

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

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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

Results

Northern Ireland

Wales

Discussion

Attempts to solve the 'problem'

Further Research

Conclusions

References

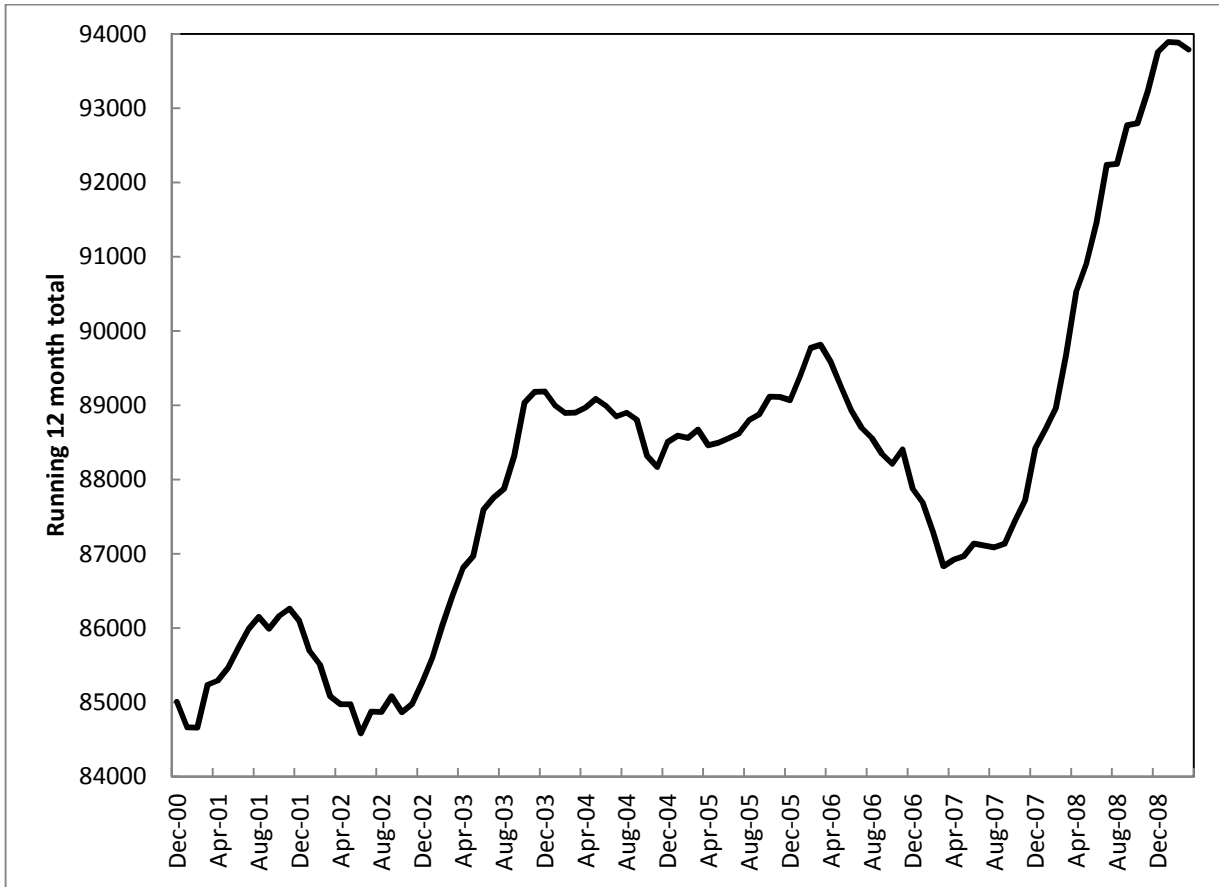
- [1] Woolhouse M, Gowtage-Sequeria S. Host range and emerging and re-emerging pathogens. *Emerging Infectious Diseases* 2005; **11(12)**. www.cdc.gov/ncidod/EID/vol11no12/05-0997.htm
- [2] Bergmire-Sweat D, Schlegel J, Marin C, Winpisinger K, Perry C, Sotir M, Harris J. Multistate outbreaks of human 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, Shuttlesworth 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’Hugin 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 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-Loebenstein 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. Cytomegalavirus 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

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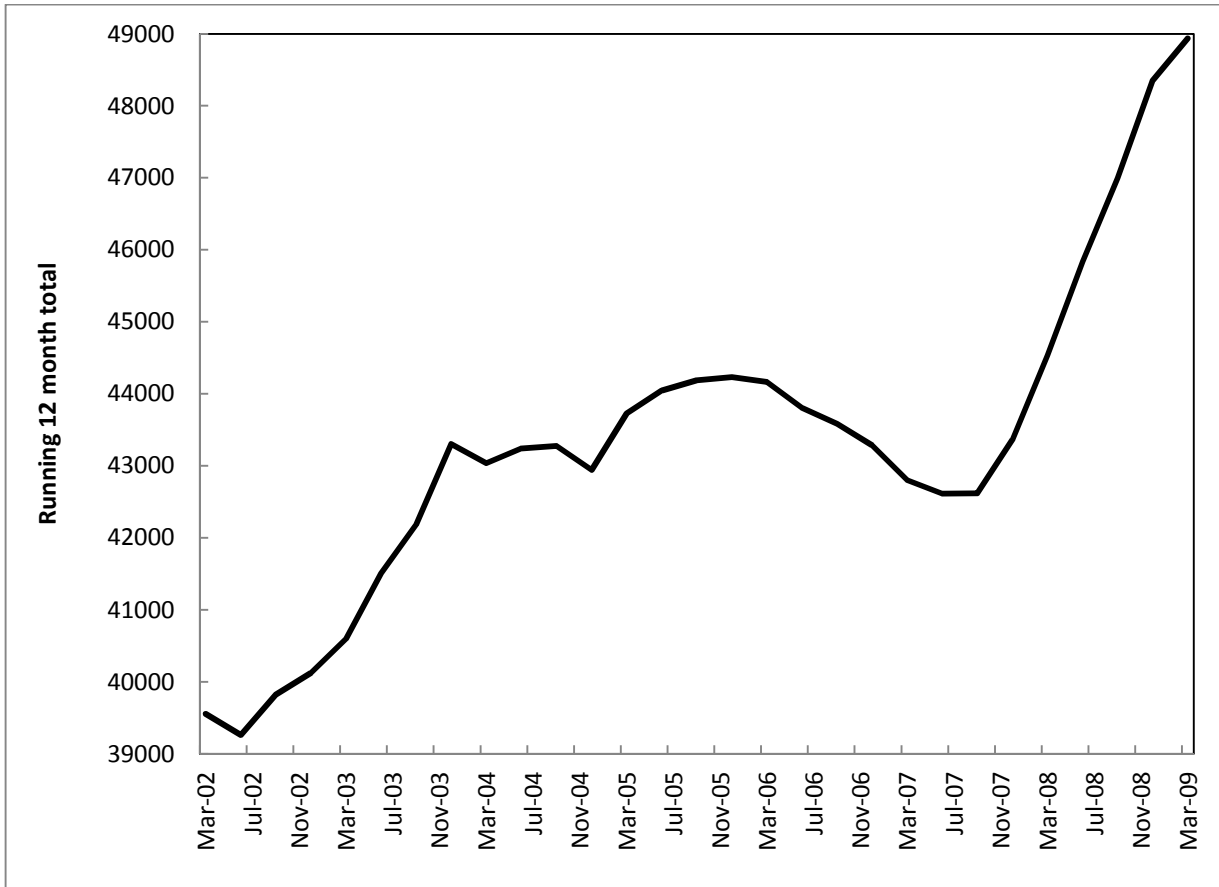
- [51] Edwards N, Hensher M. Managing demand for secondary care services: the changing context. *British Medical Journal* 1998; 317, 135-138.
- [52] New Zealand Health Technology Assessment. Acute medical admissions. A critical appraisal of the literature. NZHTA Report 6, August 1998. <http://nzhta.chmeds.ac.nz/publications/nzhta6.pdf>
- [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



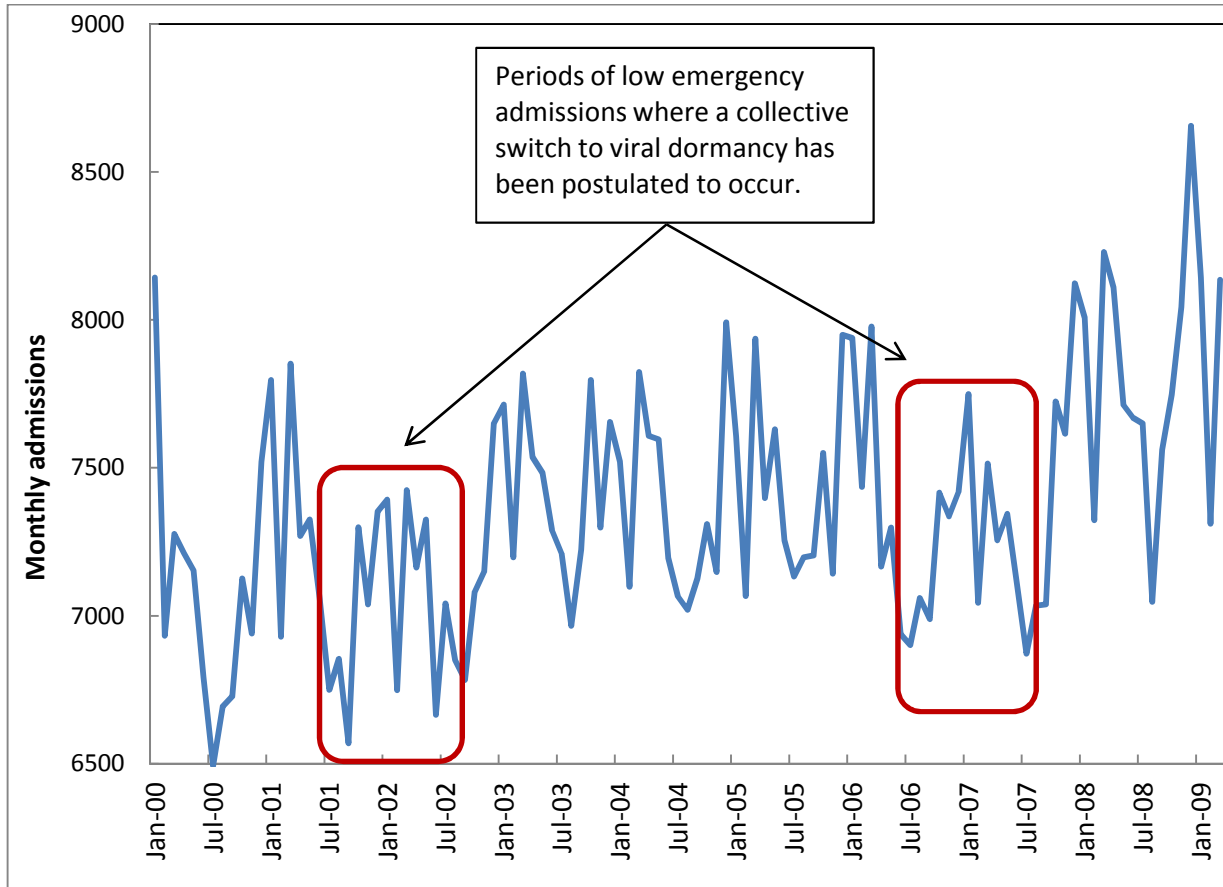
Footnote: Monthly emergency admissions (excluding same or zero day stay), to a group of non-surgical specialties (general medicine, cardiology, infectious diseases, etc) were summed to give a 12 month running total. Each point on the graph increments forward by 1 month.

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



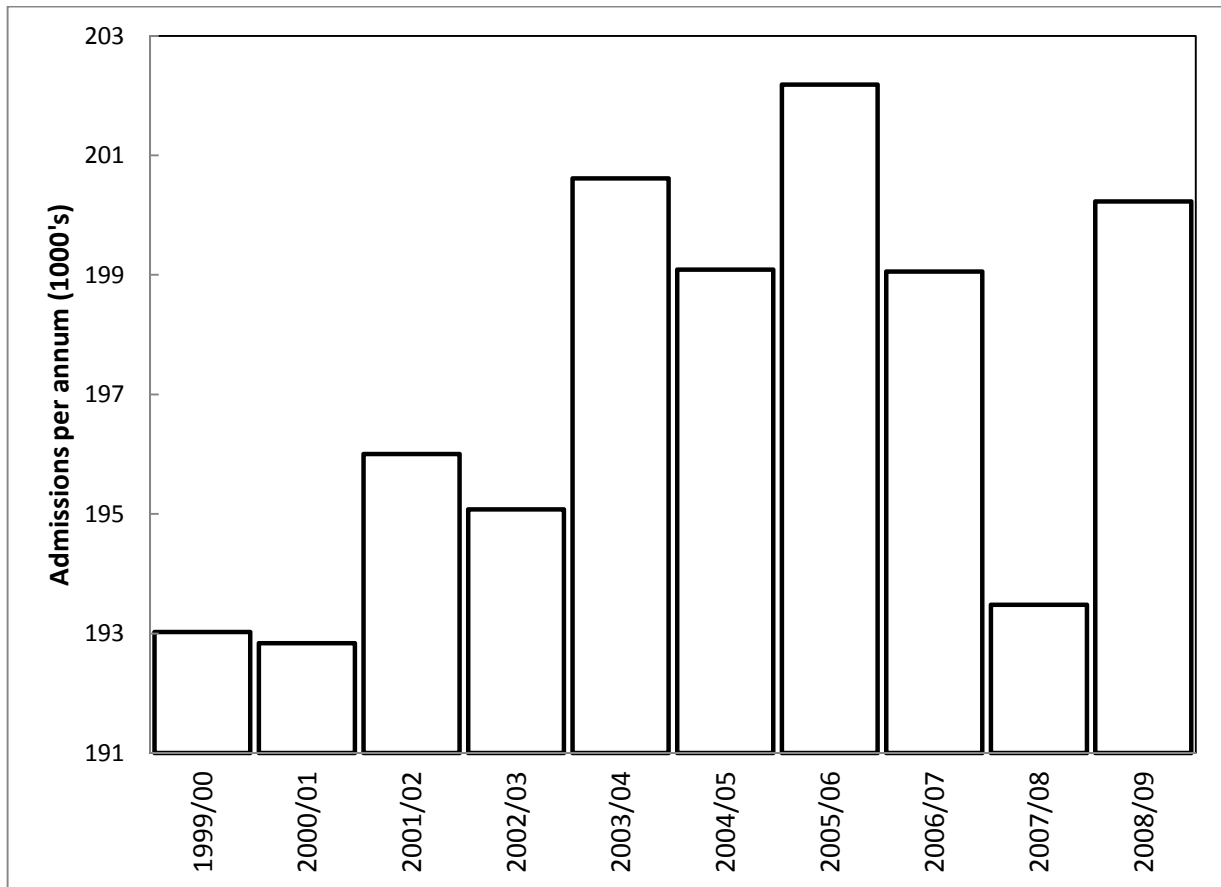
Footnote: Emergency hospital admissions (excluding same or zero day stay) relating to a list of 90 ICD-10 diagnoses identified for England [36]. Quarterly data was summed using a running annual total where the period moves forward by one quarter for each annual total.

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).