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The case for recurring outbreaks of a new type of infectious disease across all parts of the United Kingdom

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The case for recurring outbreaks of a new type of infectious disease across all parts of the United Kingdom

Abstract

The higher than expected increase in medical emergency hospital admissions has been a matter of debate for many years. While regular growth of around 1.0-1.5% per annum may be expected due to demography recent evidence has emerged from England and Scotland the increase over time appears to occur in concentrated spurts of growth at an interval of three to six years resulting in an approximate 10% step-like increase in certain medical and mental health related diagnoses. A characteristic time-related pattern in admissions then follows each step-increase. Outbreaks of a previously uncharacterised infectious disease have been proposed to account for this behaviour. Evidence is presented to show that simultaneous outbreak(s) across the remainder of the UK (Wales and Northern Ireland) are occurring with step-like increases in a similar range of diagnoses. The infectious agent is proposed to be a member of the group of persistent viruses and appears to show some form of collective switch to a dormant state around 3 ½ years after the initial outbreak. This behaviour accounts for the unique pattern of hospital admissions seen over time and is so strong that any underlying demographic trends are overwhelmed. This particular pattern of admissions will have uniquely profound financial effects upon the cost pressures experienced within the health services.

Introduction

In the process of an infectious outbreak susceptible individuals undergo chance exposure to one of around 1,400 infectious species [1] and suffer a range of acute and potentially chronic symptoms [2-3]. The issue of susceptibility and severity of the resulting illness depends on the exact infectious agent, mode of infection and on the general state of the immune system in the exposed individual.

All individuals have the potential to be in some degree of immune impairment at the point of infection due to a wide variety of factors such as age [4], prior strenuous physical activity [5], stress [6], war and trauma [7], depression [8], exposure to environmental toxins [9], poor nutrition [5, 10], acid/base imbalance [11], season of the year (including vitamin D levels) [12-13], existing autoimmune disease(s) [14], genetic factors [15], or the presence of existing persistent viral infection [16-18]. Subsequent secondary opportunistic infection(s) can then occur [19].

Over 200 viruses are known to infect humans [1] although the list is growing each year [1,20]. Of these a set of persistent viruses (HIV, Hepatitis, Epstein Barr, etc) produce a range of immune impairments [17-18, 21-23]. To complicate the picture it has recently been proposed that a wider range of viruses including influenza may be able to remain in the host in a dormant state [24] with as yet unknown effects on immune function. In this respect Cytomegalovirus (CMV) reactivation is proposed to be part of a change in the immune risk profile (IRP) which marks the hastening of biological ageing near the end of life [25-27].

An unfortunate by-product of our understanding of infectious diseases is perhaps to view them as functional silos. Hence the concept of a virus capable of producing the equivalent to a commonly infectious immune impairment has not been thought possible, i.e. capable of initiating an international outbreak similar to what may be called an 'epidemic' of prolonged 'poor health'.

However, research has suggested that a new type of infectious outbreak may be occurring at intervals of three to six years [28-36]. Each outbreak is characterised by an approximate 10% step-increase in acute hospital admissions for particular medical and mental health conditions (as opposed to surgical or trauma). There is a specific increase in the prevalence of a range of diagnoses which appear to have immune function impairment as the fundamental mechanism for the ultimate expression of a hospital admission. Hence an increase in admissions for either infection or inflammation related conditions [34-36]. The most recent of these outbreaks occurred in England & Scotland around September to November of 2002 and 2007 [31-36].

Hence, in opposition to the traditional view of a disease outbreak as a functional silo, i.e. influenza, salmonella, measles, etc, with a defined set of clinical manifestations we now have the possibility of a single entity which causes multi-dimensional effects via specific or wider ranging immune function impairment(s). In layman's terms such an outbreak could be said to be the commonly infectious equivalent to HIV (although presumably via a different mechanism) in that a range of opportunistic secondary infections occur and biological aging appears to be accelerated [21,23,37].

The administration of health care in the UK is via four health departments in the countries of (2008 population in brackets) England (51.5 million), Scotland (5.2 million), Wales (2.9 million) and Northern Ireland (1.8 million). The relevance of this to the current study is that we are dealing with independent health care systems, each holding its own healthcare data; operating using different budgets, management structures, styles and policies, and having a different emphasis on the balance between primary and secondary care. Hence only a genuine infectious outbreak would be capable of simultaneously increasing medical hospital admissions in all four countries [35]. This is especially relevant for Northern Ireland which is separated from the remainder of the UK by the Irish Sea, i.e. we are dealing with typical infectious transfer via air and sea transport [38].

Evidence has already been presented to demonstrate a series of outbreaks in England and Scotland going back to 1990 [28-36]. To demonstrate that such a wide-spread infectious outbreak has indeed occurred, the situation in Wales and Northern Ireland must be compared and shown to exhibit the same behaviour.

Methodology

Data for Northern Ireland was kindly provided by the Information and Analysis Directorate of the Department of Health, Social Services and Public Safety (DHSSPS).

Hospital admissions in Wales for the financial years 1999/00 to 2008/09 (at the level of main specialty and principal diagnosis) were downloaded from the Patient Episode Database for Wales (PEDW) website

(<http://www.infoandstats.wales.nhs.uk/page.cfm?orgid=869&pid=41010&subjectlist=Main+Specialty&patientcoverlist=0&period=0&keyword=&action=Search>;
<http://www.infoandstats.wales.nhs.uk/page.cfm?orgid=869&pid=41010&subjectlist=Principal+Diagnosis+%283+character+detail%29&patientcoverlist=0&period=0&keyword=&action=Search>).

Data was analysed in the most appropriate way to demonstrate that a step change had occurred, i.e. paired before and after comparison, graphs, running annual totals, etc as per previous studies [34].

Results

A true infectious outbreak would be expected to occur across the whole of the UK and will ignore the artificial boundaries between different regions. The existence of unique step-like increases in admissions in England and Scotland has been documented [29-36]. Evidence for similar step-changes in Wales and Northern Ireland will now be presented.

Northern Ireland

Data covering monthly emergency admissions to the medical group of specialties and quarterly admissions to a group of 90 ICD-10 diagnoses identified from the 2002 and 2007 outbreaks in England [31] are given in Figs. 1 and 2 respectively. The two step-like changes occurring at a point after September of 2002 and 2007 can be clearly seen. Note that both Fig. 1 and 2 are running annual totals, i.e. each point in the chart is a progressive moving sum of the previous 12 months or 4 quarters [34]. Running annual totals are exceedingly useful in situations where the monthly/quarterly data has a highly seasonal element [30]. However in such a chart the point of initiation of a step-like change occurs at the start of a ramp-like feature and the full extent of the step change is seen at the point one year on from the origin of the step-change, i.e. the running total at this point contains 12 full months of data after the step-change [34].

Using the monthly data for medical group admissions (Fig. 1) places the onset of the two step changes at around November 2002 and November 2007 which appears to be slightly later than that identified in England and Scotland [34-35]. In 2004 it was estimated that Northern Ireland received around 2 million visitors per annum from the UK and elsewhere (http://www.4ni.co.uk/northern_ireland_news.asp?id=25291), hence, the opportunity for the spread of an infectious disease via air and sea travel is clearly feasible [38].

Of equal interest to the step-up in admissions occurring at the onset of each outbreak is an apparent step-down in admissions occurring about 3 ½ years later. This is most readily seen in Figs. 1 and 3 and commences around November 2001 and March 2006. Recall that a running total will give the appearance of a ramp downwards at the point where a step down has occurred. Such a step down could signify a collective process, where the infectious agent is either cleared from the host population or, more likely, switches to a dormant state. Such a phenomenon can be seen in the underlying data used in previous studies relating to England and Scotland, however, the significance of this step-down was not fully appreciated.

Wales

Analysis of data for Wales at specialty level shows similar approximate 10% step changes in medical admissions as in England for the 2002 and 2007 outbreaks (Fig. 4). Analysis of the spectrum of diagnoses associated with changes in admissions around the two outbreaks show that Wales is potentially characterised by around half of the diagnoses associated with infection and inflammation identified for England [36]. However, this is probably more to do with the fact that the population of Wales is only 6% of that of England and hence the smaller numbers make it far harder to demonstrate that a statistically significant shift has occurred at the level of a single diagnosis. It is also possible that additional 20-30 diagnoses may be associated with each outbreak in Wales. These diagnoses may not have passed the high level of statistical significance required when analysing the English data [36] or may reflect different diagnostic processes in the far smaller collection of Welsh hospital sites [39].

Note that the peak in medical admissions in the 2005/06 financial year is also reflected in the data for Northern Ireland (Fig. 1) – although to a lesser extent than in Wales. This peak is almost absent in the Scottish data [32] and presumably reflects the effects of local weather and other environmental conditions. A perusal of the Welsh data relating to primary diagnosis shows that this appears to have been related to an outbreak of illnesses such as respiratory and urinary tract infection.

Discussion

This study has confirmed the existence of a step-like change in medical admissions across the whole of the UK. Slight differences in timing appear to apply with earliest onset in Scotland followed by England then Northern Ireland. Judging from the shape of Fig. 4 the most recent outbreak in Wales may have commenced toward the end of the 2007/08 financial year, however, the availability of monthly data would be needed to confirm this.

The availability of monthly and quarterly data for the medical group of specialties in Northern Ireland reveals that each outbreak initiates what is likely to be a complex time-series of changes in the incidence of various diagnoses. Hence initial infection will herald a set of immediate diagnoses which will be followed by diagnoses characteristic of more chronic exposure. This is similar to the conclusions drawn from a study of diagnoses in England [36]. It is possible that the effects are far more complex than as yet realised.

Fig. 3 for Northern Ireland uses a set of diagnoses derived from a study of English data [36]. In this previous study around half of the diagnoses showed high background growth, however, this is not evident in the data for Northern Ireland. It would therefore appear that, as suspected, certain diagnoses within the English data set are ‘contaminated’ with increasing numbers of emergency department (A&E) attendances which have been counted as zero day stay emergency ‘admissions’ due to the particular circumstances surrounding the 4 hour A&E target [40-41].

A final issue of interest relates to the seasonal pattern (summer/winter) commonly seen in emergency admissions [30-33]. It should be appreciated that a 10% step change in the case mix of medical admissions is highly likely to alter the seasonal pattern in that particular diagnoses will be more sensitive to the wider environment than others. Such a change in the seasonal pattern of bed demand was observed after the 1993 outbreak [29] and can be discerned in the monthly data for Northern Ireland (Fig. 3). This is especially true for the period where the collective switch to viral dormancy is postulated to occur. The monthly data in this period shows considerably diminished seasonal behaviour. Indeed a study of Fig. 3 appears to suggest that each outbreak is the primary factor leading to the observed highly seasonal behaviour typically expected for the medical specialties and in the short periods of dormancy the system reverts back to a state of both lower admissions and diminished seasonal behaviour which would otherwise be considered to be ‘abnormal’. It is possible that the behaviour during the ‘dormant’ period is consistent with the expected underlying 1.0-1.5% per annum growth which would be due to the effect of demographic change alone.

Viral dormancy has been recently proposed to be of greater importance than previously realised [24]. Indeed the influenza virus provides ample evidence to show that long periods of viral dormancy are possible. In this respect influenza has recently shown a nine year period of such low activity that widespread or collective dormancy is a likely mechanism to explain this behaviour. A similar extended period of low influenza activity occurred between 1879 and

1889 when a new sub-type apparently emerged similar to the emergence of swine flu in 2009 [42].

At this point it is worth while to pose the question if a step change in immune function is possible? In this respect HIV infection provides a useful model and it has been proposed that the majority of immune impairment occurs in the early days of infection [37]. Given the incredible intricacy and complexity of immune function [43-46] it is entirely feasible that AIDS-like immune impairment could be triggered via a wide variety of mechanisms.

Hence to summarise our knowledge of this infectious agent arising from this and previous studies [28-36]:

1. It is a persistent infection (most probably viral)
2. Immune function is the specific target with consequent increase in diagnoses related to infection and inflammation
3. Each outbreak leads to an approximate 10% step-like increase in acute medical admissions and knock-on effects to other health care costs
4. Time-dependant changes in the pattern of diagnoses occur
5. The effect increases with age and may show stronger effects against women
6. Approximately 3 ½ years after the initial outbreak there is a step down in admissions (viral dormancy) giving rise to a period of lower activity and cost before the next outbreak
7. The effect on admission is so strong as to by-pass underlying demographic growth
8. Outbreaks have probably occurred for at least the past 25 years
9. Spread across the entire UK implies the possibility of an international ‘pandemic’

It can be appreciated that a step-increase in inpatient medical costs is only the apex of wider ambulance, emergency department and primary and community health care costs. For this reason significant and unexpected step-changes in health care costs should therefore be a feature of those countries where such an outbreak has occurred. However health care costs are an indirect measure since in most countries the annual cost is partly constrained by government budgets and consequent reactive cost cutting measures both in-year and in later years.

In respect to the above it has been recently proposed that the cycle of surplus and deficit seen within the NHS in England is a by-product of the periodic infectious outbreaks discussed here [47-48]. Indeed the shape of the admission profile over time appears to explain the cost pressures experienced after the past two outbreaks. The drop in admissions some 3 ½ years after the initial outbreak appears to lead to a ‘lull before the storm’ where overall cost pressures appear to evaporate. An abrupt 10% increase in medical costs then ensues which appears to come ‘out of nowhere’. Indeed the heroic cost cutting measures seen in both acute and primary care during 2010 and apparent knee-jerk ‘cost-cutting’ schemes proposed by the Department of Health are most likely to be the result of the as yet un-acknowledged cost pressure arising out of the 2007 outbreak [47-49]. Tentative evidence has also been given to suggest that a similar pattern of financial pressures may have also occurred in the USA [50].

Attempts to solve the ‘problem’

The view that the increase in admissions is largely a demand management problem (i.e. due to system deficiencies which can therefore be remedied), has led the UK and other healthcare

systems to invest considerable time and money into implementing solutions based on this premise, i.e. GP referral triage and a variety of admission avoidance schemes [51-54]. This does not imply that demand management strategies are ineffective or not required; however, a recent Audit Commission report for England concluded that whatever demand management strategies were in place prior to the most recent 2007 step-change were ineffective in preventing the (full-year) increase in hospital activity seen in 2008/09 financial year [55]. Hence if the infectious disease hypothesis is correct, such demand management schemes may be largely of greatest effect in the years between the periodic outbreaks and may largely affect the zero day or short stay component of inpatient demand but cannot prevent the outbreak *per se*, i.e. we are treating symptoms arising from the outbreaks and not root causes.

It would appear that this infectious outbreak and the ensuing changes in the pattern of admissions may prove to be the single most influential factor influencing the financial pressures faced by healthcare [48-50,56] and the resulting perceived success, or otherwise, of schemes which have been initiated at different points in the cycle of each outbreak.

Further Research

It is now possible to formulate a series of research questions, which should act to direct future research in this area:

- Why the 1990 and 1999 outbreaks were mainly confined to Scotland, i.e. what are the mechanisms which regulate the onset of an outbreak and its wider spread?
- In the paired 1990 and 1993 outbreaks in Scotland and the 1993 and 1996 outbreaks in England; what factors acted to initiate a new outbreak after just 3 years and thereby circumvent the apparent collective switch to viral dormancy?
- How does the apparent collective switch to viral dormancy occur after 3 ½ years?
- Is there an autoimmune component to the outbreak?
- To what extent is the effect of this outbreak seen in primary care?

Hopefully the body of evidence to establish the existence of this new kind of infectious outbreak will be sufficient to initiate the wider research required to begin to address some of these questions.

Conclusions

Evidence has been presented to confirm the existence of a previously unrecognised type of an infectious outbreak. While additional studies will be required to confirm these findings it would seem that there is sufficient evidence to initiate the search for the actual infectious agent and to investigate the possibility of wider international outbreaks.

If we are to draw parallels with the initial identification of AIDS and the ensuing search for HIV we may presume that the isolation of the causative agent may be more challenging due to the commonly infectious element, i.e. in the absence of a readily identified host group. Elderly females may represent a reasonable starting point. Potential links to the IRP and related CMV re-activation should not be overlooked [25-27].

It would seem possible that the availability of antibiotics and wider access to acute care prevents the premature death of individuals infected with this agent and that the time-

dependant wider immune impairment may then lead to ultimate decease via one of a number of more chronic conditions.

The wider implications of this study to the areas of health care policy, public health medicine, the nature of health care costs, structure of the tariff for hospital services, anti-viral therapies and potential vaccine development should be readily apparent.

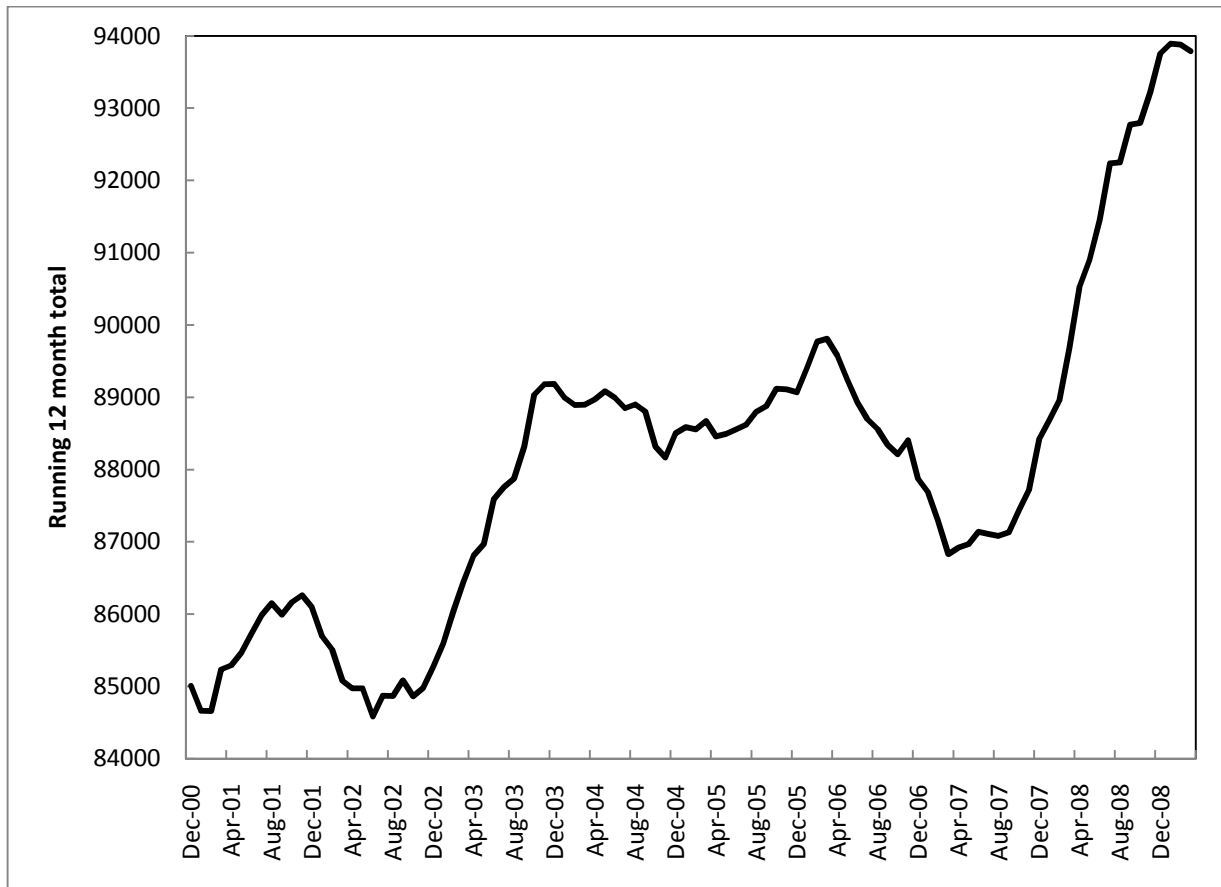
References

- [1] Woolhouse M, Gowtage-Sequeria S. Host range and emerging and re-emerging pathogens. *Emerging Infectious Diseases* 2005; **11(12)**. www.cdc.gov/ncidod/EID/vol11no12/05-0997.htm
- [2] Bergmire-Sweat D, Schlegel J, Marin C, Winpisinger K, Perry C, Sotir M, Harris J. Multistate outbreaks of human Salmonella infections associated with exposure to turtles - United States, 2007-2008. *MMWR Weekly* 2008; **57(3)**: 69-72
- [3] Voisset C, Weiss R, Griffiths D. Human RNA “rumor” viruses: the search for novel human retroviruses in chronic disease. *Microbiol Molec Biol Rev* 2008; **72(1)**: 157–196
- [4] Mayor S. Unravelling the secrets of ageing. *British Medical Journal* 2009; 338: 136-138
- [5] Gleeson M, Niemann D, Pedersen B. Exercise, nutrition and immune function. *Journal of sports sciences*. 2004; **22**: 115-125
- [6] Kiecolt-Glaser J, Glaser R, Shuttleworth E, Dyer C, Ogrocki P and Speichler C. Chronic stress and immunity in family caregivers of Alzheimer’s disease victims. *Psychosomatic Medicine*. 1987; **49(5)**, 523-535.
- [7] Ironson G, Wynings C, Schneiderman N, Baum A, et al. Posttraumatic stress symptoms, intrusive thoughts, loss and immune function after Hurricane Andrew. *Psychosomatic Medicine*. 1997; **59(2)**, 128-141.
- [8] Kiecolt-Glaser J, Glaser R. Depression and immune function – central pathways to morbidity and mortality. *Journal of Psychosomatic Research*. 2002; **53**: 873-876.
- [9] Hyams K. Developing case definitions for symptom-based conditions: the problem of specificity. *Epidemiologic Reviews*. 1998; **20(2)**: 148-156.
- [10] Haase H, Rink L. The immune system and the impact of zinc during aging. *Immunity & Ageing* 2009; 6:9 doi 10.1186/1742-4933-6-9
- [11] Lardner A. The effect of extracellular pH on immune function. *Journal of Leucocyte Biology*. 2001; **69**: 522-530
- [12] Dowell S. Seasonal variation in host susceptibility and cycles of certain infectious diseases. *Emerg Infect Dis* 2001; **7**: 369-374. <http://www.cdc.gov/ncidod/eid/vol7no3/dowell.htm>
- [13] Grassly N, Fraser C. Seasonal infectious disease epidemiology. *Proc Biol Sci* 2006; **273**: 2541-50.
- [14] Gottlieb A, Lahita R, Chiorazzi N, Kunkel H. Immune function in systemic lupus erythematosus. Impairment of in vitro T-cell proliferation and in vivo antibody response to exogenous antigen. *Journal of clinical investigation* 1979; **63(5)**, 885-892
- [15] Thomas D, Thio C, Martin M, Qi Y, Ge O, O’huigin C, et al. Genetic variation in IL28B and spontaneous clearance of hepatitis C virus. *Nature* 2009; 461: 798-801
- [16] Wills, M Carmichael, A Sissons J. Vaccines against persistent DNA virus infections. *British Medical Bulletin* 2002; 62: 125-138
- [17] Bonhoeffer S, Nowak M. Intra-host vs inter-host selection; viral strategies of immune function impairment. *Proceedings National Academy of science, USA* , 1994 91 8062-8066
- [18] Wherry E, Blattman J, Murali-Krishna K, van der Most R, Ahmed R. Viral persistence alters D CD8 T-cell immunosenescence and tissue distribution and results in distinct stages of functional impairment. *Journal of virology*, 2003, 77 (8), 4911-4927
- [19] Zuniga E, Liou L, Mack L, Mendoza M, Oldstone M. Persistent virus infection inhibits type I interferon production by plasmacytoid dendritic cells to facilitate opportunistic infections. *Cell Host Microbe* 2008; **4(4)**: 374–86
- [20] Allander T, Tammi M, Eriksson M, Bjerkner A, Tiveljung-Lindell A, Andersson B. Cloning of a human parvovirus by molecular screening of respiratory tract samples. *Proc Natl Acad Sci USA* 2005; **102(36)**: 12891–12896

- [21] Deeks S, Phillips N. HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity. *BMJ* 2010; **338**: 288-292.
- [22] Goulding C, O'Connell P and Murray F. Prevalence of fibromyalgia, anxiety and depression in chronic hepatitis C virus infection: relationship to RT-PCR status and mode of acquisition. *European Journal of Gastroenterology and Hepatology*. 2001; **13**(5), 507-511.
- [23] Evans D, Ten Have T, Douglas S, Gettes D, Morrison M, et al. Association of depression with viral load, CD8 T lymphocytes, and natural killer cells in women with HIV infection. *American Journal of Psychiatry*. 2002; **159**, 1752-1759.
- [24] Wheatland R. Viral carrier status is instilled by viral regulatory particles. *Medical Hypotheses* 2010; **74**(4): 688-691
- [25] Pawelec G, Akbar A, Caruso C, Solana R, Grubeck-Loebenstien B, Wikby A. Human immunosenescence: is it infectious? *Immunological Reviews* 2005; **205**(1): 257-268.
- [26] Pawelec G, Derhovanessian E, Larbi A, Strindhall J, Wikby A. Cytomegalovirus and human immunosenescence. *Reviews in Medical Virology* 2009; **19**: 47-56.
- [27] Derhovanessian E, Larbi A, Pawelec G. Biomarkers of human immunosenescence: impact of Cytomegalovirus infection. *Current Opinion in Immunology* 2009; **21**: 1-6.
- [28] Jones R. Emergency admissions in the United Kingdom: Trend upward or fundamental shift? 1996; <http://www.docstoc.com/docs/9258083/Increase-in-emergency-admissions---trend-or-step-change>
- [29] Jones R. Admissions of difficulty Health Services Jnl 1997; **107**(5546), 28-31
- [30] Jones R. Trends in emergency admissions. *British Jnl Healthcare Management* 2009; **15**: 188-196.
- [31] Jones R. Cycles in emergency admissions. *British Jnl Healthcare Management* 2009; **15**: 239-246.
- [32] Jones R. Cycles in emergency admissions – supplement. *Healthcare Analysis & Forecasting*, Camberley, UK. 2009; <http://www.docstoc.com/docs/5705782/Cycles-in-emergency-admissions-Supplement>
- [33] Jones R. Emergency admissions and hospital beds. *British Jnl Healthcare Management* 2009; **15**, 289-196.
- [34] Jones R. Additional studies on the three to six year pattern in medical emergency admissions. *Healthcare Analysis & Forecasting*, Camberley, UK. December 2009. http://www.hcaf.biz/Recent/Additional_Studies.pdf
- [35] Jones R. Unexpected, periodic and permanent increase in medical inpatient care: Man-made or new disease? *Medical Hypotheses* 2010; doi: 10.1016/j.mehy.2010.01.011
- [36] Jones R. Can time-related patterns in diagnosis for hospital admission help identify common root causes for disease expression? *Medical Hypotheses* 2010; doi: 10.1016/j.mehy.2010.02.09
- [37] Picker L and Watkins D. HIV pathogenesis: the first cut is the deepest. *Nature Immunology*. 2005; **6**(5), 430-432.
- [38] Hollingsworth T, Ferguson N, Anderson R. Frequent travellers and the rate of spread of epidemics. *Emerging Infectious Diseases* 2007; **13**(9), <http://www.cdc.gov/EID/13/9/1288.htm>
- [39] Jones R. Benchmarking of emergency admissions with length of stay greater than zero days in Thames Valley. *Healthcare Analysis and Forecasting*, Camberley, 2006 <http://www.docstoc.com/docs/5049802/Benchmark-overnight-emergency-admissions>
- [40] Jones R. Costing emergency assessment unit admissions. *Healthcare Analysis and Forecasting*, Camberley, 2008. <http://www.docstoc.com/docs/9721640/Costing-emergency-assessment-units>
- [41] Jones R. Costing accident and emergency department attendances. *Healthcare Analysis and Forecasting*, Camberley, 2008. <http://www.docstoc.com/docs/11550160/Costing-accident-and-emergency-department-AandE-attendances>
- [42] Thacker S. The persistence of Influenza A in human populations. *Epidemiologic Reviews* 1986; **8**: 129-142.
- [43] Ginaldi L, DiBenedetto M, DeMartins M. Osteoporosis, inflammation and aging. *Immunity & Ageing* 2:4 <http://www.immunityageing.com/content/2/1/14>
- [44] Miossec P, Korn T, Kuchroo V. Mechanisms of disease: Interleukin-17 and Type 17 Helper T cells. *New England Journal of Medicine* 2009; **361**(9); 888-898
- [45] Stout-Delgado H, Du W, Shirali A, Booth C, Goldstein D. Aging promotes neutrophil-induced mortality by augmenting IL-17 production during viral infection. *Cell Host & Microbe* 2009; **6**(5): 446-456.

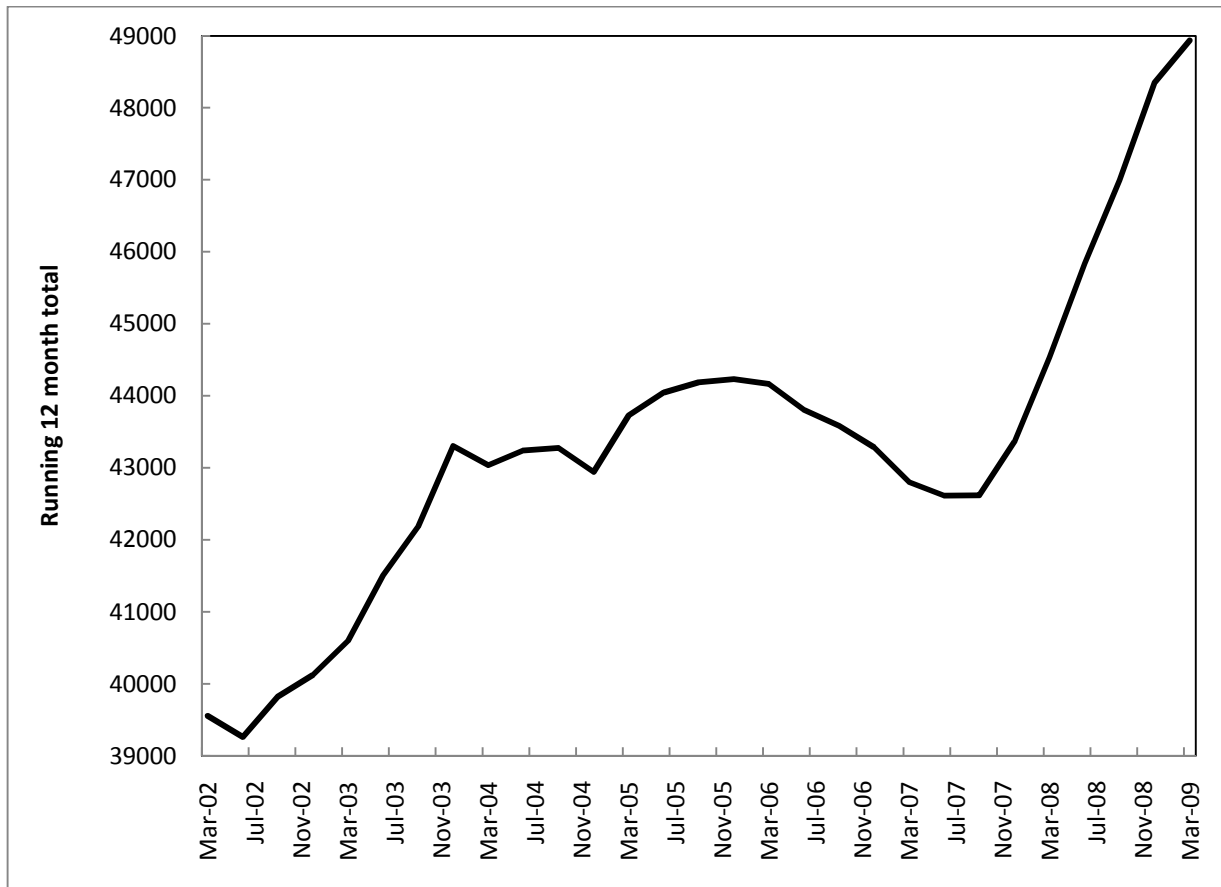
- [46] Berrington W Hawn, T. Mycobacterium Tuberculosis, macrophages, and the innate immune response; does common variation matter? *Immunology Reviews* 2007; **219**: 167-186 [Abstr]
- [47] Jones R. Cyclic factors behind NHS deficits and surpluses. *British Jnl Healthcare Management* 2010; 16(1), 48-50.
- [48] Jones R. Emergency preparedness. *British Jnl Healthcare Management* 2010; 16 (2), 94-95.
- [49] Jones R. A maximum price tariff. *British Jnl Healthcare Management* 2010; 16 (3), 146-147.
- [50] Jones R. Do NHS cost pressures follow long-term patterns? *British Jnl Healthcare Management* 2010; 16(4), 192-193
- [51] Edwards N, Hensher M. Managing demand for secondary care services: the changing context. *British Medical Journal* 1998; 317, 135-138.
- [52] New Zealand Health Technology Assessment. Acute medical admissions. A critical appraisal of the literature. NZHTA Report 6, August 1998. <http://nzhta.chmeds.ac.nz/publications/nzhta6.pdf>
- [53] Shepherd S. Integrated services: reducing hospital admissions among older people. *Health Service Journal*. Nov 2009; <http://www.hsj.co.uk/resource-centre/best-practice/integrated-services-reducing-hospital-admissions-among-older-people/5007303.article>
- [54] Anderson J, Bernath V, Davies J, Greene L, Ludolf S. Literature review on integrated bed and patient management. Centre for Clinical Effectiveness, Monash Institute for Public Health, Victoria, Australia. January 2001. <http://www.health.vic.gov.au/emergency/bgdocs/ibpmview.pdf>
- [55] Audit Commission. More for less: Are productivity and efficiency improving the NHS. *Health Briefing*, November 2009. <http://www.audit-commission.gov.uk/SiteCollectionDocuments/AuditCommissionReports/NationalStudies/20091111moreforless.pdf>
- [56] Jones R. Emergency admissions and financial risk. *British Jnl Healthcare Management* 2009; 15(7): 344-350.

Fig. 1: Admissions to the medical group of specialties in Northern Ireland



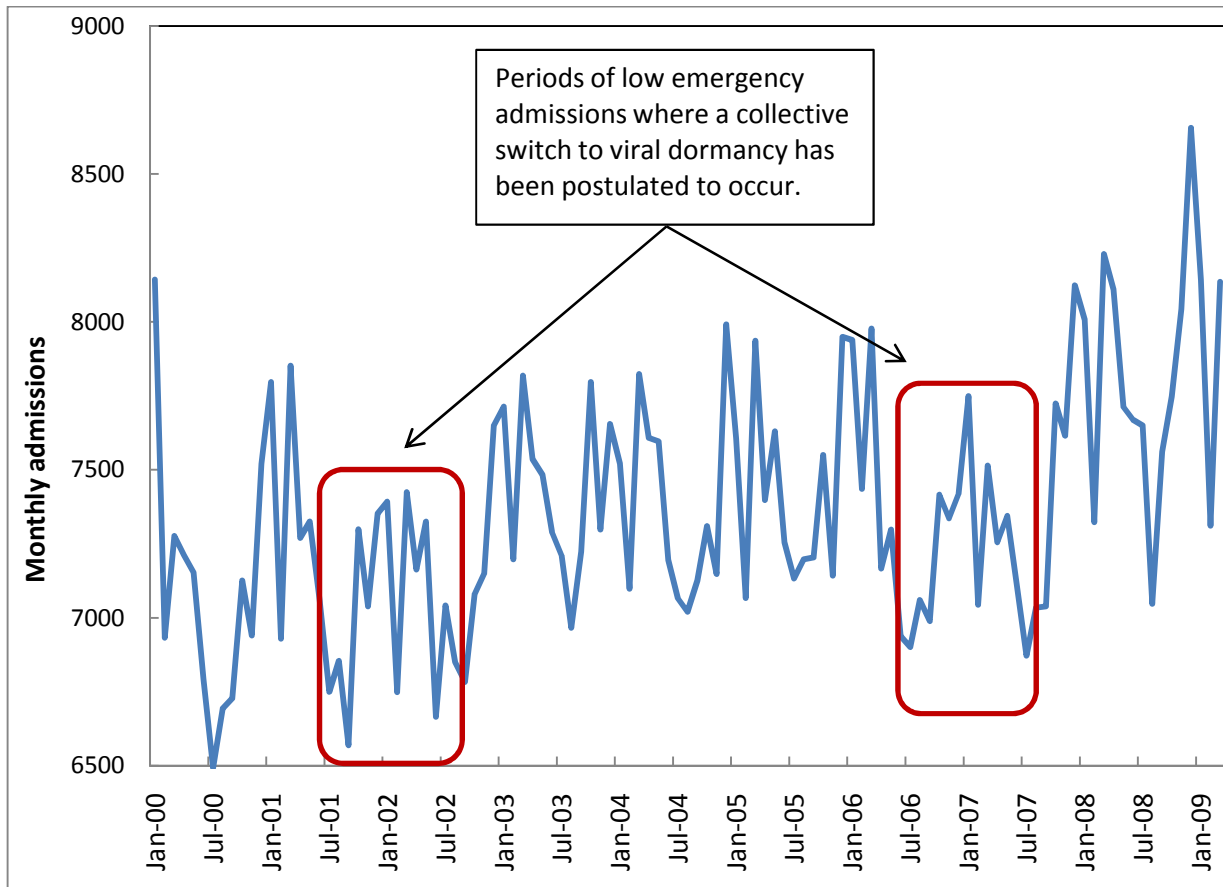
Footnote: Monthly emergency admissions (excluding same or zero day stay), to a group of non-surgical specialties (general medicine, cardiology, infectious diseases, etc) were summed to give a 12 month running total. Each point on the graph increments forward by 1 month.

Fig. 2: Annual admissions to a cluster of diagnoses in Northern Ireland



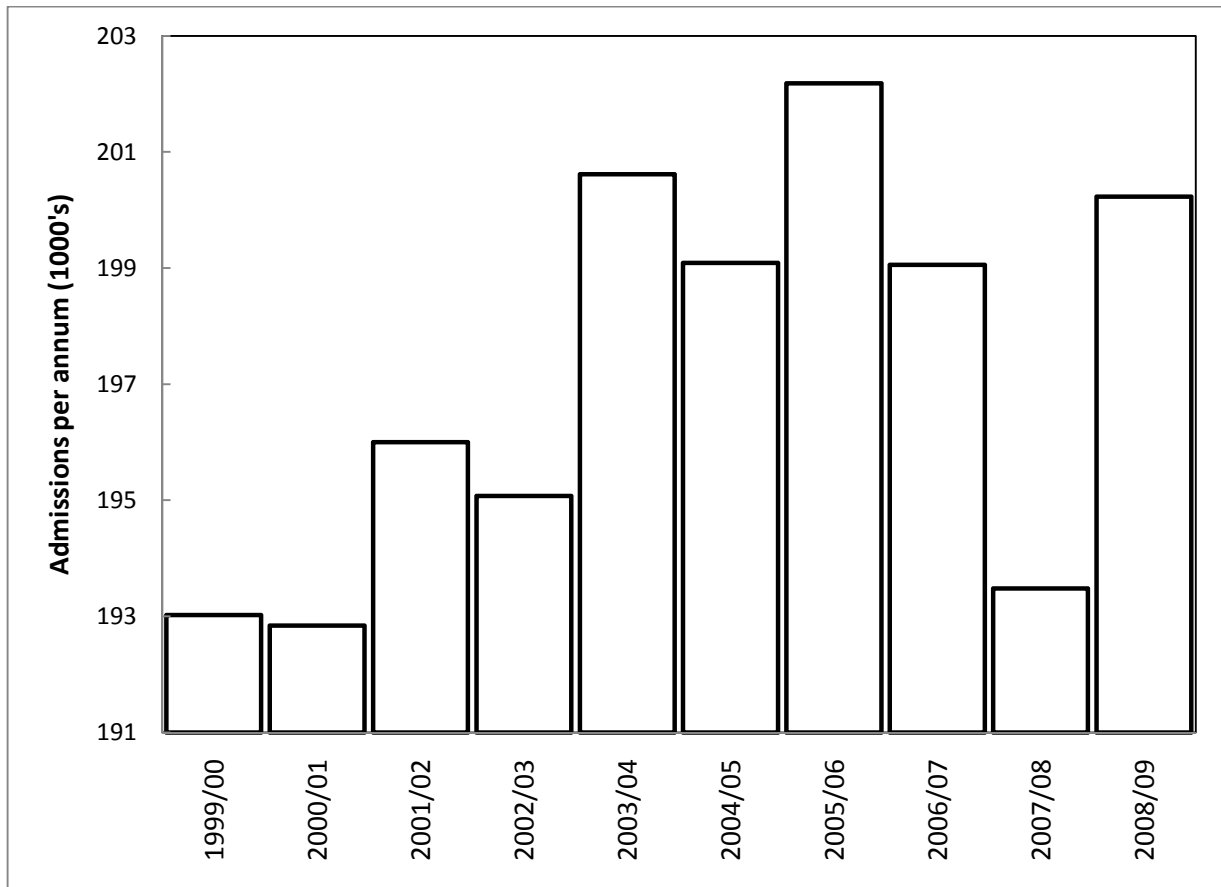
Footnote: Emergency hospital admissions (excluding same or zero day stay) relating to a list of 90 ICD-10 diagnoses identified for England [36]. Quarterly data was summed using a running annual total where the period moves forward by one quarter for each annual total.

Fig. 3: Monthly time series for medical group admissions



Footnote: Data as per Fig. 1. The high peak in January 2000 is the end of an influenza outbreak. Influenza is absent (dormant) from this point until eventual re-emergence toward the end of 2009.

Fig. 4: Annual admissions to the medical group of specialties in Wales.



Footnote: Overnight admissions to a group of 19 medical and 3 mental health specialties [34]. For the medical specialties the distinction between elective and emergency is less clear and on this occasion data includes both elective and emergency admission (excludes day case admissions but may include some zero day stay emergency admissions).