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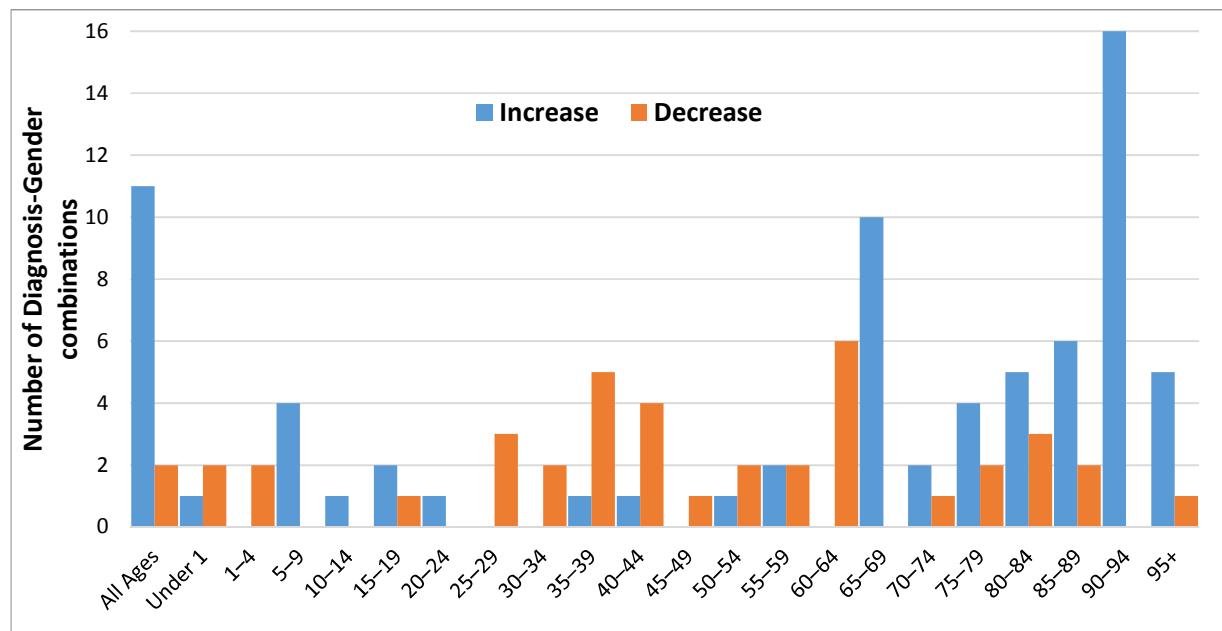
Increased deaths in 2012: which conditions?

Dr Rodney P Jones
Statistical Advisor
Healthcare Analysis & Forecasting
www.hcaf.biz
hcaf_rod@yahoo.co.uk

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BJHCM readers will already be aware that in early 2012 deaths across England and Wales showed an unexpected increase which was maintained until mid-2013 (Jones 2013c,h). This curious phenomenon commenced slightly earlier in Scotland (Jones 2013j) and showed evidence for an infectious-like spatial spread within Scotland, England and Wales (Jones 2010b, 2013b,c,j). Simultaneous to the increase in deaths there was an increase in A&E attendances (specifically for those who were admitted) and an even larger increase in total medical emergency admissions (Jones 2012b, 2013d-g) and a curious parallel cycle in the gender ratio at birth (Jones 2013i). These parallel increases in deaths and medical admissions have been characterized across all parts of the United Kingdom and appear to occur in a long-term time series going back to 1993 and possibly earlier (Jones 2012, 2013b,d,j).

Figure 1: Diagnosis-gender combinations by age band showing high increases in deaths



Footnote: A significant increase was defined as any increase where the difference between the two years was greater than 3 standard deviations apart while a significant reduction was set at 2.4 standard deviations. The standard deviation was calculated using Poisson statistics with $SD = (\text{deaths in 2012} - \text{deaths in 2011})/\sqrt{\text{deaths in 2011}}$.

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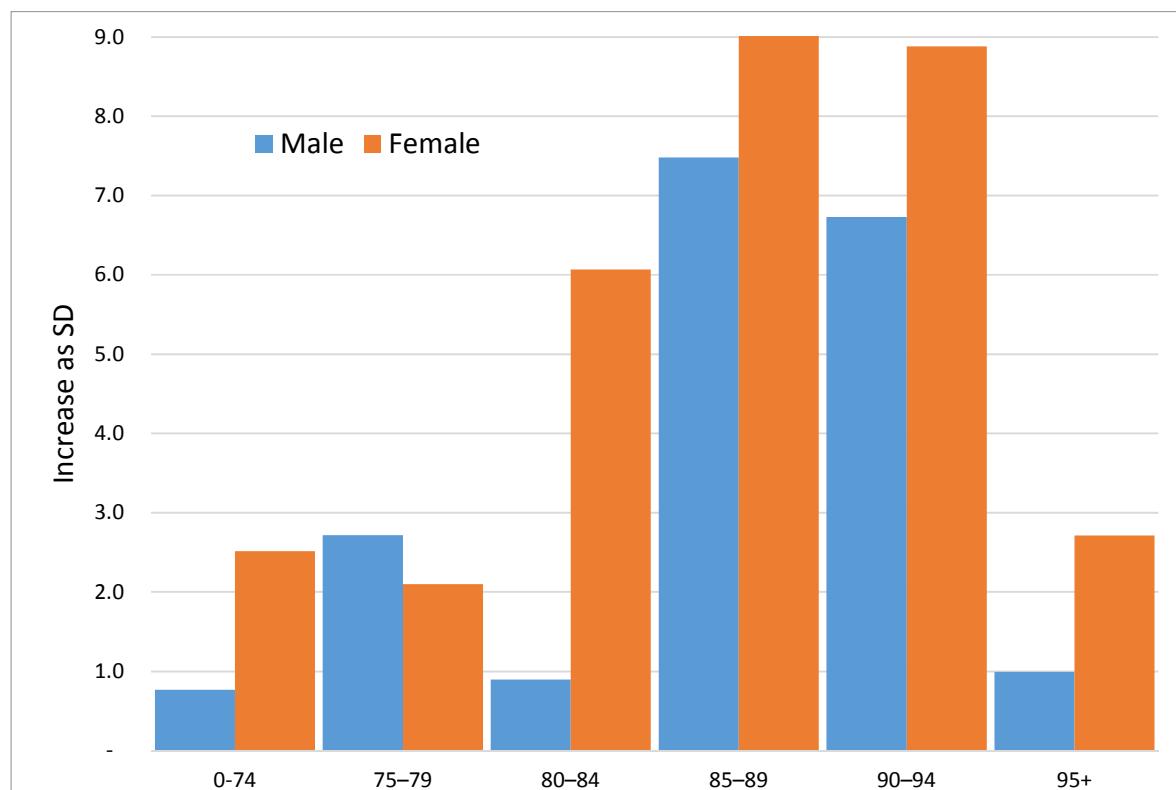
Specific increases for particular diagnoses were characterized following the previous 2007 event for patients who had been admitted to hospital and subsequently died (Jones 2012c-d). This record-linkage data is not available for the 2012 event however cause of death data (both in and out of hospital) is available for all deaths from the Office of National Statistics for deaths registered in England and Wales. Given that the event occurred very early in the 2012 calendar year it is possible to investigate which diagnosis-age combinations showed a specific increase in 2012 compared to 2011.

Table 1: ICD chapter (cause of death) showing significant increases

Chapter	Gender	Increase (SD)	Increase (%)
V Mental and behavioural conditions	F	22.1	15.2%
V Mental and behavioural conditions	M	16.1	16.1%
VI Diseases of the nervous system	F	15.1	15.0%
VI Diseases of the nervous system	M	12.0	13.1%
X Diseases of the respiratory system	F	8.4	4.5%
X Diseases of the respiratory system	M	8.0	4.5%
IX Diseases of the circulatory system	F	6.5	2.5%
II Neoplasms	M	5.0	1.8%
XVIII Symptoms and signs	F	4.1	4.5%
XVIII Symptoms and signs	M	3.4	6.7%
II Neoplasms	F	3.2	1.2%

Footnote: SD = standard deviation difference between 2011 and 2012

Figure 2: Increase in deaths from Alzheimer's



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Since there are large differences in the number of deaths for different ages and diagnoses this article has used Poisson statistics to transform the difference between one year and the next into a common currency of standard deviations of difference. Anything with more than a three standard deviation difference can be considered statistically significant. Figure 1 shows the pattern of statistically significant increases and decreases at ICD chapter level following the 2012 event where there were 35 specific female age band-diagnosis increases but only 27 for males while Table 1 shows which ICD chapters were specifically associated with a high increase in deaths across all age bands. The increase is generally higher for females except for neoplasms. Since there are 19 ICD chapters describing cause of death it should be apparent that the source of the increase in deaths is highly diagnosis specific and is largely limited to just 6 of these 19 chapters. From Table 1 we also notice that the deaths are also highly age specific with those aged 90-94 and 65-69 showing increases across the highest number of gender-diagnosis combinations and involve some surprisingly large percentage increases especially for mental health and nervous system. Across all diagnoses the highest percentage increase was seen in the 90-94 age group with 13.0% increase for males and 12.7% increase for females.

One theory for the increase is that a succession of years with 'mild conditions' leads to the accumulation of higher numbers of potentially frail persons who then die en masse when such mild conditions cease. This theory fails to explain the roughly similar cycle time seen in the Scottish data over many years or the apparent infectious-like spread across the UK which has now been documented at very small area level (Jones 2014a). The alternate infectious theory seems to correspond with the spatial spread as well as the age and diagnosis specificity. In this respect Figure 3 presents the situation for Alzheimer's disease where a higher increase for females is observed across elderly age bands especially age 80-84. The highest percentage increase occurred in age band 90-94 of 32.8% for males and 24.6% for females.

In an attempt to explain the time-based response of both deaths and emergency admissions a potential role for cytomegalovirus (CMV) has been proposed (Jones 2013b,d, 2014b). In this respect for Alzheimer's it has been noted that higher CMV antibody levels were associated with neurofibrillary tangles and central nervous system (CNS) interferon γ was only detected in CMV seropositive individuals (Lurain et al 2013) The percentage of senescent T cells was higher in CMV positive individuals. In another study Alzheimer patients who were CMV seropositive had lower levels of naïve CD8 and a higher proportion of effector CD8 T cells (Westman et al 2013). High CMV antibody levels were associated with frailty in psycho-geriatric patients (Haesker et al 2013). While these do not prove that CMV is the causative agent they merely suggest that CMV could be involved. Further studies are needed. However it should also be noted that the spectrum of action of CMV does correspond fairly closely with those ICD chapters highlighted in Table 1 (Rafailidis et al 2008, Jones 2014b). CMV also potentially explains the curious reduction in deaths seen in the 95+ group across nearly all diagnoses in that the long lived are either CMV free or have very low levels of CMV antibodies indicating strict immune control (Derhovanessian et al 2010).

On a more pragmatic level such large (for specific age-diagnosis combinations) and totally unexpected increases in deaths and medical admissions do have catastrophic effects against the budgets of NHS organisations (Jones 2010a,b, 2012a, 2013a,b, 2014a) and it is suspected that these outbreaks have inequitable effects against organisations in different locations (Jones 2010b, 2012a, 2014a). For these reasons all concerned need to know exactly what is happening and why. Pretending that nothing has happened in the name of political expediency is not a real option given that the health of far too many people appear to be affected. Both patients and NHS organisations need real answers.

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