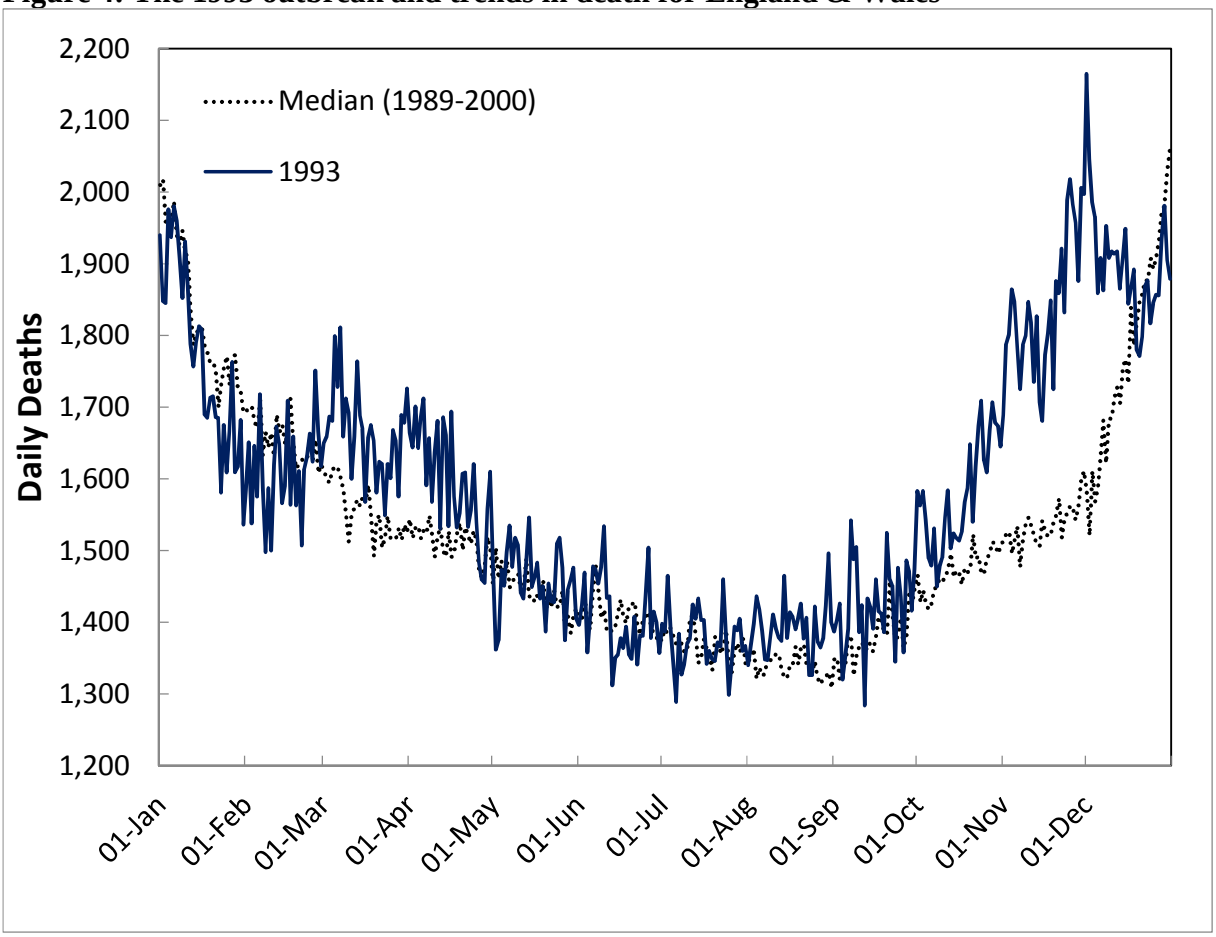
An infectious outbreak

Are we dealing with a genuine infectious outbreak? I have consistently stated that we are dealing with the equivalent to a slow-burn infectious outbreak of a subtle persistent agent (as opposed to spike events such as an influenza epidemic or extreme temperatures) and this has been discussed in recent reviews (Jones 2013a,e, 2014). Such an outbreak has been demonstrated in Figure 4 for the 1993 event which for the whole of England & Wales commences with an early increase in deaths in late February of 1993 through to the end of April. This outbreak was characterized in Reading, Berkshire to occur in the middle of March 1993 with a dramatic 15% step-increase in medical admissions (Jones 1996, 1997). After this point deaths are consistently slightly higher than the median of daily deaths between 1989 and 2000 and winter mortality is greatly elevated from October onward. This outbreak (and indeed all other outbreaks) has been documented to initiate slightly earlier in Scotland (Jones 2013d).

Figure 4: The 1993 outbreak and trends in death for England & Wales



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The reasons why this outbreak may be due to the common herpes virus cytomegalovirus have been explored elsewhere (Jones 2012b, 2013a,d). In summary, this virus has powerful immune evasive and modulating properties, is a known risk to the immunosuppressed (HIV/AIDS, transplant recipients, etc), during pregnancy where infection of the fetus can lead to neurological defects and is now increasingly recognized as a risk to other members of the population, especially the elderly. Hospital case reports indicate increasing mortality in those age over 55 and in those with conditions affecting the immune response such as diabetes, renal failure and untreated non-hematological malignancy (Rafailidis et al 2008).

A recent study on the trend in deaths in Scotland between 1990 and 2012 noted the apparent change in the shape of the time trend for each outbreak from before 2000 to after. One possible cause is the fact that early in 2000 influenza activity declined to a 100 year minimum, an event which had only occurred previously between 1879 to 1889 (Thacker 1986). Based on analysis of the 1996 outbreak in England it was concluded that there may be some degree of additive or synergistic interaction between the two infectious agents especially when the proposed outbreak occurs prior to an influenza outbreak (Jones 2012a). In this respect recent research has shown that those aged 65+ with the highest CMV antibody titre have over a 4-times lower response to influenza vaccination (McElhaney et al 2012) indicating impaired ability to withstand a winter influenza event. Other research indicates that CMV induced immune changes in the elderly may be responsible for delayed clearance of the influenza virus from the lung (Alonso et al 2013). In addition children infected with CMV are known to have statistically higher infections with the common respiratory viruses (RSV, rhinovirus, enterovirus) identified in the PHE report (Chomel et al 2001).The increased respiratory deaths demonstrated in Figure 1 of the PHE report is consistent with this observation and is in agreement with a potential role for cytomegalovirus (CMV) where CMV pneumonitis may not be recognized and misdiagnosed as unspecified pneumonia (Jones 2013a,e). Regarding excess deaths for the over 65s the PHE report states that ‘A similar observation was made in several countries across Europe’.

However the subtle shift in deaths documented in Figure 4 and also correctly identified after the 2012 outbreak are not detectable by the EuroMOMO approach (especially with the addition of

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the incorrectly upward sloping baseline) because it was designed to look for a different type of event.

Indeed the life insurance industry is well aware of the unusual increase in deaths commencing in early 2012 - they have, after all, been paying out for life policies. They are also aware that deaths (and policy payments) have now returned to what may be considered normal levels.

On a more technical note I would argue that the impact of these infectious outbreaks diminishes with time and hence the shape of the baseline probably changes over time. To establish if this is the case will involve correcting the historic data for temperature (Hajat et al 2007).

Conclusions

In conclusion, the method of analysis has to suit the particular characteristics of the outbreak in question. Thank goodness that a public health analyst, using tried and tested public health methods, was alert enough to spot the onset of the increased deaths emanating out of the 2012 outbreak.

Where does all this leave us? The excess deaths are still there, EuroMOMO is valid for what it was designed to do and can be left to do that, but the rest of us need to be aware that there is probably more to infectious outbreaks and epidemiology than is currently in the textbooks. So why are PHE seemingly adverse to the possibility of a genuine infectious outbreak of a type not previously characterized?

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