

A time series of infectious-like events in Australia between 2000 and 2013 leading to extended periods of increased deaths (all-cause mortality) with possible links to increased hospital medical admissions

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Received: 19/Apr/2015 Accepted: 25/Aug/2015

Original article

ABSTRACT

Background and aims: Trends in deaths and medical admissions in the UK and Europe show evidence for a series of infectious-like events. These events have been overlooked by traditional surveillance methodologies. Preliminary evidence points to a rise in medical admissions in Australia around the same time as those observed in Europe, and this study was aimed to evaluate whether the deaths are occurred in similar way.

Methods: Both monthly and annually deaths in the states of Australia and smaller local authority geographies were analyzed for evidence of large and abrupt step-like increases which endured for a minimum of 12 months. Monthly data were analyzed using a 12-month running total of deaths, while annual data compared one year to the next by converting changes in deaths into standard deviation equivalents in an assumed Poisson distribution.

Results: At State and Local government level, there was evidence for spatial spread of an agent causing step-like changes in deaths which endured for 12 to 18 months before returning to the expected time-trajectory for deaths. The maximum step-like change ranged from 4.1% in New South Wales to 11.7% in the Northern Territory. The magnitude of the step-change was reduced with the size of the spatial geography and followed a power law function with size.

Conclusion: The same events leading to increased deaths and medical admissions in the UK and Europe (Northern Hemisphere), also appeared to be operating in Australia (Southern Hemisphere) at roughly the same points in time. A common infectious source appeared to be implicated.

Keywords: Death, Spatial spread, Medical admissions, Emerging infectious diseases, Age-standardization, Trend analysis.

INTRODUCTION

With more over than 1,400 human pathogens¹ this possibility exists that there are hidden epidemics of a novel nature. Current surveillance methodologies tend to focus on spike events typically caused by winter infections or periods of extreme heat or cold.²⁻⁴ There are a number of persistent

infectious agents⁵ which could cause novel epidemics. For example, it has been noted that the incidence of syphilis rises and falls in an approximate nine year cycle.⁶ Many persistent infections, for example the herpes group of viruses, are eventually bought under immune control with sporadic reactivation.⁷

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In Australia there is some evidence that the incidence or severity of herpes simplex virus episodes, as determined by GP consultation, may be cyclic.⁸ Indeed all agents provoking an immune response have their own particular periodicity for outbreaks.⁹⁻¹⁰

If a hidden epidemic with a persistent agent were to exist, the time response would consist of an initial and then sustained increase in deaths and hospital admissions, followed by eventual decline as the infection is bought under immune control. Indeed the presence of an active persistent infection could even increase the susceptibility of the host to other infections and may act to increase the number of admissions/attendances during the winter months – which may then be incorrectly attributed to winter infections. This period of sustained activity could endure for many months. This type of response can be detected using a 12-month running total of deaths or admissions.

Due to the highly seasonal nature of deaths and medical admissions,^{9,11-13} a 12-month running total of deaths also has the benefit of de-seasonalising the time series and of reducing the level of background Poisson scatter.¹⁴ In a running 12-month total the arrival of a step-like change leads to a ramp. The slope of this ramp is equal to the average increase in the monthly deaths or admissions. The duration of the ramp indicates the time period before the agent is eventually bought under immune control. Hence the ramp will be 12 months long if the infectious agent maintains active for 12 months. If the active phase continues longer than 12 months, the ramp then levels off at a new and higher rate of admission/attendance.

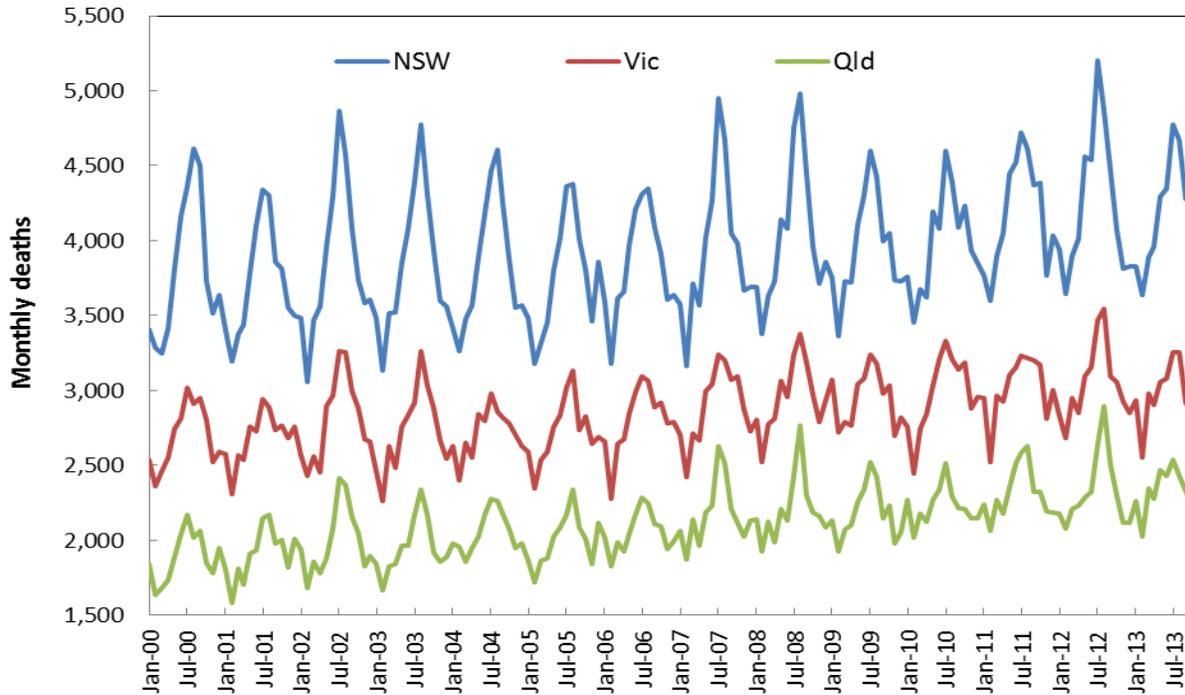
Without the application of a 12-month running total of deaths, the outbreak would be missed since it would be concealed within the dominant seasonal pattern and its associated Poisson will be scattered. Figure 1 gives an example of monthly deaths in three

Australian states where the years 2002/2003, 2007/2008 and 2012 appear to have higher peak than the general time series, however, it is difficult to discern if this is exclusively a winter effect. Note the higher background Poisson-based scatter in the smaller monthly numbers for Queensland.

The potential existence of one such outbreak has recently been deduced from the study of 12-month running total of deaths, medical emergency admissions and GP referral in both the UK and the 27 EU countries.¹⁵⁻¹⁹ Each additional death in these outbreaks appears to generate around 10 extra emergency medical admissions.²⁰⁻²¹ The increase in deaths is of such a magnitude as to induce a temporary reversal in ongoing reduction in age-standardized mortality.^{21,22} Both deaths and medical admissions appear to cluster around a common range of conditions, which could best be described as the exacerbation of existing conditions which are immune sensitive, via infection, inflammation and autoimmunity.^{15,20,22-26} The agent appears to show strain specific characteristics,²⁶⁻²⁷ and exhibits very small area spread consistent with an infectious etiology.²⁸⁻³³ Increased hospital bed occupancy also shows spatial spread,³¹ and a sudden and unexpected increase in medical bed occupancy is a characteristic feature of these events.^{21,34}

Analysis of 12-month running total deaths in England and Wales suggest a series of outbreaks dating back to the 1950's and perhaps earlier, with around two events per decade but occasionally more.^{17,35} Similar events have been demonstrated in the 27 EU countries, Canada and the USA.^{15,17,34,36-38}

These outbreaks exhibit relatively slow spatial spread and outbreaks in the UK and Europe initiate across a two-year window, with some countries appearing to consistently initiate earlier than others.^{15,17,21,26,28-33,35,37}



Footnote: NSW= New South Wales, Vic= Victoria, Qld= Queensland.

Figure 1: A time series of monthly deaths in three Australian states

The presence of these infectious-like events has already been inferred to occur in Australia. In the first instance, occupied hospital beds in Australia were observed to increase in a step-like manner around the times of the proposed outbreaks.³⁴ Data from Queensland also demonstrated step-like increases in medical admissions and occupied beds arising from the 2002 and 2007 outbreaks.³⁴ A review of bed requirements at the Royal North Shore Hospital (RNSH) in Sydney, used 12-month running total of medical admissions to demonstrate a similar event following the 2007 outbreak with preliminary evidence for condition specificity.³⁸ The shape of the 12-month running total of medical admissions suggested relatively slow spread across the rather dispersed catchment area of this hospital.

This paper examined a 12-month running total of deaths for Australian states

from Jan 2000 to Oct 2013, to determine if events already documented to occur across the rest of the Western world (Canada, USA and the 27 EU countries) in 2002/2003, 2007/2008, 2009/10 and 2012/2013 were also occurred in Australia. The increase in deaths/admissions/attendances attributable to these events endure for a minimum of 12 months before abating.³⁵

METHODS

Monthly deaths for Australian states were obtained from the Australian Bureau of Statistics (ABS) covering the years 2000 to 2013³⁹. A running 12-month total was calculated through to September 2013 (beyond which death registrations tend to decline, especially in December). Annual deaths for Local Government Areas (LGAs) from 2001 to 2013 were obtained from the same source.

Unusually large spike events can affect a running 12-month total and the top 10% of 'spike' months were trimmed back to the 90th centile value. See Figure 1 in supplementary material. This was achieved by calculating the successive difference from one month to the next. Values for the successive difference between months were then ranked and the top 10% were assumed to be spikes of unusual magnitude. The spike was then trimmed by deducting the 90th centile value, and this trimmed value was then subtracted from the actual number of deaths in that month.

The underlying trend in the running 12-month total was determined by putting a third order polynomial trend line through the points of minimum death, and the actual data was then compared to this expected trend. See Figure 2 and Table 1 in the supplementary material. The results of growth-adjusted totals running for all States are given in Figure 3 in the supplementary material.

The month of onset with a large step-like increase in deaths was determined by comparing successive 12-month blocks, i.e. June 2000 to May 2001 versus June 2001 to May 2002, etc. The difference percentage was calculated. The point of maximum percentage difference indicates the presence of a step-like change. Where the onset and magnitude of a step-change may have been obscured by a previous spike-event, the onset/magnitude was determined by visual inspection of the charts. This method has been used elsewhere.^{17,18,21,28-30}

Evidence for spatial spread between LGAs was assessed for the 465 largest LGA with more than 10 average deaths per annum (2001 to 2013) and no zero values in any year. Successive difference between years were calculated as the equivalent to a Poisson standard deviation (STDEV)

difference, i.e. $(\text{Year 2} - \text{Year 1})/\text{square root}(0.5 \times [\text{Year 1} + \text{Year 2}])$. By definition the standard deviation of a Poisson distribution is equal to the square root of the average. See Table 2 in the supplementary material for additional details.

RESULTS

It is important to remember that a step-like change in a monthly time series is transformed into a ramp in a running 12-month total. For example, before an outbreak of the persistent agent, there was an average of 100 health care events per month (the annual total is 1,200). An outbreak of the persistent agent occurs and events rise to an average of 120 per month (20 per month higher). In the first month after the outbreak there will be a total of $100 \times 11 + 120 = 1,220$ events, while in the 11th month of the running total there will be $120 \times 11 + 100 = 1,420$ events and then finally in the 12th month $120 \times 12 = 1,440$ events, which will continue until the outbreak is brought under immune control and a ramp down will then occur. The onset of any step-like event will therefore lie at the foot of any ramp increase, while the magnitude of the step change is revealed in both the slope of the ramp, and also at the point 12 months on from the foot of the ramp. The ensuing step-down in deaths at the end of the event can be detected in the same way.

The first step in this analysis is to eliminate the null hypothesis, namely that the trends in the running 12-month total charts are simply artefacts of spike events due to winter infectious outbreaks or periods of extreme heat or cold. Table 1 displayed all the relevant information to eliminate this hypothesis.

Table 1: Maximum monthly spike difference and trim value, and maximum possible effect of a spike event on the running 12-month total, with a frequency of 1 in 13 years

State	Maximum monthly spike	Date for maximum	Trim	97.5% CI Poisson†	Maximum possible contribution
NSW	686	Jul-07	380	126	1.4%
Vic	447	Mar-11	249	107	1.3%
Qld	396	Jul-07	189	92	1.5%
SA	213	Mar-13	109	64	1.8%
WA	278	Jul-12	102	63	2.1%
Tas	86	May-10	46	37	2.0%
NT	32	May-09	15	18	3.5%
ACT	52	Aug-03	25	23	3.5%
Aust	1,795	Jul-12	981	214	1.2%

Footnote: The value of the trim point is set at the 90th centile in each State. † 97.5% Confidence Interval (Poisson) calculated on average monthly deaths in last six years. The maximum spike value (before trimming) over the 13 year period was matched to the running 12-month total to calculate the maximum possible effect of a spike. Vic= Victoria, WA= Western Australia, ACT= Australian Capital Territory, Qld= Queensland, Tas= Tasmania.

The ‘maximum monthly spike’ column presented the highest value in each State for the difference between one month and the next. This was followed by the date (which was different in every State but usually in the winter) and then the ‘trim’ value (the value of the 90th centile). The trim value was subtracted from the monthly spike to give the actual adjusting factor used in all the following analysis. The 97.5% confidence interval (CI) was the value of a ‘spike’ arising from chance variation based on Poisson variation around the monthly average deaths. The trim had to be higher than the 97.5% CI since we were dealing with genuine spike events. This occurred in all but the two smallest States where the Trim and the 95% CI were roughly similar. The final column displayed a hypothetical maximum possible contribution from the maximum spike (without applying the trim value) to a running 12-month total. This inflated value was well below any deviation or step-like feature observed in this study – which in any case used adjusted data to avoid the contribution from such spikes. In addition, the contribution of a spike event in a running 12-month total did not lead to ramp-like trends. This issue is addressed

further in the discussion. However, the null hypothesis can be categorically rejected.

The monthly trends in Figure 1 indicated evidence for possible peak years, plus underlying growth in deaths over time. To demonstrate the nature of the peaks in death, the running 12-month total for Australia and several states have been corrected for both spike events (as above) and growth using a third order polynomial and are presented in Figure 2.

To calculate the polynomial, the peaks were first removed and the number of deaths in the troughs were used to estimate the trend upward over time (see supplementary material Table 1 and Figure 2). The actual (adjusted for spike values) and expected deaths were then compared and the difference calculated as a percentage deviation. The polynomial method is seen to be adequate in that there is no residual trend in any direction in the deaths relative to the trend (other than the unexplained peaks and troughs).

Four large deviations away from the trend line could be seen in the years 2002/2003, 2007/2008, 2010/2011 and 2012/2013, although depending on the spatial unit the 2010/2011 and 2012/2013 peaks could be merged into each other.

There was evidence for timing differences regarding the onset of each step-event and differences in the magnitude (percentage change) of each event in different States. These deviations also showed evidence of multi-modal behaviour which would be

expected from relatively slow spread throughout a relatively dispersed population structure and resulting clustering effects at whole State level. Charts for each State are available in Figure 3 in the supplementary material.

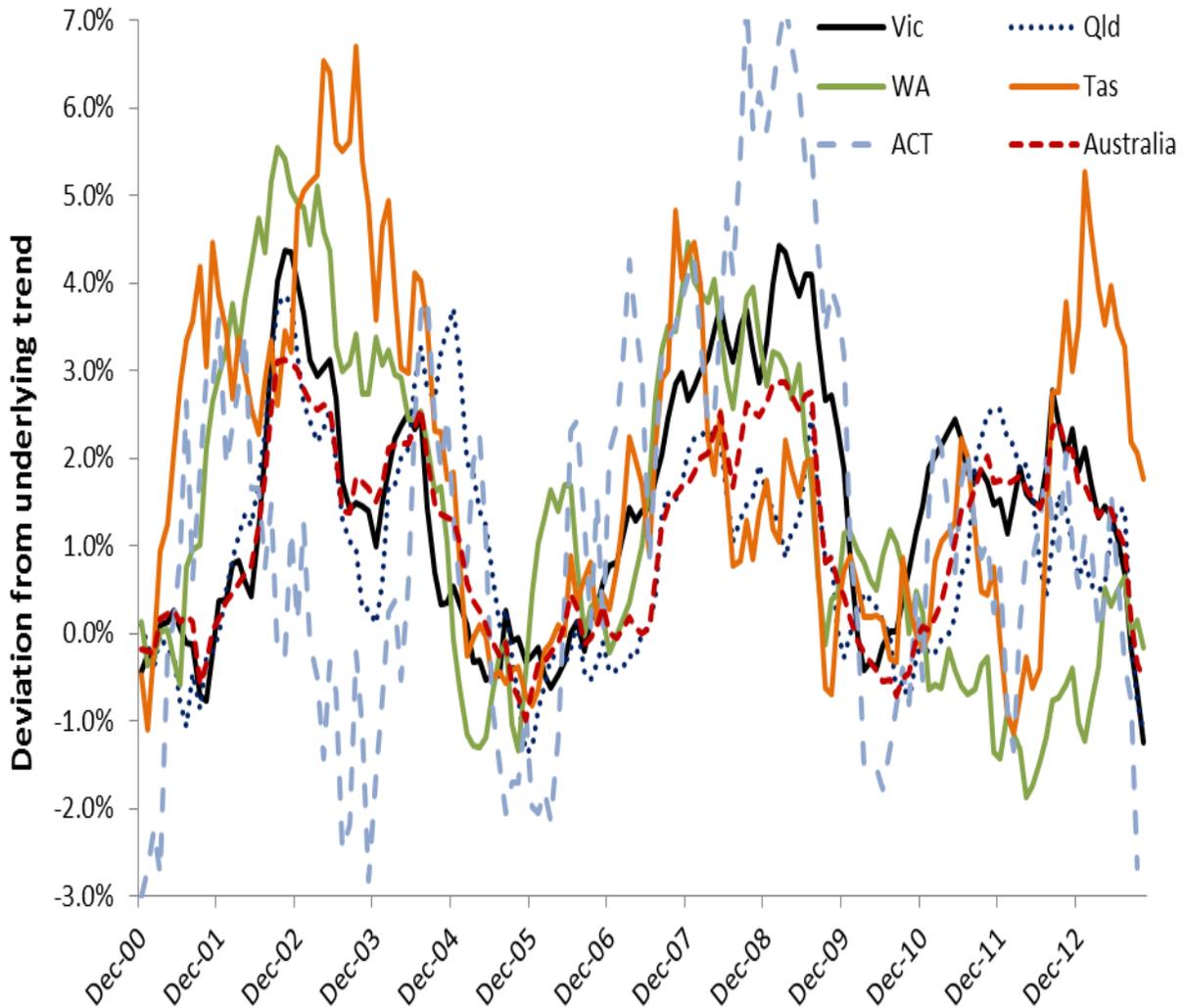


Figure 2: Growth-adjusted running 12-month totals for deaths in several states and for Australia.

Table 2 presents a summary of results for the most recent outbreaks. For the sake of simplicity only the first of any multi-modal features are documented, i.e. the leading edge of the composite effect observed at State level aggregated numbers. The values for the percentage increase shown in Table 2 were

derived from comparing 12-month blocks of data each side of the step-like change, i.e. the before and after situation. It has the limitation that it is assumed that there are no unusual events in the 12 months prior to the step-change, however, it seems that on most occasions this holds true.

Table 2: Summary of results for the last 4 events

State	Latitude [†]	Deaths [‡]	2001/2002		2007/2008		2009/2010		2012/2013	
			Onset	Increase	Onset	Increase	Onset	Increase	Onset	Increase
Australia		137,740	Oct-01	4.10%	Feb-07	4.10%	Sep-10	3.60%	Jun-12	>2.4% H
NSW	33.9	47,240	Mar-02	3.80%	Jun-07	3.70%	Oct-10	5.50%	Dec-11	3.8% H
Vic	37.8	34,270	Nov-01	5.60%	Nov-06	4.10%	Jun-10	4.40%	Sep-11	>2.7% H
Qld	27.5	25,370	Oct-01	6.00%	Feb-07	6.10%	Nov-10	5.00%	Jul-12	3.00%
SA	34.9	12,300	Jul-02	2.40%	Jun-07	4.30%	May-10	2.80%	Jun-12	3.70%
WA	31.9	11,980	Jul-01	6.90%	Jan-07	6.70%	Oct-09	2.90%	Dec-11	5.00%
Tas	42.9	4,080	May-02	4.60%	Nov-06	7.00%	Oct-09	3.70%	Feb-12	7.80%
NT	12.5	960	Sep-01	5.70%	May-07	11.70%	Aug-10	7.70%	Jul-12	4.10%
ACT	35.3	1,550	Aug-03	9.90%	Apr-06	10.50%	Jul-10	6.90%	Mar-12	3.80%

[†]Latitude of capital city, [‡]Average deaths per annum 2000 to 2013, [†] Increase estimated from step-like reduction after the event. NSW= New South Wales, Vic= Victoria, Qld= Queensland, SA= South Australia, WA= Western Australia, Tas= Tasmania, NT= Northern Territory, ACT= Australian Capital Territory.

A random walk type process within the larger State geography appears to determine the apparent onset when looking at State level data. While the percentage increase shows variation between each event, the maximum increase appears to increase with decreasing deaths, i.e. smaller population or fewer social networks for disease spread. All percentage increases are statistically significant at the 95% confidence interval, except for the 2 smallest increases in the ACT and NT (least number of deaths).

Figure 3 investigates the effect of size on the apparent maximum increase seen for each state. As can be seen in Figure 2 every state does not experience the full extent of potential increase on every occasion and hence the maximum increase during the 12-year period has been selected to reveal this potential. As can be seen all states lie reasonably close to a power law function,

except for the low value seen for South Australia and the higher value seen for the Northern Territory, where the population is largely clustered in Darwin.

Figure 4 investigates if initiation occurs more frequently at particular times of the year. As can be seen, initiation occurs most frequently during the winter months. The power law function in Figure 3 was then used to adjust all states to the equivalent to 10,000 deaths; however there was insufficient data to determine if there was a statistically significant difference in the percentage increase throughout the year.

After correcting for the effect of size (Figure 3), neither the date of onset or percentage increase shows any correlation with latitude (results not shown), i.e. time of year rather than latitude seems to be the more important factor behind spread of the agent.

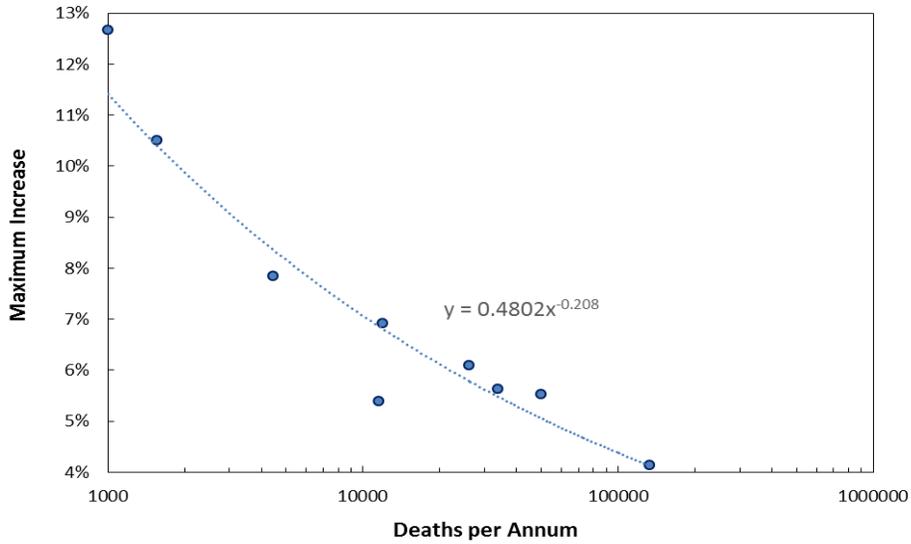


Figure 3: Maximum step-like increase in each State and number of deaths as a measure of size

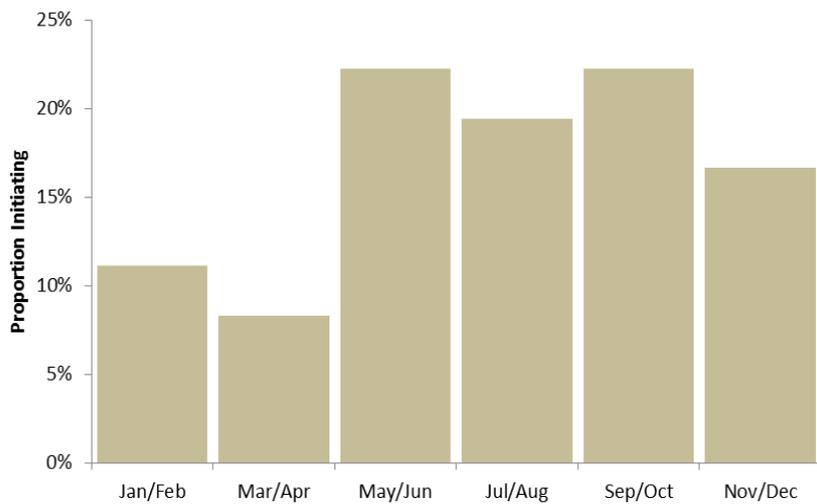


Figure 4: Month of initiation for 4 events/outbreaks

The issue of spatial spread at LGA level is investigated in Figure 5. As indicated in the Methods section the difference between one year and the next can be transformed into standard deviation equivalents assuming Poisson statistics. This allows percentage differences (which vary with size due to underlying Poisson effects), to be expressed as standard deviation equivalents. Hence anything with less than 1 standard deviation

difference can be considered to have arisen from chance alone. Greater than 3 standard deviation (STDEV) difference is highly likely to indicate that the step-change occurred very close to the start of a calendar year, while > 2 STDEV probably indicates commencement in the first half of the year. Likewise < -3 STDEV indicates that the step-down has occurred very late in the previous calendar year or at the start of the

calendar year in question, etc. In Poisson statistics any value beyond ± 2 STDEV lies outside the 95% confidence interval and can be assumed to arise from special causes.

Evidence for spatial spread can be discerned. For example, the large positive shift starting in 2006 appears to move across the LGA's within Australia in 2006, 2007 and 2008. The 2010 event spreads in 2010 and 2011. As an example, the LGAs showing greater than ± 4 STDEV step-like changes are listed in Table 3 in the supplementary material. It should be noted that 92% of Australian LGAs show less than ± 0.5 STDEV equivalent to the slope of the trend line for change in deaths per annum between 2001 and 2013, and hence the step-like events are largely unaffected by any long-term background trends in deaths. The clear message is that the method is detecting highly statistically significant step-up and step-down events in the context of spatial spread. Influenza

outbreaks or similar can be discounted simply because large step-up and step-down events occur in the same year within different parts of Australia consistent with the observed relatively slow spread seen within the UK and across Europe. Additional analysis for all LGA with greater than ± 4 standard deviation equivalent step-change is presented in Table 2 in the supplementary material.

From Table 2 it can be seen that in Torres Strait Island and the Northern Peninsular area the 2010 event occurs very early in 2010 and remains high for the whole of that year and is then followed by a corresponding step-down to the usual level of deaths. However in Brisbane (a very large urban area) the 2007 outbreak probably occurs mid-way through 2007 and continues into 2008, with the step down in 2009. This sequence has been confirmed by a study of emergency medical admissions in Queensland.³⁴

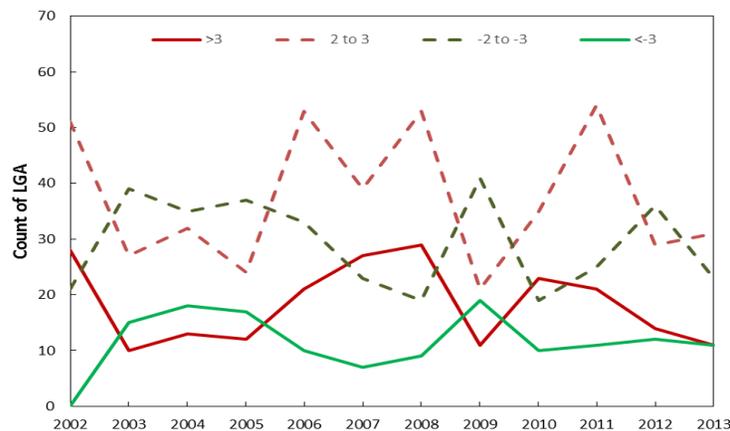


Figure 5: Large positive and negative step-like shifts observed in Australian Local Government Areas (LGA) expressed as standard deviation (STDEV) equivalents

DISCUSSION

Before discussing the implications of the various Figures and Tables in more

detail it is necessary to understand why the data have been analyzed in this particular

manner and why age-standardization has not been applied.

In the field of actuarial science it has become increasingly apparent that the current models are failing to capture non-standard or unexplained behaviour in the trends in death (all-cause mortality),⁴⁰ and that this anomalous behaviour may partly involve age cohorts.⁴⁰ Put simply, the periods of higher death revealed in this study should not exist. The usual explanation is that periods of higher death are due simply to the spike events occurring in some winters and/or to periods of extreme heat or cold. By their very nature these are short-term and temporary events. There is some evidence to suggest that a short-term period of higher deaths in winter will be compensated for by a short-term period of lower deaths in the following summer,¹¹ and so, in theory, the net effect should not unduly affect a running 12-month total. Something like a very large influenza epidemic may override this general rule, however, it is generally accepted that even influenza does not have large scale effects which would endure for 12 consecutive months. The null hypothesis that the effects observed in this study are due to spike events has been shown to be false in the results section.

However, in a running 12-month total the effect of a spike event, such as an influenza epidemic, does not create a ramp-like trend (as observed in this study), but creates a plateau or rectangle shaped feature in the running 12-month series. For example, if there are an average of 100 deaths per month and in one month an outbreak of influenza leads to 160 deaths, i.e. 60 influenza-attributable deaths. Before the 'spike' influenza event there are 1,200 deaths per 12 months in a running total. The spike of 60 extra influenza deaths then results in a running total of 1,260 deaths which endures for 12 months, i.e. the plateau

or rectangle shaped event in the running total. At the end of 12 months the spike drops out of the running total which then reverts from 1,260 back to 1,200. Visual inspection of Figure 3 in the supplement clearly shows that the resulting trends (after correcting for the effect of spike events) are a mix of a few small residual plateau features - where the method has failed to entirely remove the effect of the spike events - plus additional ramp-like features arising from these unknown and seemingly infectious-like events.

However it has been observed that initiation of one of these infectious-like outbreaks just before a spike event can accentuate the magnitude of any spike event(s) in the following winter.⁴¹⁻⁴² This possibility requires further studies. The key message is that the ramp-like features are the result of these 'anomalous' and previously unexplained infectious-like events.

The second question to address is why age standardization has not been applied? The answer to this question has a two-fold aspect. Firstly, time-series in deaths (all-cause mortality) are normally expected to follow continuous trends. An example of these continuous trends can be seen in the Office for National Statistics (ONS) forecast trends in death at Local Authority level in England and Wales where there are no large single year changes.⁴³ Hence the analysis of trends in death over 10 to 15 year periods of time (as in this study), does not need to involve age standardization since anticipated trends do not show evidence for large shifts over very short periods of time (as implied by the step-like changes leading to periods of higher death revealed in this study).

The second aspect to this issue lies in the fact that during these infectious-like events it has consistently been observed that both deaths and medical admissions show curious single-year-of-age specificity.^{26-28, 30} Age-standardization typically involves the

use of 5-year age bands, and this intrinsic single-year-of-age behavior appears to invalidate the hidden assumptions behind the use of 5-year age bands. Such single-year-of-age specificity has been proposed to arise from the phenomena called 'antigenic original sin'.²⁷ In antigenic original sin, infection with a series of strains of the same agent is known to produce cohorts of patients with patterns of antigenic specificity, which may or may not be beneficial when exposed to a new strain of the same agent.⁴⁴⁻⁴⁷ It is for this very reason that influenza vaccines, for example, are multivalent and contain a mix of antigens likely to mimic the influenza strains most likely to be prevalent in the coming winter. Occasionally this antigenic mix does not reflect the mix of influenza strains that actually emerge in the following winter, and in certain persons this can actually lead to increased sensitivity to influenza resulting in hospitalization.⁴⁸

The authors own unpublished analysis of medical admissions during the 2008 event in one part of Australia showed this same single-year-of-age specific behaviour, and this observation led to the more detailed studies conducted in the UK. Hence on this basis, the use of traditional 5-year age band standardization is not recommended, and the pragmatic approach adopted in Figure 2 and Figure 3 allows the actual running 12-month total to be compared to an estimate of the continuous trend in running 12-month total deaths which may arise in the absence of these step-like events.

Returning to the Tables and Figures, the analysis has attempted to reveal a time series of previously hidden periods of higher death in Australia which coincides with events documented in the UK and the 27 EU countries. The 2009/2010 event is only partly evident in the UK¹⁷ and Europe (unpublished) but is strongly evident in Australia (Figure 2). As is the case in

England and Wales, the 2009/2010 event can partly obscure the 2012/13 event and the percentage increases in Table 1 for 2012/2013 may be underestimated. This arises due to a weakness in the running 12-month total methodology, namely, it relies on a 12-month period prior to the step-like increase which is free from extraneous effects. However, for the moment it has served the purpose of demonstrating these events which can now be further investigated using alternative methods perhaps similar to the growth-adjusted trend demonstrated in Figure 2, or other more sophisticated approaches.

The effect of size (Figure 3), has also been documented in the UK and Europe for both deaths and medical admissions, and appears to arise from the slow spatial spread of the agent.^{17,21,30} The resulting range in initiation dates leads to a situation where peaks and troughs can average out as the spatial unit gets larger. This is an outworking of the effect of scale in the modifiable areal unit problem (MAUP).⁴⁹ The fact that not every event achieves its maximum possible increase in each State requires further investigation which could reveal roles for weather and climatic influences on modulating the spread of the agent in different locations.

The role of month of the year in the apparent percentage increase is some interest. As opposed to the northern hemisphere the winter in Australia occurs in June/July, and Figure 4 demonstrates that, as in Europe and the UK,^{17,21,30} the point of initiation most commonly occurs (but not exclusively) in the winter months. This winter preference strongly suggests a common infectious/immune etiology.⁵⁰ Further study using smaller geographic areas will be needed to determine if there is a relationship between time of year and percentage increase in Australia. While it requires around 300 deaths in the spatial

unit to demonstrate statistically significant increases, it is possible to demonstrate the point of onset with only 30 deaths or medical admissions. Analysis of the timing of the step-like increases across the 565 Australian local council geographies should be adequate to demonstrate spatial spread. This can be achieved using monthly or weekly data.

Regarding the role of season, it was noted that the 2012 outbreak in the UK had very little effect on most of London and some other parts of the UK.¹⁷ The outbreak appears to have been delayed to around June of 2014 in these locations, and initiation is at the start of summer rather than the more common winter initiation.¹⁷ Other partial outbreaks have also been observed in the UK,²¹ and there are mechanisms regulating spread of this agent which need to be understood.

With respect to the relationship between size of the spatial unit (number of deaths) and percentage increase Figure 3 presents a power-law relationship which is approximately the same as that observed across Local Authority (LA) areas in the UK – there are roughly 1,000 deaths per LA in the UK,^{17,21,30} i.e. it is the same phenomena and can be transferred between countries (as observed in Europe). It will be appreciated that the population of Australia is concentrated mainly in the capital cities and surrounds, and it is this effective population density which facilitates spread of infectious agents.

Spatial spread within the UK has been demonstrated at both local authority and small area levels and similar spatial spread can be seen between LGAs in Australia (Figure 5 and Table S2). Explanations based on weather patterns, government policy or societal factors can be discounted and infectious spread is highly likely.

The link with emergency medical admission requires comment. This link is a key feature of the events in the UK and has already been inferred by the link with bed

occupancy and medical admissions seen to occur during the times at which deaths increase in Australia.^{34,38} Periods of high bed occupancy have been consistently observed to occur during these presumed infectious events.^{21,26,31,34} This study has used deaths as an indicator, however, deaths are the top of a disease apex. Hence the relevance of the observation of 10 extra medical admissions per extra death, and probably 100 extra primary care consultations per extra death,^{20,52} along with increases in GP referral for a consultant opinion.^{18,35}

Lastly, we need to address the issue as to why these events have remained undiscovered for so long? Table S2 clearly shows that very large (greater than 4 standard deviation equivalent) step-like events are very common and occur in 18% of all LGAs. A further 41% contain events between 3-4 standard deviation equivalent. In the absence of a conceptual model explaining their existence, it would appear that such events have simply been assumed simply not to exist, and hence no one went looking for them. It is only by the application of a running 12-month total that their existence emerges from the confusing monthly patterns (as in Figure 1). The message for epidemiologists must be, take nothing for granted.

CONCLUSION

In conclusion, an infectious-like phenomena seems to exist across the western world with evidence for relatively slow spatial spread over a period of around 2 years. A further outbreak in 2014 has recently been documented to occur in the UK.³⁵ Hospital bed pressures appear to be directly linked to these events seemingly via a relationship between end of life and bed occupancy,⁵¹ and also by the 10 extra medical admissions per extra death.⁵² Analysis using the Australian 565 Local Council geographies or the 185

Local Government Areas with greater than 30 deaths per annum should be sufficient to demonstrate infectious-like spread of deaths and medical admissions using monthly or weekly data (preferred). Larger areas such as Brisbane will need to be analysed at suburb level. Demographers, actuaries, epidemiologists, clinicians and public health researchers in all Countries should investigate these events with some urgency as it is highly likely that they extend beyond Western countries.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

ACKNOWLEDGEMENT

We are grateful to thank all people who kindly helped us in conducting this research.

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How to cite the article: Jones R.P. A time series of infectious-like events in Australia between 2000 and 2013 leading to extended periods of increased deaths. *Int J Epidemiol Res.* 2015; 2(2): 53-67.