

Role of social group and gender in outbreaks of a novel agent leading to increased deaths, with insights into higher international deaths in 2015

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Abstract

Considerable evidence has accumulated for outbreaks of a novel type of infectious agent. Deaths, medical admissions, bed occupancy, ED and outpatient attendances, NHS staff sickness absence, stillbirths, the gender ratio at birth, and certain types of congenital malformations all simultaneously increase. This study uses social groups across the whole of England and Wales to demonstrate that female deaths are especially increased during these presumed infectious events, and that the pattern of deaths over time appears to be influenced by social behaviours. The effect upon NHS staff sickness absence appears to occur before that upon deaths. A very significant increase in deaths in 2015 is also investigated. Evidence suggests that this increase was due to an interaction between influenza and the proposed novel infectious agent. Analysis by social group demonstrates that white British bore the primary brunt of this unique event. The social group most affected (with around an 8% increase in deaths over 2014) was older people living in communal establishments (nursing homes and retirement homes), where proximity and the movement of staff appears to have led to enhanced person to person transmission with catastrophic consequences. The increase in 2015 was replicated across most of Europe with a few notable exceptions. The potential role of immune switching and of the immune modifying virus, cytomegalovirus, in these outbreaks is discussed.

Key Words:

Death, emerging infectious diseases, social groups, volatility, social behaviours, deaths in 2015, immune switching

Introduction

Recent research has highlighted the role of outbreaks of a presumed infectious agent which leads to on/off (up/down) switching of deaths, medical admissions, hospital bed occupancy, emergency department and outpatient attendances, staff sickness absence, human fertility, the gender ratio at birth, stillbirths, and the incidence of certain congenital conditions [see references in 1-29]. Females are affected more so than males via spontaneous abortion of the female foetus and medical admissions in the elderly [27]. Complex very small area spatial spread of mini-epidemics (occurring all the time) is involved leading to larger national level events every 2 to 5 years [3,5,7,8,11,13,14,20]. These events are international in scope and have been demonstrated across the whole of Europe and all other Western countries

[10,15]. Far wider scope appears entirely likely, and this agent may eventually be recognised as the ultimate source or exacerbating factor behind more deaths than influenza and other large scale sources of mortality.

This study aims to provide insight into the role of social behaviours in the magnitude and timing of the outbreaks, and to investigate an unusual increase in deaths in 2015 which swept across most of Europe and elsewhere in the world.

Methods

Data Sources

Annual deaths were obtained from the following sources: Australia (2003 to 2015, Australian Bureau of Statistics), 45 European countries (2013 to 2015, Eurostat deaths (total) by month), England and Wales (2013 to 2015, Office for National Statistics deaths by area of residence), Scotland (2013 to 2015, National Records of Scotland).

Output area annual deaths for males and females in England and Wales (2001 to 2015) from the Office for National Statistics. Output Area Classification lookup tables for England and Wales from the Office for National Statistics (ONS).

NHS staff sickness absence was obtained from NHS Digital.

Analysis

Direct year-on-year percentage differences for local government areas in the UK, Europe and Australia.

Output Area (OA) deaths were aggregated into social groups using the Output Area Classifications for England and Wales, and for London, from the ONS and the London Data Store. Difference between successive years were calculated as Standard Deviation equivalents (STDEV) using Poisson statistics as per previous studies [11-15,20].

The ratio of male to female deaths was calculated for various LOAC. A simple linear trend line (Microsoft Excel) was then fitted to this trend after excluding high years. The excess of female deaths relative to the trend was then calculated.

Results

Analysis of the data is presented in two sections. In the first, social groups from England and Wales are used to investigate the roles of gender and social behaviours on the magnitude and timing of the infectious events.

In the second part, data on deaths is examined across the UK, Europe and Australia. Potential causes behind an unusual international increase in deaths in 2015 are examined.

Female Specificity

Figure 1 investigates the magnitude of the year-to-year volatility in deaths for males and females in each of 76 social groups (determined from 2011 census variables) in England and Wales. Difference between years was calculated as a standard deviation equivalent (STDEV) [24,27] relative to the average deaths between 2001 to 2014, and the average volatility calculated over the 15-year period. Converting the year-to-year differences into STDEV equivalents adjusts all social groups for size [24], enabling like-for-like comparison.

Figure 1 illustrates the principle that female deaths are generally more volatile than males, i.e. outbreaks of the agent generally affect females more than males. Volatility needs to be understood in the context that outbreaks of the presumed infectious agent lead to on/off switching in deaths, and it is the resulting high/low behaviour which generates additional

year-to-year volatility. Certain social groups show higher volatility due to higher sensitivity to the presumed infectious agent.

Highest and lowest volatility female groups were 5b2 (communal retirement) and 2c2 (migrant commuters) respectively, while highest and lowest male volatility was found in 8c1 (hard pressed ageing industrious workers) and 8b2 (hard pressed rented terraces). Social deprivation per se seems to not play a major role since both high and low volatility male groups are from socially deprived areas. However, both male and female high volatility groups are from aged communities. It is also clear that males and females within the same social group show differential volatility, and this confirms the observation that the genders respond to different social factors [24].

Higher Deaths in Certain Years

Figure 2 illustrates the principle that deaths are higher in certain years. The social group in Figure 2 is high in persons with a black ethnic origin. As can be seen female deaths are greater during the outbreaks, and peak at almost 2-times higher than seen in males. Genetic, cultural and social network factors may be involved in this difference.

After excluding high years, a second order polynomial was used to estimate the baseline trend in Figure 2. While there is a general downward trend in deaths after 2001 in most social groups in England and Wales there are exceptions, and it is sometimes difficult to know if the baseline trend follows a second order polynomial on all occasions.

To remedy this issue the ratio of male to female deaths was calculated, high years excluded, and a linear fit was used to calculate the trend line. The ratio of female to male deaths (a dimensionless ratio) appears to avoid some of the uncertainty regarding the underlying trend in deaths. This analysis shows years in which there are an excess of female deaths relative to the baseline ratio. A negative value represents a period of excess male deaths.

Figures 3 to 5 illustrate the different profiles between males and females observed across three diverse social groups. Differences in both magnitude and timing can be inferred. Recall that annual data is made more difficult to interpret due to part year effects, and the possibility that onset in males and females can lag behind each other [24].

Unusual Deaths in 2015

In the UK the year 2015 saw the largest increase in deaths (+5.6%) over the previous year since the 1960s [30]. No official explanation has ever been offered.

Table 1 shows the social groups in England and Wales which experienced a statistically significant (> 3 STDEV) increase in 2015. Females occur in Table 1 on 35% more occasions than males. As a generalization, the social groups most affected are of white British ethnic origin, especially elderly. Ethnicity (genetic factors?), social or cultural behaviours and female gender are clearly implicated. At the opposite end of the spectrum (data not shown) are student and several Eastern European social groups who experience a reduction rather than an increase – on both occasions younger age is the common factor.

International Scope

The outbreaks of a presumed infectious agent are international in scope, with Australia being no exception [15,31]. Figure 6 shows the trend in total deaths in Australia between 2003 and 2015. Due to very different patterns of immigration after World War II Australia shows a general increase in total deaths, as opposed to the general decrease in the UK. However, certain years are clearly higher than the trend such as 2008 and 2014/2015.

The suggestion is that whatever led to higher deaths in 2015 in the UK may have commenced in mid-2014 in Australia. Recall that the winter occurs in mid-year in Australia, and that the population of Australia is highly dispersed which would facilitate slower spread.

Is there any evidence that similar dispersion occurred elsewhere?

Common Patterns

To investigate this possibility Figure 7 shows the difference in deaths between 2013 to 2014 and 2014 to 2015 seen at local authority level across the UK and at country level across Europe. To limit statistical scatter analysis is restricted to local authority/countries with over 2,000 deaths per annum. As can be seen the change in 2015 (over 2014) is greatly influenced by the magnitude of the change seen in 2014 (over 2013), i.e. areas experiencing a large increase in deaths in 2014 generally did not show the large increase in deaths in 2015, and vice versa. The effect was clearly not limited to the UK, although UK government agencies have not made this clear and all concerned have been left to speculate.

This pattern is further investigated in Figure 8 for social groups in London with more than 2,000 deaths per annum. Figure 8 also contains a male/female split where it can be seen that a higher proportion of females within social groups had a reduction in deaths in 2014 (over 2013), while the opposite is true for males. Hence females tended to experience a higher increase in deaths in 2015.

A similar situation is observed when using smaller output area data (OA) for England and Wales (excluding London) – data not shown. When converted to STDEV equivalents this smaller OA data shows the following linear relationship $2015 \text{ (as STDEV)} = 0.33 - 0.42 \times 2014 \text{ (as STDEV)}$. Hence any small area experiencing no change between 2013 and 2014 will on average experience a 0.33 STDEV equivalent increase in 2015. A small area experiencing a -5 STDEV reduction in 2014 would on average show a +2.2 STDEV increase in 2015. Females show a similar preference for a reduction in 2014 as in Figure 8.

Understanding Annual Patterns

Due to the data availability at output area (OA) level in England and Wales this study has been restricted to calendar year totals. Several of the above sections contain comments regarding interpreting such annual totals in the context of smaller area movement of the suspected pathogen.

Figure 9 illustrates these issues with running (moving) 12-month total deaths for two local authorities in Berkshire, namely Slough and West Berkshire. West Berkshire is a predominantly affluent white British community with the majority of the population living in Newbury and nearby Thatcham. Slough has a very large Pakistani community, and due to its close proximity to Heathrow and London attracts new immigrants and asylum seekers. There is a thriving black market in the provision of sub-standard accommodation (with poor sanitation) including converted garden sheds. The Slough council has claimed for many years that the true population of Slough (as measured by the weight of refuse as a proxy for human habitation) is far higher than the census figures represent.

A previous study of the 2012 outbreak in Berkshire, using mid super output area (MSOA) data for medical admissions, demonstrated that Slough and West Berkshire respond to the outbreaks in different ways [8,11]. As can be seen in Figure 9 the pattern over time in West Berkshire shows clearer saw-tooth behaviour which is indicative of on/off switching, while that in Slough is more complex due to the greater diversity of social networks and far higher proportion of other ethnic groups.

The 2002 outbreak shows anti-phase behaviour in Slough and does not commence until 2003. Between 2006 and 2009 Slough demonstrates indeterminate behaviour, which is assumed to arise when male/female outbreaks go out-of-phase. It is only from 2010 onward that the series of outbreaks in 2010, 2012, 2014 and 2016 can be seen in high synchrony in both locations. The ongoing 2016 outbreak in the UK, mixed with a cocktail of bad policy, led to chaos in the NHS during the winter of 2016/17.

The interaction with influenza in 2015 shows as a 'table top' shaped feature added on top of the saw-tooth pattern arising from the 2014 outbreak, however, the strength of this interaction differs between the two locations.

Calendar year totals are the total every December in the running (moving) 12-month total chart. Hence year-on-year comparisons can be blurred depending on when each event initiates and the annual total can contain a mix of partial year effects.

It is these partial year effects which generate the scatter in Figures 7 and 8, and can lead to the volatility observed in the other charts. The effects at national level therefore depend on the sum total of all small areas and the degree of synchrony. For example, a high proportion of anti-phase behaviour can 'hide' an outbreak which was largely the case for the 2010 outbreak when observed at national level [7,14].

Wider Links with Illness

It has been previously observed that the effects of these events on the gender ratio at birth, Emergency Department attendance and medical admissions occur slightly earlier than the effect upon deaths [19]. Effects against NHS staff sickness absence have also been observed [29]. Figure 10 explores the issue regarding the timing of the effect against NHS staff sickness absence relative to deaths (all-cause mortality) in England. As can be seen in Figure 10, sickness absence tends to initiate slightly before the increase in deaths, and that the relative effects against sickness absence and deaths are different during each event.

Discussion

The previous study in this series [24], established the principles that these outbreaks occur continuously over time in very small areas, with around 1% of small areas having a mini-outbreak at any point in time. Males and females behave as separate compartments with magnitude seemingly influenced by different population characteristics, i.e. deaths in women were more sensitive to the presence of children, etc. Male or female outbreaks can occur simultaneously but more commonly lag-behind each other. Chance appears to play a major role in all these behaviours.

This study has used annual totals to illustrate broad principles, however, these outbreaks do not occur in neat calendar year temporal patterns. Hence as in Figure 6 (deaths in Australia) the trends are a mix of part-year and full-year effects which depend on timing and magnitude, and upon wider spread across the whole of Australia. Figure 9 illustrated this effect using monthly data from two socially diverse local authority areas in Berkshire (England), while Figure 10 used monthly deaths and NHS staff sickness absence to demonstrate that for the whole of England (a composite of all small areas) the increase in sickness absence commenced before the increase in deaths.

However, the behaviour of countries, local authority areas, social groupings and very small areas all display similar patterns suggesting a common source for the behaviour. As suggested in previous studies [1-30], and confirmed in Figure 10, these events are highly likely to be of an infectious origin. There is a cascade of morbidity and mortality with the effects upon pregnancy seeming to occur first. This is followed by increased ED attendance,

medical admissions, and staff sickness absence, with deaths rising last in this cascade of poor health.

Figures 1 and 2 have re-emphasized the central role of gender differences in these outbreaks. All studies conducted in the future need to split the data by gender.

Figures 2 to 5 show that different social groups and/or population dispersion patterns can show male or female peaks in different years. However, superimposed on this are larger (inter)national events which occur roughly around 2003, 2008 and more recently 2012, 2014, 2016 in the UK. The data for Australia (Figure 6) is a composite for a dispersed population, however, the detail becomes clearer using monthly data in 12-month running totals at State and local government geographies [15,30].

Figures 7 and 8 demonstrated that the outbreaks occur at all geographic levels from very small spatial units (output areas) through to local government and national geographies.

Another study has suggested that an interaction between the presumed infectious agent and influenza led to the jump in deaths in January 2015, which then had ongoing effects upon mortality for an extended period [28]. A further study demonstrates that the magnitude of the increase in 2015 in both the UK and Europe is strongly influenced by the difference in deaths between December 2014 and January 2015 [32], which seemingly arose from an influenza outbreak following vaccination of the population with a poorly matched antigen vaccine [28,32].

These infectious events appear to occur as on/off switching. The switch-on leads to higher deaths for a 12-month period, followed by switch-off until the next event is initiated. At very small area level the switch-on occurs at very approximate two year intervals [24]. It has been suggested that this on/off switching has an immune system basis [27,34].

This presumably partly explains why the timing of events has such a profound effect on the magnitude of the 2015 increase. Those countries/locations which experienced switch-on for most of 2014 therefore went into switch-off in 2015, and apparently, this prevented any interaction with influenza and/or vaccination with the incorrect antigen mix.

In the UK, it has been proposed that the increase in deaths in 2015 was due to reduced funding of social care [35-37]. This proposal is contradicted by the small-area and international behaviour demonstrated in this study and elsewhere [32].

The potential involvement of the immune modifying virus, cytomegalovirus, has been discussed elsewhere, both in terms of adult deaths, medical admissions, and stillbirths in the foetus [1,2,4,6,9,19,22,23,27].

Conclusion

Current models for expected number of deaths need to be modified to include the effects of the outbreaks of this presumed pathogen. Sophisticated spatial and fractal analysis is required to investigate how transmission occurs in different social groups. The male/female difference is clearly of fundamental importance, as is the degree of in-phase and anti-phase behaviour.

Given the seeming ability of this pathogen to increase stillbirths and certain congenital conditions [27], urgent international research is required to confirm the pathogen and develop a workable vaccine. Government agencies in the UK remain in (public) denial regarding the presence of this pathogen [38].

Another outbreak of influenza A(H3N2) has occurred in December 2016 to February 2017 similar to that which was seemingly involved in the 2015 increase in deaths [33]. It remains to be seen if the events in 2015 will be repeated in 2017.

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Figure 1: Average year-to-year volatility in deaths (as STDEV equivalents) for social groups in England and Wales by gender, 2001 to 2015

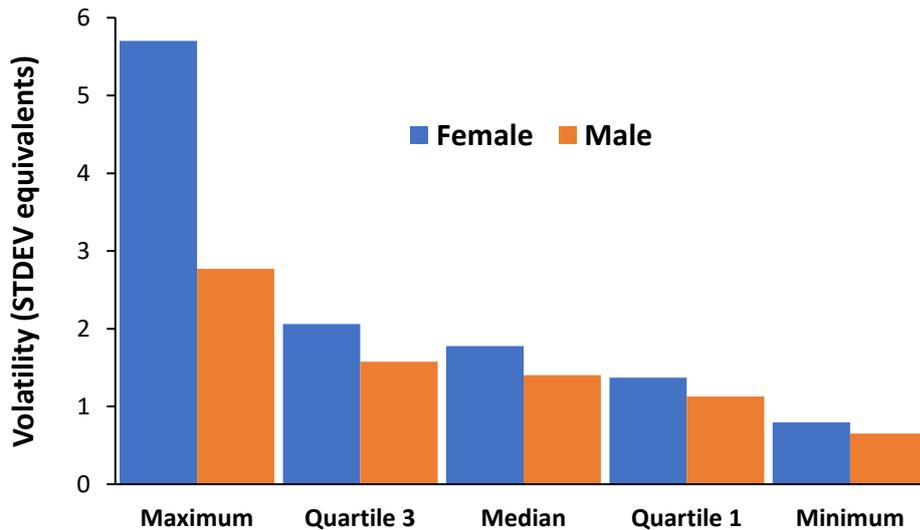


Figure 2: Deaths relative to the underlying trend for social group 8d2 (hard pressed ethnic mix, high in black ethnic origin)

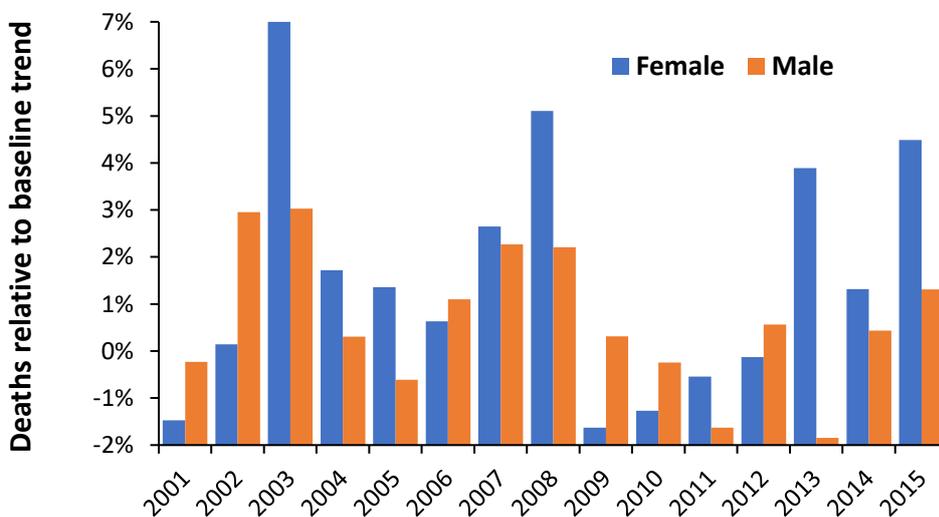


Figure 3: Excess female relative to male deaths in group 5b2 (ageing communal retirement)

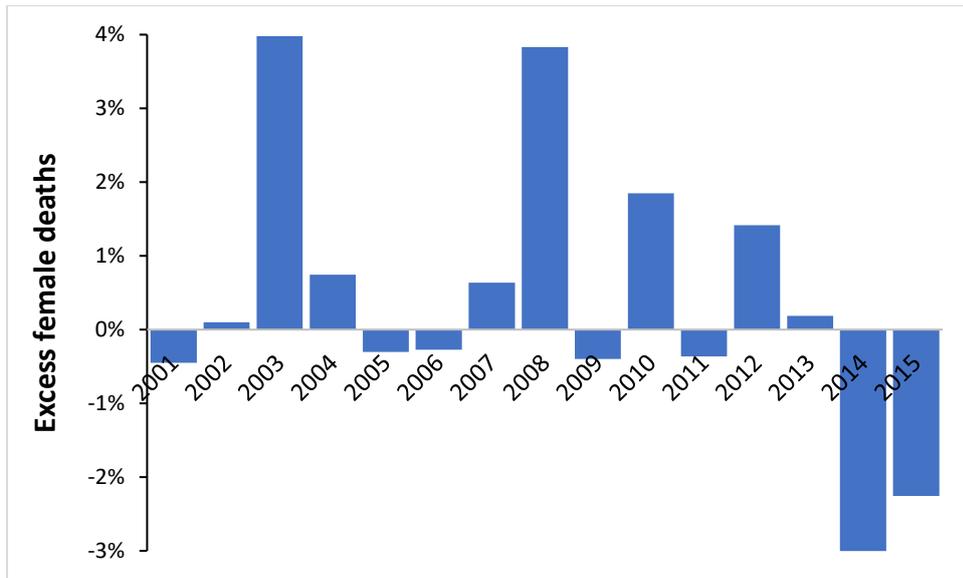


Figure 4: Excess female to male deaths in group 6b2 (white suburban semi-detached communities)

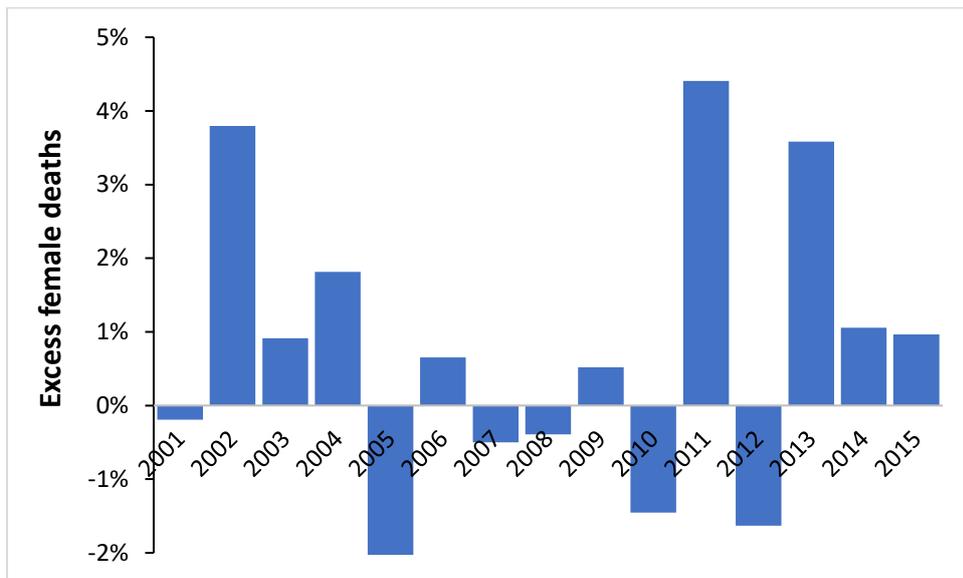


Figure 5: Excess female relative to male deaths in group 8b2 (hard pressed rented terraces)

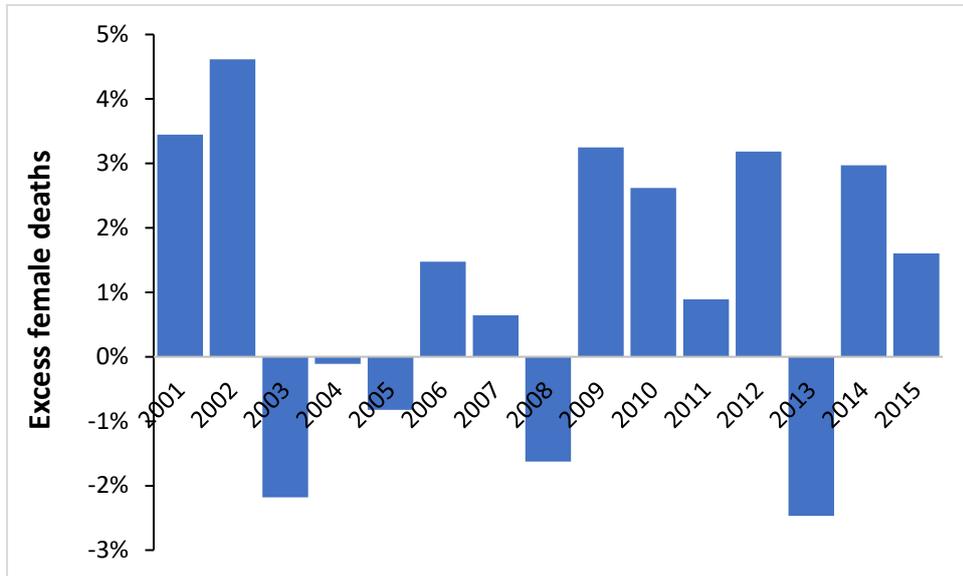


Figure 6: Annual deaths in Australia, 2003 to 2015

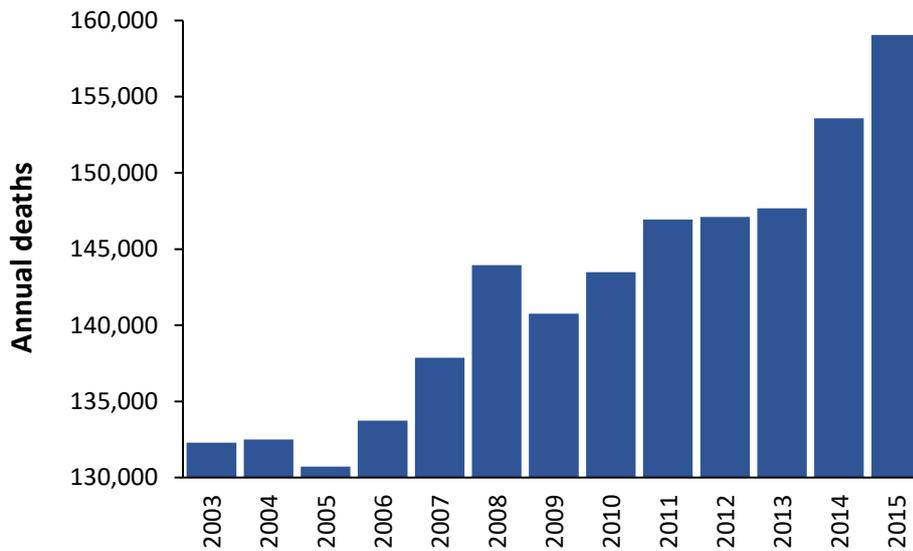


Figure 7: Annual deaths in European countries and UK local government areas (>2,000 deaths per annum), change between 2014 to 2015 versus change 2013 to 2014

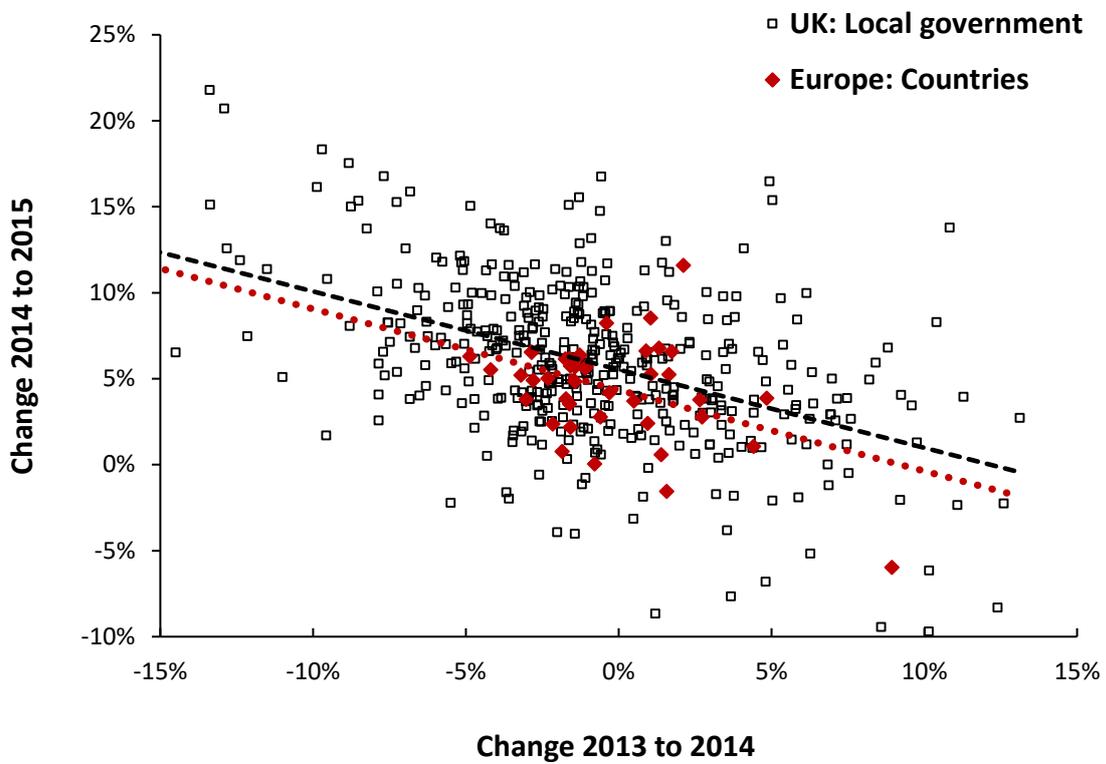


Figure 8: Annual male or female deaths in social groups within England and Wales (>2,000 deaths per annum), change between 2014 to 2015 versus change 2013 to 2014

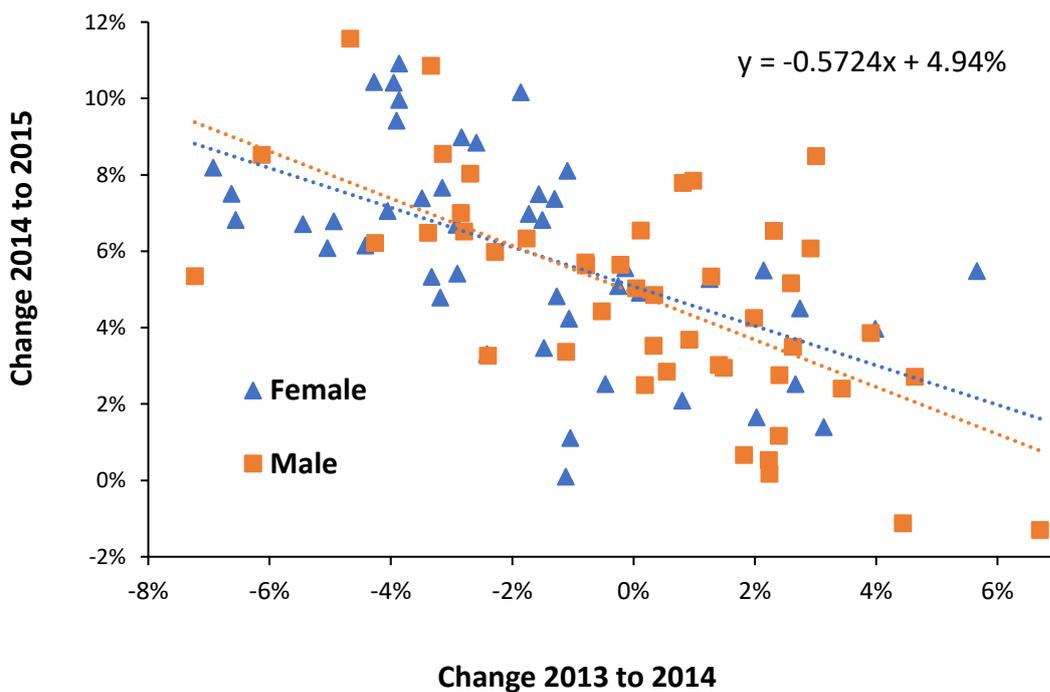


Figure 9: Running (moving) 12-month total deaths in Slough and West Berkshire

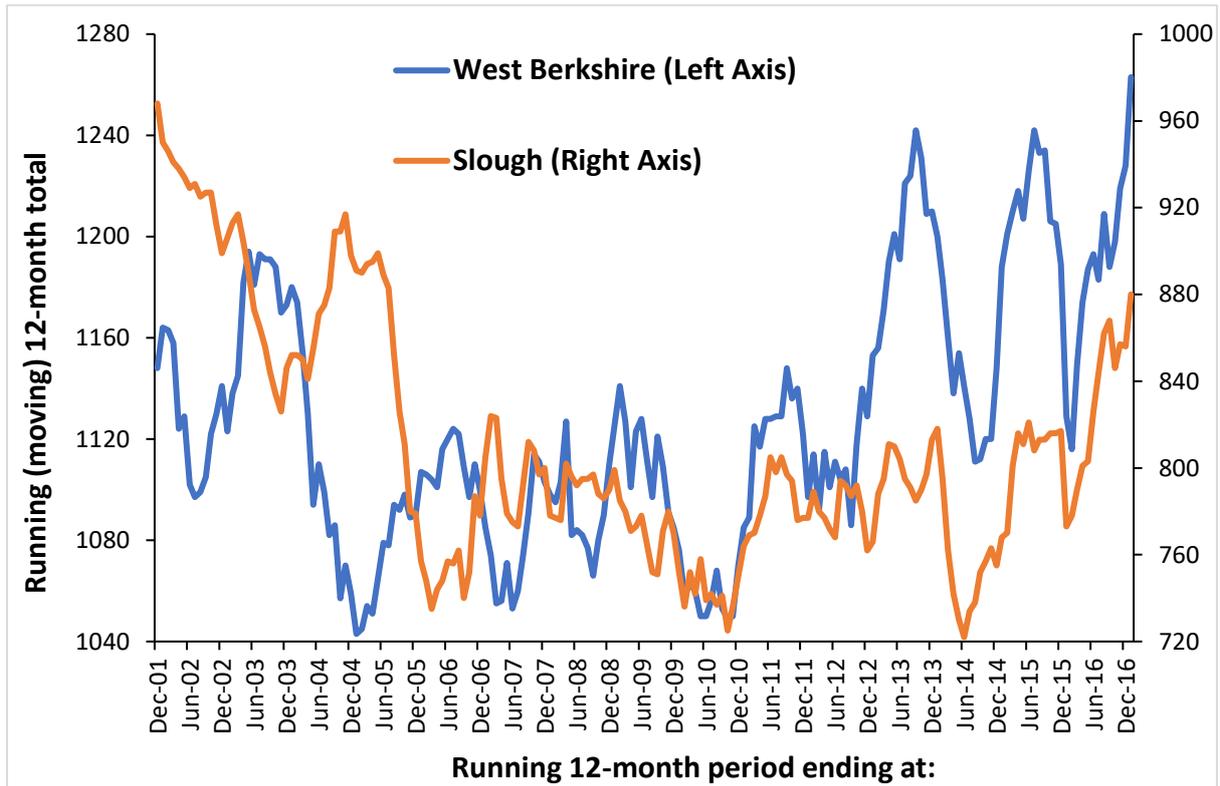


Figure 10: Running (moving) 12-month average NHS staff sickness absence rate and deaths (all-cause mortality) in England

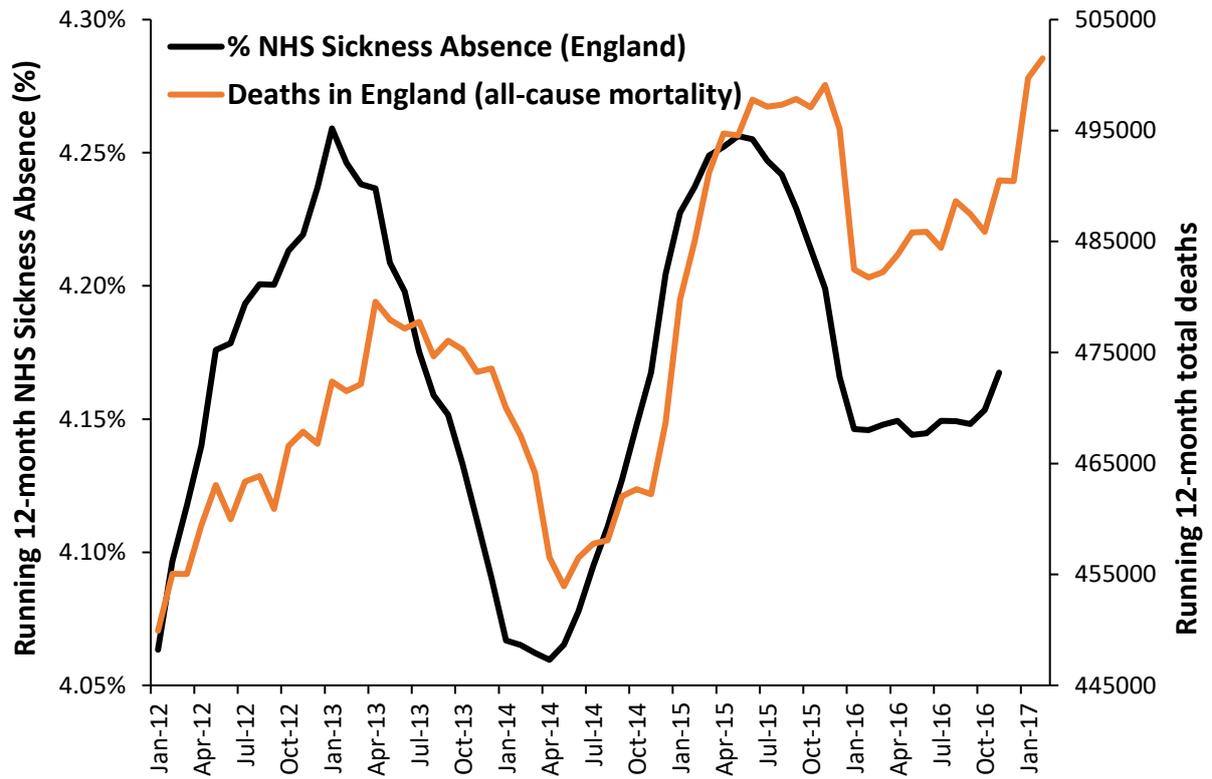


Table 1: Social groups in England and Wales showing a statistically significant change between 2014 and 2015

Sex	OAC	Supergroup	Group	Subgroup	2014	Change	STDEV
F	5b2	Urbanites	Ageing Urban Living	Communal Retirement	21,477	7.4%	10.8
M	5b2	Urbanites	Ageing Urban Living	Communal Retirement	11,887	7.8%	8.5
F	1c3	Rural Residents	Ageing Rural	Detached Rural Retirement	5,821	10.0%	7.6
F	5b3	Urbanites	Ageing Urban Living	Self-Sufficient Retirement	9,622	7.5%	7.4
F	6a3	Suburbanites	Suburban Achievers	Detached Retirement Living	7,886	8.1%	7.2
F	1c2	Rural Residents	Ageing Rural	Renting Rural Retirement	5,754	9.4%	7.1
F	1b1	Rural Residents	Rural Tenants	Rural Life	4,666	10.4%	7.1
F	7a2	Constrained City	Challenged Diversity	Hampered Aspiration	4,249	10.4%	6.8
F	4a1	Multicultural Metropolitans	Rented Family Living	Social Renting Young Families	5,621	9.0%	6.7
F	8d1	Hard-Pressed Living	Migration and Churn	Hard-Pressed Family	3,509	10.9%	6.5
F	6b3	Suburbanites	Semi-Detached Suburbia	Semi-Detached Ageing	8,843	6.8%	6.4
M	5b3	Urbanites	Ageing Urban Living	Self-Sufficient Retirement	9,227	6.5%	6.3
M	6a3	Suburbanites	Suburban Achievers	Detached Retirement Living	8,467	6.3%	5.8
F	5a1	Urbanites	Urban Professionals and Families	White Professionals	6,147	7.4%	5.8
F	6a4	Suburbanites	Suburban Achievers	Ageing in Suburbia	6,650	7.0%	5.7
F	8c1	Hard-Pressed Living	Hard-Pressed Ageing Workers	Ageing Industrious Worker	7,735	6.2%	5.4
M	7d3	Constrained City	Ageing City	Retired Communal City	2,101	11.6%	5.3
M	6b2	Suburbanites	Semi-Detached Suburbia	White Suburban	8,596	5.6%	5.2
M	8b1	Hard-Pressed Living	Challenged Terraced Workers	Deprived Blue-Collar	3,401	8.5%	5.0
M	1c2	Rural Residents	Ageing Rural	Renting Rural Retirement	3,356	8.6%	5.0
F	1a2	Rural Residents	Farming Communities	Established Farming	2,323	10.2%	4.9
F	8c2	Hard-Pressed Living	Hard-Pressed Ageing Workers	Ageing Rural Industry	3,009	8.8%	4.8
M	1b3	Rural Residents	Rural Tenants	Ageing Rural Flat Tenant	3,473	8.0%	4.7
F	3b1	Ethnicity Central	Endeavouring Ethnic Mix	Striving Service Workers	1,008	14.9%	4.7
F	6b2	Suburbanites	Semi-Detached Suburbia	White Suburban Communities	7,987	5.3%	4.7
M	7d1	Constrained City	Ageing City	Ageing and Families	1,852	10.9%	4.7
M	1c3	Rural Residents	Ageing Rural	Detached Rural Retirement	3,491	7.8%	4.6
M	6a2	Suburbanites	Suburban Achievers	Comfortable Suburbia	2,099	9.8%	4.5
M	8c1	Hard-Pressed Living	Hard-Pressed Ageing Workers	Ageing Industrious Workers	6,937	5.3%	4.5
M	6b4	Suburbanites	Semi-Detached Suburbia	Older Workers/ Retirement	5,969	5.6%	4.4
F	4a2	Multicultural Metropolitans	Rented Family Living	Private Rent New Arrivals	2,821	8.2%	4.3
F	7d3	Constrained City	Ageing City	Retired Communal City	3,715	7.1%	4.3
F	4a3	Multicultural Metropolitans	Rented Family Living	Commuters with Young Families	3,132	7.7%	4.3
F	8a1	Hard-Pressed Living	Industrious Communities	Industrious Transitions	7,051	5.1%	4.3
F	1c1	Rural Residents	Ageing Rural	Rural Employed/ Retirees	1,175	12.4%	4.3
M	8a1	Hard-Pressed Living	Industrious Communities	Industrious Transitions	6,959	5.0%	4.2
M	5a3	Urbanites	Urban Professionals and Families	Families in Terraces/ Flats	5,012	5.7%	4.0
M	6a4	Suburbanites	Suburban Achievers	Ageing in Suburbia	5,696	5.3%	4.0
M	3a1	Ethnicity Central	Ethnic Family Life	Established Renting Families	2,155	8.5%	3.9
M	3b2	Ethnicity Central	Endeavouring Ethnic Mix	Bangladeshi Mixed Employment	568	16.4%	3.9
F	5b1	Urbanites	Ageing Urban Living	Delayed Retirement	5,141	5.3%	3.8
F	1b3	Rural Residents	Rural Tenants	Ageing Rural Flat Tenant	3,198	6.7%	3.8
F	6a2	Suburbanites	Suburban Achievers	Comfortable Suburbia	1,682	9.2%	3.8
M	4c1	Multicultural Metropolitans	Asian Traits	Achieving Minorities	2,799	7.0%	3.7
F	1b2	Rural Residents	Rural Tenants	Rural White-Collar Worker	4,448	5.6%	3.7
M	6b1	Suburbanites	Semi-Detached Suburbia	Multi-Ethnic Suburbia	3,809	6.0%	3.7
M	2c3	Cosmopolitans	Comfortable Cosmopolitans	Professional Service	181	26.5%	3.6
M	6b3	Suburbanites	Semi-Detached Suburbia	Semi-Detached Ageing	9,710	3.5%	3.5

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Sex	OAC	Supergroup	Group	Subgroup	2014	Change	STDEV
M	8c2	Hard-Pressed Living	Hard-Pressed Ageing Workers	Ageing Rural Industry	2,793	6.5%	3.4
F	7c1	Constrained City	White Communities	Challenged Transitionaries	1,187	9.8%	3.4
M	1c1	Rural Residents	Ageing Rural	Rural Employment/ Retired	1,182	9.7%	3.3
M	4a3	Multicultural Metropolitans	Rented Family Living	Commuters with Young Families	2,997	6.1%	3.3
F	6b1	Suburbanites	Semi-Detached Suburbia	Multi-Ethnic Suburbia	3,617	5.5%	3.3
F	6a1	Suburbanites	Suburban Achievers	Indian Tech Achievers	3,714	5.4%	3.3
F	2a2	Cosmopolitans	Students Around Campus	Student Digs	244	20.9%	3.3
F	7d1	Constrained City	Ageing City	Ageing and Families	2,269	6.8%	3.2
M	1a4	Rural Residents	Farming Communities	Older Farming Community	1,827	7.6%	3.2
M	7a3	Constrained City	Challenged Diversity	Multi-Ethnic Hardship	5,547	4.3%	3.2
F	8d3	Hard-Pressed Living	Migration and Churn	Hard-Pressed European	2,220	6.7%	3.2
F	1a4	Rural Residents	Farming Communities	Older Farming Community	1,572	7.9%	3.1
F	3d1	Ethnicity Central	Aspirational Techies	New EU Tech Workers	810	11.0%	3.1
F	7a3	Constrained City	Challenged Diversity	Multi-Ethnic Hardship	5,404	4.2%	3.1
F	7a1	Constrained City	Challenged Diversity	Transitional E. European	1,719	7.5%	3.1