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A New Type of Infectious Outbreak?

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Abstract

In the UK, hospital medical admissions have been rising for many years. Many explanations have been offered but none adequately explain why the increase appears to occur in bursts. However during these bursts both medical admissions and all-cause mortality appear to rise and fall in a synchronous manner.

This study looks at the trend in age-standardized mortality in Scotland for women between 1994 and 2013, and male and female mortality for diseases of the circulatory system in 2012 and 2013 versus 2011 in England and Wales.

A steady downward trend in the mortality rate is observed with higher than expected mortality in the years 1995, 1999, 2002/2003, 2007/2008 and 2012/2013. Similar findings have been reported in England, Wales and Northern Ireland. In England and Wales mortality due to circulatory system diseases showed age-dependent patterns similar to the saw tooth patterns observed in 'antigenic original sin', which suggests the different strains of the same agent are involved.

A new type of infectious outbreak appears to be implicated with a broad-based effect against all-

cause mortality and increased admissions for a wide range of medical conditions.

Keywords: Emerging infectious outbreaks, all-cause mortality, immune impairment, cytomegalovirus, medical admissions, gender.

Introduction

A long-term and unexplained increase in medical hospital admissions (but not surgical or trauma), has characterised most Western health care systems [1,2]. Many potential explanations have been offered including breakdown of the traditional family, higher expectations, more cautious physician behaviour, poor integration between health and social care and an ageing population [1-4]. However none of these explain why medical admissions increase as a regular series of surges which coincide with a regular series of unexplained increases in all-cause mortality [1,2,5-8], or why the gender ratio at birth also changes during these times [9].

Recent research has shown that these surges in admissions and deaths show spatial spread along with age and condition dependence [2,10-19]. All of which are highly suggestive of a new type of infectious outbreak which may have a *modus operandi* based on immune manipulation, leading to changes in susceptibility to infection, inflammation and autoimmunity [1-3,8,18,20].

The last outbreak which occurred across 2012 and 2013 led to a minimum of 45,000 deaths in England and Wales, and appears to be part of a longer series which can be traced back to the early 1950's [21].

This short study will demonstrate the effect of these presumed infectious events on the time trend in age-standardized all-cause mortality among females in Scotland, and the age and gender specific effects of the last outbreak upon vascular system deaths in England and Wales.

Materials and Methods

Age standardized all-cause mortality rates (per 1000,000 population), for females between 1994 and 2013 (using the 2013 European standard population) were obtained from the General Register Office for Scotland website (http, //www.gro-scotland.gov.uk/statistics/theme/vital-events/deaths/age-standardised-rates.html).

Deaths in England and Wales (Series DR) due to vascular system diseases were obtained for the years 2011, 2012 and 2013 from the Office for National Statistics website (http, //www.ons.gov.uk/ons/rel/vsob1/mortality-statistics--deaths-registered-in-england-and-wales--series-dr-/2013/stb-deaths-registered-in-england-and-wales-in-2013-by-cause.html). Mortality rates are presented as a trend. The underlying trend line was calculated as a second

order polynomial using Microsoft Excel with exclusion of years affected by the outbreaks, namely, 1999, 2002, 2003, 2007, 2008, 2012, 2013.

Age and gender specific vascular deaths are presented as the percentage difference between the average deaths in 2012 and 2013 versus 2011 (the year just before the outbreak).

Results and Discussions

Up to the present, the trends in all-cause mortality have been assumed to reflect a wide range of environmental (temperature, humidity, etc) and infectious events (mainly winter respiratory infections). Unexplained deviations have been assumed to be 'one of those things'. However, with the benefit of hindsight, it is now known that certain years are characterised by the spatial spread of an apparently new type of infectious condition [2,21]. A baseline trend can therefore be calculated by excluding these years from the calculated trend, and the results of one such calculation are presented in Figure 1.

As can be seen, the trend is remarkably smooth and is very close to the data points (typically less than ± 1% deviation) for those years not affected by the presumed outbreaks. Also observed is the fact that the outbreaks typically affect two consecutive years and are responsible for 2% to 5% deviations away from the trend line for mortality rate. The overall trend line is not greatly affected by these events simply because the excess deaths are a small proportion of the total population of living persons, and hence the trend approximates to sampling with replacement.

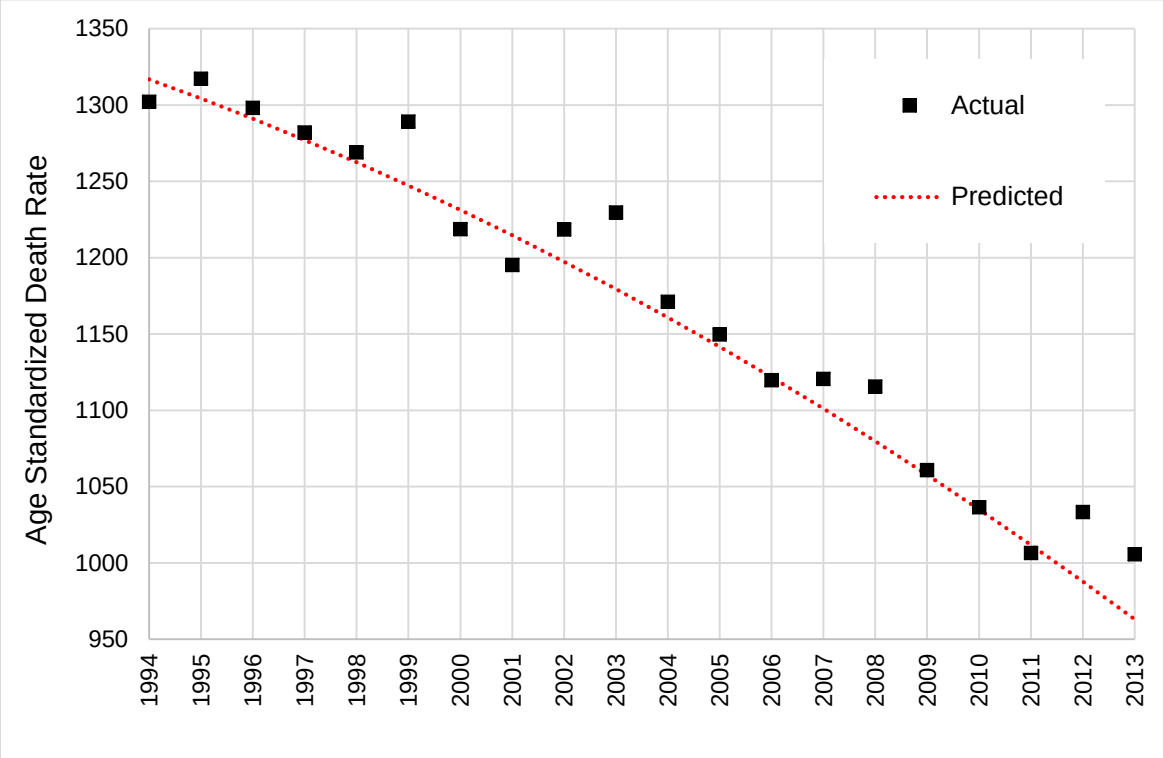
The 2012/2103 event accounts for a cumulative 9% increase in the mortality rate and represents the worst cumulative effect since 1994, an effect which is also observed in England and Wales [21]. Corresponding increases in emergency department attendances and medical admissions are observed during these events [2,22-24]. We are clearly dealing with something of profound public health importance, and it has been estimated that each event adds £6 billion of unexpected costs into the NHS in England alone [25].

Having demonstrated a profound effect upon all-cause mortality, Figure 2 now investigates specific effects against vascular system diseases. The International Classification of Diseases (ICD) chapter covering vascular system diseases includes both vascular and cardiac conditions.

In 2013 total deaths due to vascular system conditions accounted for 29% of male and 27% of female deaths, and hence this one chapter has a profound influence on the total all-cause mortality.

Deaths due to cardiac conditions have been falling for over two decades due to a variety of medical and drug developments. This ongoing downward trend acted to obscure the fact that there were considerable effects on vascular system deaths. In Figure 2, the downward trends have not been used to adjust the data simply because they have an unknown effect on the particular age-gender combinations.

Figure 1. Age standardized mortality for females in Scotland (1994 to 2013).

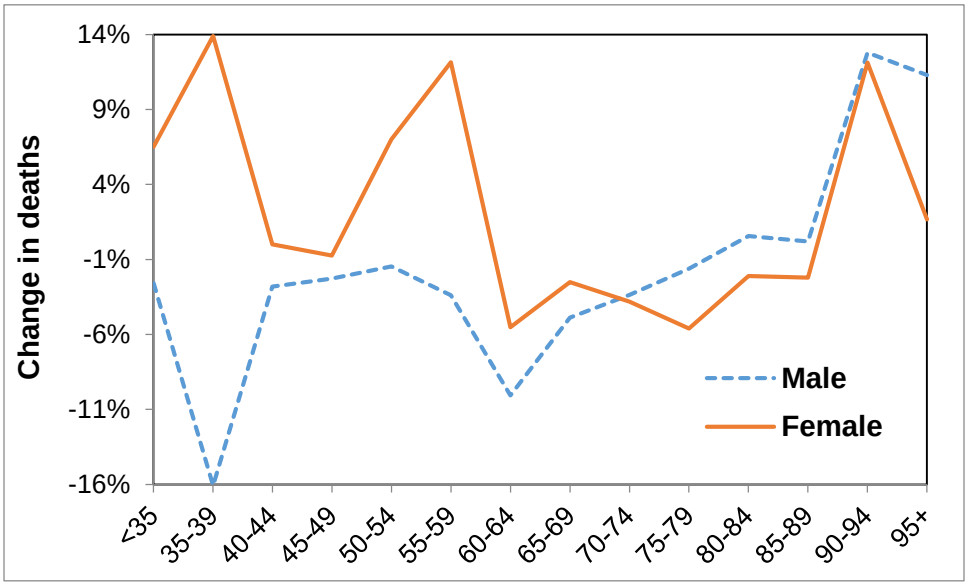


Once again, with the benefit of hindsight, we now understand that these outbreaks have specific age-gender effects, hence, some age-gender combinations in Figure 2 will be unaffected by the outbreak and hence will show as a negative change relative to 2011 (the year before the outbreak), while those specifically affected will show a large positive deviation [26]. Ages less than 35 have been grouped together to give more than 200 male and female deaths, i.e. to prevent statistical volatility from confounding the analysis. Highest deaths are for females in the 85-89 age band with more than 16,000 deaths in any year.

However, clearly seen in Figure 2 are saw tooth patterns in the changes in deaths experienced by various age groups. Hence there are peaks in female deaths around ages 35-39, 55-59 and 90-94. Male deaths are relatively unaffected except for a large reduction for those aged 35-39 and a peak for those aged over 90. Such saw tooth patterns were first reported for influenza deaths by Frances in 1960 [27], and arise from repeated exposure of populations to a series of different strains of the same infectious agent. Exposure to a particular strain primes the adaptive immune system to the antigen pattern of that strain, which can be beneficial or unhelpful upon exposure to a new strain, hence the saw tooth patterns in mortality.

Based upon the pattern of diagnoses associated with both deaths and hospital admissions during these outbreaks, it has been proposed that the immune modulating virus, cytomegalovirus

Figure 2. Deaths due to vascular system diseases in England and Wales (average of 2012 and 2013 versus 2011)



Recent research has suggested that these patterns may be single year of age specific and that the use of five year age bands may be acting to obscure the true complexity of the response [17,23,26].

(CMV), may be in some way associated with these outbreaks [2,5,8,16,18,28]. This may be via the introduction of a new strain, or may be via opportunistic reactivation in the presence of another infectious agent. Further work is required to determine exactly how CMV may be involved, however, it is clear that whatever is happening is affecting a wide range of medical conditions, and is clearly of great medical significance.

Conclusion

Evidence to suggest that something 'unusual' was happening has been around for many years, but lacked a conceptual framework for the correct explanation [1,2,21]. The effect of outbreaks of a type of infectious agent upon age standardized mortality rates, and upon age-gender associated deaths due to vascular system conditions, has been demonstrated in this study. Small area spread consistent with infectious transmission has been demonstrated elsewhere [17,19,23]. Outbreaks have been demonstrated across the whole of Europe (leading to around 470,000 deaths), North America (USA and Canada), Australia and New Zealand [1,2,30], and further research is urgently required to determine the extent of these outbreaks in other countries. The role of these outbreaks in hastening condition acuity and death suggests that the agent is playing a significant role in disease expression.

Acknowledgement

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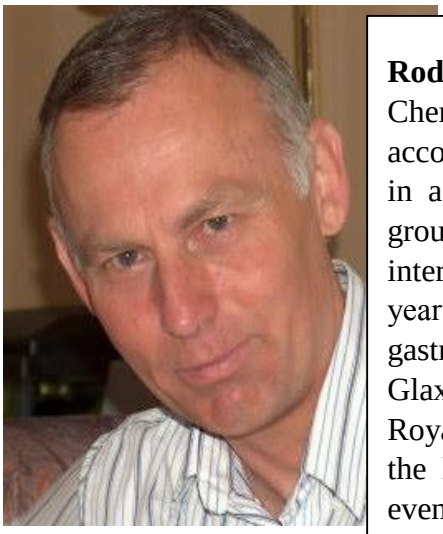
Authors Column



Rod has a B.Sc. (Hon) in Microbiology/Biochemistry and a Ph.D. in Chemical Engineering (Biochemical); is a chartered management accountant (ACMA, CGMA). His career outside the NHS covers 7 years in academia (Biochemical Engineering) and 10 years in industry as a group process development engineer and general manager of an international laboratory proficiency testing organisation. He has over 22 years' experience in healthcare. A disease management study in gastrointestinal bleeding & ulcers won an international award within Glaxo plc. In 1996 he completed a review of bed requirements for the Royal Berkshire Hospital. The forecast bed numbers were contested by the local health authority and a smaller hospital was built. The Trust eventually submitted a further business case (due to chronic bed shortages) to bring bed provision in line with the original forecast.

His research has led to the development of many innovative and new methods for understanding the operational and financial challenges in healthcare. He is the author of hundreds of papers, articles & reports, is an invited speaker at national conferences, is a member of the editorial board of the British Journal of Healthcare Management and runs a regular feature 'Money Matters' which investigates the application of statistical methods and trends into the understanding of how costs behave in the real world of health care. Since 2008 he has been investigating international outbreaks of a new type of infectious immune disease. This disease has gone unnoticed due to a unique type of spatiotemporal spread which appears to involve a series of local mini-epidemics facilitated by a respiratory phase of infection. Details of this research can be found at: http://www.hcaf.biz/emergencyadmissions.html