

Unexpected, periodic and permanent increase in medical inpatient care: man-made or new disease?

Rodney P Jones, Ph.D. (ACMA)

Healthcare Analysis & Forecasting

Honister Walk, Camberley, Surrey, UK GU15 1RQ

Telephone: +44 (0)1276 21061

Email : hcaf_rod@yahoo.co.uk

Website: www.hcaf.biz

Competing Interests: None

Source of Funding: None

Abstract

For many years medical admissions to acute hospitals have been increasing at a rate far higher than expected from demographic change. Factors such as emergency re-admission, GP thresholds, breakdown of the family unit and deficiencies in community and social care have been suggested to explain this widening gap. Solutions to the problem have revolved around demand management strategies. While such strategies do result in a relative reduction in demand they are unable to prevent the underlying long-term behaviour. Analysis of daily admissions in Scotland, England and at individual hospitals over the past 25 years shows that the admissions tend to increase in a step-like manner at an interval of three to six years. This causes a typical 10% step-increase in physician workload and inpatient medical costs and across England adds over 1,200,000 occupied bed days of additional bed demand into the health service within the space of around three months. There are knock-on effects to demand for ambulance services, accident and emergency attendance and GP referral. The step increase is characterised by a cluster of diagnoses, increases with age and effects women more than men. Such behaviour has similarities to an infectious outbreak and the evidence for this and alternative hypotheses are discussed.

Introduction

Around the world there has been an enduring trend to increasing numbers of hospital medical admissions that is far above that explained by demography. Factors such as increasing re-admission, GP thresholds, breakdown of the family unit, deficiencies in primary and social care have been proposed as contributing to the gap [1-5].

In England the wider group of medical specialties account for around 2,300,000 overnight stay admissions per annum and around 18,700,000 occupied bed days (equivalent to 51,000 fully occupied beds). The latter represents around 60% of total acute hospital occupied beds (excluding maternity and mental health). Unexpected changes in admissions to the medical group therefore have the potential to disrupt health service workload and finances.

It is the almost universally accepted belief that the growth in emergency admission arises from the sum of emerging trends, i.e. re-admissions for those with chronic conditions and changes in admission threshold which are overlaid onto basic demographic growth [1]. However this is unable to explain the observed trend which is discontinuous with bursts of growth which typically increase the overall number of genuine overnight stay emergency admissions by around 10% at an interval of between three to six years [1,6-10]. Contrary to expectation the new and higher level of admissions continues until the next step change. Fig. 1 illustrates the magnitude of the effect upon occupied beds and also demonstrates a gradual recovery after the step change as length of stay efficiency measures are introduced to cope with the unacceptable increase in bed occupancy.

It has been tentatively proposed that this step-change in admissions could be the result of a previously uncharacterised infectious outbreak. However a more cautious view would be that the effect is simply due to some policy or operational change. The evidence for and against each of these two hypotheses for this unique phenomenon will now be explored.

Policy and Organisational Explanations

When confronted with an observed step-change in admissions the usual response is some form of change due to a policy, organisational or admission threshold phenomena [11] or to some form of data artefact. Indeed in the early aftermath of the 1993 step-change the hospital where the author was then working was accused by the local health authority of admitting more patients to increase income. Such anecdotes aside any possibility of a data artefact is easily dismissed given the national nature of the change and the virtual impossibility of

manufacturing such large numbers of overnight stay admissions which can be traced back to individual patients with a unique NHS number. The effect has been demonstrated at specialty level and the likelihood that an incorrect specialty has been assigned to an admission is very low [12].

It is likewise difficult to establish a linkage to any common administrative or policy change within the NHS, and even if this were possible, policy is implemented in piecemeal fashion over an extended time period. Organisational change in healthcare likewise occurs after considerable planning and implementation [11]. In this respect the phenomenon has repeated over a very long time frame and on each occasion appears to come unexpectedly to both provider and purchaser, i.e. it is totally unplanned. Furthermore the health services in Scotland and England are run independently with different policies and administrative arrangements.

To demonstrate the unplanned nature of this phenomenon it should be noted that general and acute (all specialties excluding mental health and maternity) available beds actually declined from 2007/08 to 2008/09 while the occupied beds increased by 1,584 (equivalent to 580,000 occupied bed days) [13]; i.e. most hospitals were expecting the downward trend in occupied beds seen between 2003/04 and 2007/08 to continue. This observation is the opposite of conventional wisdom which indicates that fewer available beds will lead to fewer occupied beds, i.e. demand is supposed to expand to fill supply and vice versa, and a new mechanism is needed to explain this reversal in behaviour.

There is no evidence of a change in the statistical behaviour of admissions surrounding any of the step-changes, i.e. the admission rate steps up to the new level with admissions continuing to behave (from a dynamic viewpoint) in a similar way to that seen before the step change [9]. To put this in context, over the past 25 years the health service has coped with numerous influenza outbreaks, unusually hot summers, etc and the rate of admissions and bed demand has always returned back to normal after such disturbances. The effect leading to the step changes is therefore of a fundamentally different type.

An alternative suggestion could be a general reduction in the threshold to refer within primary care. Referral from primary care is always filtered by a first outpatient attendance or by A&E or assessment unit triage. Elective inpatient demand has been shown to follow a trend which is independent of changes in GP referral, i.e. the outpatient to inpatient conversion ratio declines as inappropriate referrals are filtered out [14-15]. Another explanation could be that A&E and

This article has been published as: Jones R (2010) Unexpected, periodic and permanent increase in medical inpatient care: man-made or new disease. *Medical Hypotheses* 74(6), 978-983. Please use this to cite.

assessment unit admission thresholds are simultaneously reduced across the UK. This implies that A&E and medical consultants (but not consultants in other specialties) have for no apparent reason somehow acted in unison to increase admissions.

It is important to note that the average length of stay (ALOS) for the additional patients arising from the step change in admissions is around 10 days. This is well above the ALOS for general medicine (6.3 days) but below that for elderly medicine (15.6 days), but is above the average for both of 8.5 days (elderly medicine is only 23% of the combined total) and by implication the patients are seriously ill and this immediately discounts any attempt to explain the step change as some trivial shift in admission or referral threshold.

The final possibility for such a step increase in the average acuity of admitted patients could lie within the remit of an earlier suggestion that the effect is due to demand exceeding the capacity of community health and social services [16]. This could be expanded to include bed capacity in community hospitals and nursing homes. Such a suggestion is equivalent to an increase in admissions for the long-stay (elderly rehabilitation) component of the elderly care admissions within medicine [11]. These sources of potential knock-on inpatient admissions could indeed lead to a step-like change although it is unlikely to simultaneously occur on a national basis given the wide range in such resources within different local authorities. This final hypothesis requires detailed analysis of both the source of the admission and the destination after discharge to see if there has been a fundamental shift in the pattern of care. However the question still remains as to why the gap between capacity and demand for such services would increase to such an extent in the first place; i.e. is the step change in admissions a cause or a consequence?

In summary, the evidence for a consistent type of policy- or organisational-based change operating over a 25 year time frame is somewhat weak but requires further investigation if only to fully eliminate this alternative. The alternative hypothesis for a unique type of infectious outbreak will now be discussed.

Infectious Agent Hypothesis

Periodic infectious outbreaks are well recognised phenomena. The period between outbreaks is determined by vector population dynamics and immune responses in the host [17-20]. The key mechanism behind the periodic nature is the ability of the host to acquire immunity to the infectious agent and hence even within sexually transmitted diseases, syphilis shows a typical nine year period between what would be called an 'outbreak' while gonorrhoea (no acquired immunity) shows a typical continuous trend [19-20]. An outbreak of an infectious disease can lead to an increase in emergency hospital admission, but after the outbreak it would normally be expected that the level of admissions would revert back to that prior to the outbreak [21].

However it is also known that an increasing number of viruses maintain a state of permanent infection in the host by utilising a range of immune evasive or suppressive mechanisms [22-28] and viral infection of this type could account for the step-like change in emergency admission rates which will arise from the pool of infected persons. For consistency, this section will refer to the phenomenon in the terms of an infectious 'outbreak'. Further discussion regarding viral-induced immune dysfunction will be presented later; however, the specific factors which are suggestive of an infectious outbreak are as follows [1,6-9,29]:

1. The unique periodic behaviour has been consistent over a very long time period of 25 years or more.
2. The timing for each outbreak is variable (February/March, December/January, September dates have been observed) and does not correspond to the end of a financial year. Major organisational changes in English hospitals typically in April (the start of a new financial year) due to the potential effect on financial flows arising from Payment by Results (PBR).
3. Within a very short space of time (six to eight weeks at a single location) the admission rate steps up to a new and higher rate.
4. Regional variability in the timing and extent of the step increase is suggestive of an infectious outbreak.
5. Each outbreak is characterised by an increase in excess deaths which lasts for around six to eight weeks in a local area.
6. The increase in emergency admissions is accompanied by a step-change increase in occupied beds. Analysis of the 1993 outbreak revealed that the magnitude of the winter/summer peaks and troughs in medical bed occupancy also appeared to be

accentuated in the three years following this event and such factors are not under the control of administrative or policy initiatives.

7. The outbreak appears to coincide with a non-specific increase in GP referral for an outpatient appointment and this could be interpreted as an increase in general poor health which appears to accompany the outbreak.

8. The step-change is specific to particular medical (and mental health) specialties as opposed to wider surgical, trauma or paediatric, i.e. it is not due to some generalised factor effecting all admissions in an indiscriminate manner.

9. The step-change increases in magnitude with age and leads to an increase in female admissions which gradually reduces until the next step change.

10. Of great interest is the fact that a range of specific diagnoses were noted to increase during the outbreak but with no change in diagnoses unrelated to medicine or mental health.

While all of the above are highly suggestive of an infectious outbreak the nature of the last key feature, namely, shifts in the pattern of diagnosis, will now be investigated in greater detail.

Shifts in Diagnosis

A phenomenon of this magnitude must be demonstrated to have some specificity with respect to its mode of action. Table 1 presents the results of recent analysis of the changes in primary diagnosis which occurred after the 2002 and 2007 outbreaks using the 148 high-level International Classification of Diseases (ICD) groups [9]. A cluster of 48 diagnostic groups seem to be associated with the step change in admissions and bed occupancy.

The increased incidence of general and non-specific diagnoses associated with each outbreak is perhaps best understood in the context that there are at least 61 medical conditions with vague symptoms (wrongdiagnosis.com/sym/vague-symptoms.htm#intro) and this key marker should not be disregarded. The work on symptom-based conditions may shed light regarding such diagnoses and their association with the outbreak [30].

The national average length of stay for R69 (unknown causes of morbidity) in 2008/09 was 35 days which implies that at least one group of patients (perhaps with significant co-morbidities) are specifically affected. This is both a symptom of the organisational dysfunction arising

from the 10% step increase in incoming demand and of the potential diagnostic uncertainty associated with an uncharacterised infectious disease/syndrome.

Indeed the apparently disparate group identified in Table 1 does have a set of common themes:

1. Increased susceptibility to a wide range of infections (including post procedural)
2. Increased prevalence of inflammation (including post procedural)
3. General symptoms and signs for 'illness'
4. Mental health problems
5. General vascular problems

The step increases for respiratory tract infections (RTI) is an interesting marker since both GP consultations and prescriptions for RTI have shown a reduction over the period 1997 to 2006 [31] which is the total opposite to acute admissions, i.e. the condition is severe enough to warrant hospital admission and a reduction in primary care thresholds are not implicated in that the threshold to prescribe has increased.

The common theme would appear to be that of immune system dysfunction which is known to be initiated by trauma (i.e. war and natural disaster), prolonged anxiety (i.e. carer's of debilitated relatives), biological stress due to infection (Hepatitis C and HIV infections) and depression [32-38]. Enhanced symptoms of anxiety and depression are also a by-product of immune dysfunction [34-36,38]; hence, the occurrence of increased mental health issues stemming from enhanced anxiety and depression (i.e. self harm, attempted suicide, drug misuse, etc) and the step increase in admissions and bed days observed in adult mental health, forensic psychiatry and old age psychiatry [6,9].

At this point it may be relevant to point out that the higher step change in admissions seen for women [9] may be consistent with the known higher susceptibility of women to auto-immune diseases [39]. Indeed for all ages over 60 years (accounting for 70% of medical admissions) the relative excess of women to men in the population of England has been steadily declining since 1996 [40]. This is the exact opposite of the trend in admissions shown in the cluster of 48 diagnostic groups and we must therefore conclude that some mechanism is at work which transcends policy, general changes in admission thresholds or other structural explanations.

Research into the way in which the AIDS virus infects its host suggests that viral infections can lead to a rapid initial decline in general immune function [41]. Recent research into

immunosenescence in the elderly has identified that Cytomegalovirus (CMV) infection is highly implicated in the decline in immune function [42-44] and an Immune Risk Profile (IRP) has been established which appears to be able to detect the transition to a state of increased immune debility (both with or without CMV seropositivity), i.e. increased susceptibility to infection and ultimately to disease. Hence it is an entirely feasible hypothesis to suggest that infection with an additional virus can trigger the higher incidence of immune dysfunction implied by these findings perhaps even via secondary CMV re-activation. Indeed this may be an as yet unrecognised role for one of the more common viruses known to infect the general population or may be an as yet uncharacterised virus. In this respect infection with one virus can open the way for opportunistic secondary infection [28]. We can probably exclude a role for the influenza virus given the numerous influenza outbreaks resulting in no permanent increase in hospital admissions.

The final issue is that of the apparent constant rate of admissions between the step changes. A constant rate can be achieved if the decline in the infected sub-population (via a higher rate of disease as indicated by the IRP) roughly matches the underlying growth in need via demographic change in the non-infected population.

International Scope

An infectious disease/condition of this magnitude is unlikely to be confined to one country. A similar phenomenon may be occurring in the USA where the cost of care for insured individuals was known to follow a periodic pattern of step increases in cost over a 42 year period from 1960 onward [45-47]. Best estimate for the outbreaks (sudden increase in cost) in the USA are dates either in or around the years (± 1 year) 1963, 1967, 1973, 1978, 1986, 1994 and 2000. This cycle in costs led to a corresponding lagged cycle in underwriting profit and loss [45-47], which once recognised, led to a change in underwriting processes such that premiums were based on the here and now [48] rather than the usual historical analysis and assumptions around demographic change which is inappropriate for a periodic phenomenon. It has been recently proposed that this same effect may be responsible for the cycle of surplus and deficit also seen in the NHS [48]. The existence of this periodic increase in cost did not appear to be widely communicated outside the underwriting industry and hence did not attract the interest of epidemiologists and other researchers.

Notwithstanding the difficulties of using whole year data the above studies suggest that additional international research is required. If an infectious agent is responsible then the timing of the outbreak in different countries would depend on the mode of transmission and the process for achieving sufficient mass action to initiate an outbreak. Irrespective of the source of this phenomenon the existence of step changes as a fundamental mechanism for the growth in medical demand (and cost) has been established and therefore requires explanation.

Testing the Hypothesis

Analysis of daily or weekly data for a range of hospitals from a variety of UK and international locations looking at shifts in age, sex, diagnosis, source of admission and discharge destination for both admissions and bed occupancy are required. In the UK postcode level data requires analysis to determine if the 'outbreak' has a profile consistent with the spatial spread of an infection. The point of onset of each outbreak needs to be linked with measured levels of various infectious agents to establish if there is any link with a known agent or vector.

The author has recently analysed bed occupancy data for the intensive care unit (ICU) at one outer London hospital and a step increase occurred in the last half of 2007. National data for the 2002 outbreak appears to confirm the feasibility of this observation with a 5% increase in adult occupied intensive care beds in 2003/04 v 2002/03 [13]. A change in the way bed data was collected prevents wider confirmation of the national picture for adult intensive care beds in 2008/09.

The hypothesis around enhanced rates of decease especially in females is easily tested using monthly deaths split by gender either at a national or local level.

The re-evaluation of published longitudinal studies for specific diseases may give further insight. For example, admission for anaphylactic shock (an auto-immune condition) showed a distinct step change in 1993/94 versus the 1992/93 financial year, i.e. at the point surrounding the March 1993 outbreak [49]. At this point it should be noted that the majority of longitudinal studies have not looked for step changes in admissions and hence such events may have gone unreported.

It is suggested that the research into the role of light intensity due to month of the year (season) and solar cycles as factors leading to the disposition toward certain diseases may

This article has been published as: Jones R (2010) Unexpected, periodic and permanent increase in medical inpatient care: man-made or new disease. *Medical Hypotheses* 74(6), 978-983. Please use this to cite.

offer the ability to select for cohorts within the population and study the differential effects of each step change [50-53]. This would establish biological rather than organisational causes for the step change.

Lastly, studies utilising the Immune Risk Profile (IRP) discussed above need to be extended to determine if such a shift in immune function is associated with this phenomenon.

Conclusions

This study has investigated two sources for this phenomenon. The evidence for a policy- or organisation-based source generally appears to be weak. The possibility of an emerging capacity gap within community-based services requires further investigation. Evidence for a unique type of infectious outbreak has been given. It is apposite to recall that prior to 1980 patients with symptoms of HIV infection presenting to their GP or hospital would have been regarded as yet another patient with unexplained 'vague' symptoms, i.e. 'unwell' for no apparent reason. If an infectious agent is implicated then appropriate public health measures can be applied as the solution to the real root cause.

Whatever the cause, each 'outbreak' is highly infectious in the sense that the medical admission rate moves rapidly from a lower to a permanently higher rate in a matter of weeks and will have enormous implications to the financial pressures and physician work-load within the health service. Indeed it has fundamental implications to how we view the role of immune function in the wider context of public health and primary care policy.

Finally, there is a need for the wider appreciation of the possibility of step changes in longitudinal studies on the incidence of conditions/diseases especially where immune system function may be primarily or secondarily involved.

It is hoped that the hypothesis presented here will promote wider interest in this fascinating but poorly understood mechanism for unexpected growth in demand for medical inpatient care and cost which presumably also has fundamental effects across multiple aspects of primary care.

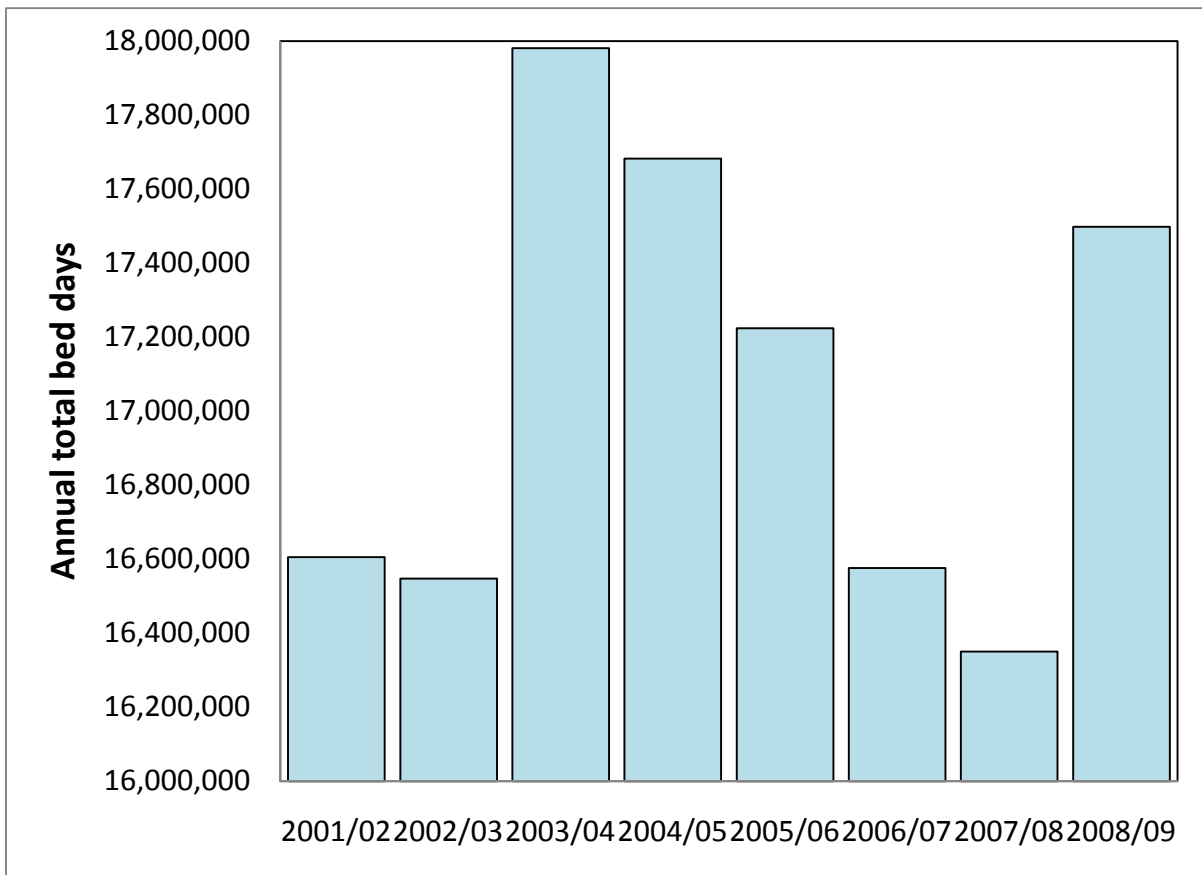
References

- [1] Jones R. Trends in emergency admissions. *Brit J Healthcare Management* 2009; **15**: 188-196.
- [2] Edwards N, Hensher M. Managing demand for secondary care services: the changing context. *British Medical Journal* 1998; **317**: 135-138.
- [3] New Zealand Health Technology Assessment (1998) Acute medical admissions. A critical appraisal of the literature. NZHTA report 6, August 1998.
<http://nzhta.chmeds.ac.nz/publications/nzhta6.pdf>
- [4] 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>
- [5] 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>
- [6] Jones R. Emergency admissions in the United Kingdom: Trend upward or fundamental shift? *Healthcare Analysis & Forecasting*, Camberley, UK. 1996;
<http://www.docstoc.com/docs/9258083/Increase-in-emergency-admissions---trend-or-step-change>
- [7] Jones R. Cycles in emergency admissions. *British Journal of Healthcare Management* 2009; **15**: 239-46.
- [8] Jones R. Cycles in emergency admissions – supplement. *Healthcare Analysis & Forecasting*, Camberley, UK. 2009; <http://www.docstoc.com/docs/5705782/Cycles-in-emergency-admissions-Supplement>
- [9] 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
- [10] Jones R. Admissions of difficulty. *Health Service Journal* 1997; **107**(5546): 28-32.
- [11] Millard P, Rae B, Busby W. Why noskinetics? Measuring, modelling the process of care. In 'Intelligent Patient Management'. Eds S McClean, P Millard, E El-Darzi & C Nugent. Berlin, Heidelberg, Springer 189: 3-23.
- [12] Jones R. Getting the best from hospital patient information. *Healthcare Analysis & Forecasting*, Camberley, UK. 1996
- [13] Department of Health – Performance & Statistics. Average daily number of available and occupied beds by ward classification, England'; 2002/03, 2003/04, 2007/08, 2008/09.
<http://www.dh.gov.uk/en/Publicationsandstatistics/Statistics/Perfomancedataandstatistics/Beds/index.htm>
- [14] Jones R. How many patients next year? *Healthcare Analysis & Forecasting*, Camberley, UK. 1996
- [15] Jones R. Does growth in general practitioner referral link directly to growth in inpatient demand? *Healthcare Analysis & Forecasting*, Camberley, UK; 2006.
<http://www.docstoc.com/docs/5049799/Outpatient-to-Inpatient-Conversion-Ratio>
- [16] Kendrick S. Emergency admissions: what is driving the increase? *Health Serv J* 1995; **105**(5451),26-28.
- [17] Dowell S. Seasonal variation in host susceptibility and cycles of certain infectious diseases. *Emerg Infect Dis* 2001; **7**: 369-74.
<http://www.cdc.gov/ncidod/eid/vol7no3/dowell.htm>

- [18] Koelle K, Pascual M. Disentangling extrinsic from intrinsic factors in disease dynamics: A nonlinear time series approach with an application for cholera. *Am Nat* 2004; **163**: 901-13.
- [19] Grassly N, Fraser C, Garnett G. Host immunity and synchronised epidemics of syphilis across the United States. *Nature* 2005; **433**: 417-21.
- [20] Grassly N, Fraser C. Seasonal infectious disease epidemiology. *Proc Biol Sci* 2006; **273**: 2541-50.
- [21] Earnest A, Chen M, Ng D, Sin L. Using autoregressive integrated moving average (ARIMA) models to predict and monitor the number of beds occupied during a SARS outbreak in a tertiary hospital in Singapore. *BMC Health Serv Res* 5:36. Doi:10.1186/1472-6963-5-36
- [22] Alcamí A, Koszinowski U. Viral mechanisms of immune evasion. *Immunol Today* 2000; **21**(9): 447-55
- [23] 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): 12891-6
- [24] de Graaf M, Osterhaus A, Fouchier R, Holmes E. Evolutionary dynamics of human and avian metapneumoviruses. *J Gen Virol* 2008; **89**(Pt 12): 2933-42
- [25] Kumar D, Erdman D, Keshavjee S, Peret T, Tellier R, Hadjiladis D, et al. Clinical impact of community-acquired respiratory viruses on bronchiolitis obliterans after lung transplant. *Am Jnl Transplant* 2005; **5**(8): 2031-6
- [26] Voisset C, Weiss R, Griffiths D. Human RNA “rumor” viruses: the search for novel human retroviruses in chronic disease. *Microbiol Mol Biol Rev* 2008; **72**(1): 157-96
- [27] Xu X, Sreaton G, McMichael A. Virus infections: escape, resistance and counterattack. *Immunity* 2001; **15**(6): 867-70
- [28] 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
- [29] Jones R. Emergency admissions and hospital beds. *Br Jnl Healthcare Management* 2009; **15**, 289-96.
- [30] Hyams K. Developing case definitions for symptom-based conditions: the problem of specificity. *Epidemiologic Reviews* 1998; **20**(2): 148-156.
- [31] Gulliford M, Latinovic R, Charlton J, Little P, van Staa T, Ashworth M. Selective decrease in consultations and antibiotic prescribing for acute respiratory tract infections in UK primary care up to 2006. *Journal of Public Health*. 2009; doi:10.1093/pubmed/fdp081
- [32] Vojdani A, Thrasher J. Cellular and humoral immune abnormalities in gulf war veterans. *Environmental Health Perspectives* 2004; **112**(8): 840-846.
- [33] Hyams K, Wignall F, Roswell R. War syndromes and their evaluation: from the US Civil War to the Persian Gulf War. *Annals of Internal Medicine* 1996; **125**(5): 398-405.
- [34] Goulding C, O’Connell P, 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 & Hepatology* 2001; **13**(5): 507-511.
- [35] Kiecolt-Glaser J, Glaser R. Depression, immune function – central pathways to morbidity, mortality. *Journal of Psychosomatic Research* 2002; **53**: 873-876.
- [36] 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.
- [37] Kiecolt-Glaser J, Glaser R, Shuttleworth E, Dyer C, Ogrocki P, Speichler C. Chronic stress and immunity in family caregivers of Alzheimer’s disease victims. *Psychosomatic Medicine* 1987; **49**(5): 523-535.

- [38] 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.
- [39] Fairweather D, Rose N. Women and autoimmune diseases. *Emerging Infectious Diseases*. 2004; **10**(11) www.cdc.gov/ncidod/EID/vol10no11/04-0367.htm
- [40] Office for National Statistics, United Kingdom. Mid-1996, Mid-2002, Mid-2006 population estimates. United Kingdom estimated resident population by five year age group, sex. <http://www.statistics.gov.uk/statbase/Product.asp?vlnk=15106>
- [41] Picker L, Watkins D. HIV pathogenesis: the first cut is the deepest. *Nature Immunology* 2005; **6**(5): 430-432.
- [42] 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.
- [43] Pawelec G, Derhovanessian E, Larbi A, Strindhall J, Wikby A. Cytomegalovirus and human immunosenescence. *Reviews in Medical Virology* 2009; **19**: 47-56.
- [44] Derhovanessian E, Larbi A, Pawelec G. Biomarkers of human immunosenescence: impact of Cytomegalovirus infection. *Current Opinion in Immunology* 2009; **21**: 1-6.
- [45] Gabel J, Formisano R, Lohr B, Di Carlo S. Tracing the cycle of health insurance. 1991; <http://content.healthaffairs.org/cgi/reprint/10/4/48.pdf>
- [46] Born P, Santerre R. Unravelling the Health Insurance Underwriting Cycle. University of Connecticut, Business School, USA. 2005; <http://tinyurl.com/cwazlw> (accessed 30 Nov 2009)
- [47] Rosenblatt A. The underwriting cycle - The rule of six. *Health Affairs (Millwood)* 2004; **23**(6): 103-106.
- [48] Jones R. Cyclic factors behind NHS deficits and surpluses. *British Journal of Healthcare Management* 2010; **16**(1), 48-50.
- [49] Sheikh A, Alves B. Hospital admissions for acute anaphylaxis: time trend study. *British Medical Journal* 2000; **320**, 1441.
- [50] Davis G, Lowell W. Chaotic solar cycles modulate the incidence and severity of mental illness. *Medical Hypotheses* 2004; **62**(2), 207-214.
- [51] Davis G, Lowell W. The sun determines human longevity: teratogenic effects of chaotic solar radiation. *Medical Hypotheses* 2004; **63**, 574-581.
- [52] Davis G, Lowell W. Solar cycles and their relationship to human disease and adaptability. *Medical Hypotheses* 2006; **67**(3), 447-461.
- [53] Davis G, Lowell W. Peaks of solar cycles affect the gender ratio. *Medical Hypotheses* 2008; **71**, 829-838.

Fig. 1: Total bed days in England for the cluster of diagnoses identified in Table 1.



Footnote: Data for 2008/09 has been adjusted downward to account for a change in the way bed days in the HES standard tables are allocated when the admission spans the end of a financial year. See [9] for details of the adjustment and data sources. The downward trend in bed days between 2003/04 and 2007/08 is due to ongoing reductions in the average length of stay via a range of efficiency measures which are especially to do with the movement of elderly patients back into the community after their acute phase has ended. As can be seen such efficiency gains have been largely lost via the 2007 outbreak and the resulting increase in occupied beds seen in 2008/09.

Table 1: A group of 48 high level diagnoses showing evidence of a step change for the residents of England (size of the step as a percentage).

ICD Codes	Description of Diagnostic Group	Bed days		Admissions		2008/09	
		03/04	08/09	03/04	08/09	ALOS	Admissions
A20-A49	Certain bacterial diseases	114%	102%	107%	103%	12.9	24,746
A50-A64	Predominantly sexual infections	108%	141%	100%	99%	4.4	1,029
B20-B24	Human immunodeficiency virus disease	107%	102%	102%	104%	12.1	3,831
B25-B34	Other viral diseases	103%	112%	104%	111%	1.1	51,602
B35-B49	Mycoses	113%	111%	108%	105%	7	2,535
E15-E90	Endocrine nutritional and metabolic diseases	109%	110%	110%	112%	6.8	69,085
F10-F19	Disorders due to psychoactive substances	109%	104%	107%	101%	7.4	48,903
G00-G09	Inflammatory diseases, central nervous system	116%	113%	99%	107%	17	4,110
G10-G13	Other degenerative diseases (incl. Alzheimer)	115%	115%	96%	97%	43.2	10,276
G20-G26	Movement disorders (incl. Parkinsonism)	101%	111%	98%	105%	19.2	7,844
G40-G47	Epilepsy, migraine & other episodic disorders	98%	108%	103%	107%	3.2	96,295
H10-H13	Disorders of conjunctiva (incl. conjunctivitis)	117%	108%	109%	97%	1.5	1,539
I00-I09	Rheumatic heart disease	96%	119%	95%	115%	13.3	3,787
I10-I15	Hypertensive diseases	100%	104%	101%	110%	6.1	19,914
I26-I28	Pulmonary heart disease & circulation	100%	108%	102%	110%	9.2	20,719
I95-I99	Other & unspecified circulatory disorders	107%	104%	110%	109%	7.4	14,574
J00-J06	Acute upper respiratory infections	109%	98%	114%	101%	0.9	117,014
J10-J18	Influenza & pneumonia	112%	118%	109%	115%	11.2	133,768
J20-J22	Other acute lower respiratory infections	109%	109%	108%	112%	5.7	120,533
J40-J47	Chronic lower respiratory diseases	110%	106%	110%	110%	5.9	190,837
J60-J70	Lung diseases due to external agents	123%	110%	120%	105%	16.8	9,853
J80-J99	Other diseases of the respiratory system	103%	106%	104%	106%	9.3	53,241
K70-K77	Diseases of liver	106%	104%	103%	101%	11.7	21,341
K90-K93	Other diseases of the digestive system	100%	107%	102%	106%	5.6	51,602
L00-L14	Other infections and disorders of the skin	106%	105%	106%	103%	6.3	136,234
M40-M54	Dorsopathies	103%	102%	108%	110%	4.8	100,536
M60-M79	Soft tissue disorders	105%	103%	106%	107%	1.8	116,393
N00-N08	Diseases of the kidney	105%	107%	105%	108%	5.1	32,887
N17-N19	Renal failure	103%	104%	123%	103%	10.7	39,027
N20-N23	Urolithiasis	106%	100%	111%	105%	2.2	47,501
N25-N29	Other disorders of kidney & ureter	95%	113%	103%	108%	5.3	3,605
N30-N39	Other diseases of the urinary system	109%	111%	107%	108%	7.9	157,128
N99	Other disorders of the genitourinary system	114%	95%	107%	102%	4	2,853
R00-R09	Symptoms & signs - circulatory/respiratory	100%	99%	108%	107%	1.6	395,688
R20-R23	Symptoms & signs - skin & subcutaneous tissue	104%	102%	102%	106%	1.3	33,644
R25-R29	Symptoms & signs - nervous & musculoskeletal	103%	111%	105%	111%	6.5	20,583
R40-R46	Symptoms & signs - cognition, perception, etc	108%	108%	112%	113%	6.4	54,735
R47-R49	Symptoms & signs - speech & voice	106%	112%	100%	118%	4.2	6,318
R50-R68	General symptoms & signs	102%	106%	109%	110%	4.2	293,437
R69	Unknown & unspecified causes of morbidity	120%	158%	119%	110%	35.2	116,827
R70-R89	Abnormal findings of bodily fluids or samples	116%	98%	91%	109%	2.7	8,949
T36-T50	Poisonings by drugs & medicaments	107%	100%	112%	101%	1.3	111,600
T66-T78	Other and unspecified effects of external causes	104%	126%	114%	104%	1.8	12,971
T79	Certain early complications of trauma	115%	112%	97%	98%	8	2,104
T80-T88	Complications of surgical & medical care	108%	105%	107%	105%	7.2	137,642
T90-T98	Sequelae of injuries	92%	178%	71%	125%	17.9	137
Z00-Z13	Examination and investigation	96%	142%	102%	114%	1.8	64,579
Z80-Z99	Health hazards related to family	120%	140%	90%	77%	13.6	1,194

Footnote: Diagnoses in red bold show a step change in both admissions and bed days for both outbreaks, other diagnoses meet the criteria in some years or in one of the criteria. Columns headed 03/04 and 08/09 give the percentage increase in bed days or admissions seen between 2002/03 v 2003/04 and 2007/08 v 2008/09 respectively. ALOS = average length of stay for 2008/09. Note the frequency of diagnoses with a relatively high ALOS. Admissions and bed days include both elective and emergency admissions which represent a continuum of care especially in the medical specialties. See [9] for details of data sources and methods.