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ОСОБЛИВОСТІ УРОДИНАМІКИ НИЖНІХ СЕЧОВИВІДНИХ ШЛЯХІВ У ДІТЕЙ З НЕЙРОГЕННИМ СЕЧОВИМ МІХУРОМ ЗА УМОВИ ВПЛИВУ ТРАНСКРАНІАЛЬНОЇ МАГНІТНОЇ СТИМУЛЯЦІЇ

Порушення сечовиведення в дитячому віці досить розповсюджене і трапляється майже у третини дітей віком від 4 до 15 років, тому метою роботи було вивчення показників урофлоуметрії у дітей з нейрогенним сечовим міхуром за умови застосування транскраніальної магнітної стимуляції (ТМС).

Обстежено 90 дітей (42 дівчинки і 48 хлопчиків) віком 5?12 років. Для урофлоуметрії застосовували уродинамічну систему “ACS 180 Plus” (MENFIS BioMed., США). Визначення психоемоційного стану проводили за тестом Спілбергера — Ханіна, ТМС здійснювали за допомогою приладу «Нейро МС/Д» компанії «Нейрософт» (індукція 2,0 Тл) щодобово однократно двома курсами по 10 діб.

У результаті дослідження дійшли висновку, що ТМС (2,0 Тл, 5 Гц), яка здійснюється на ліву префронтальну кору головного мозку, викликає позитивні лікувальні впливи щодо розладів уродинаміки нижніх сечовивідних шляхів у дітей з нейрогенним сечовим міхуром, вираженість яких має обернену залежність від рівня реактивної тривоги.

Ключові слова: діти, уродинаміка нижніх сечовивідних шляхів, урофлоуметрія, тривожність, транскраніальна магнітна стимуляція.

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PECULIARITIES OF LOW URINARY TRACT URODYNAMIC IN CHILDREN WITH NEURIGENIC BLADDER UNDER CONDITION OF TRANSCRANIAL MAGNETIC STIMULATION

Disturbances of urodynamic occurred in one third of children of 4 to 15 years old.

The aim of work was to investigate urflowmetric indices in children with neurogenic bladder under conditions of transcranial magnetic stimulation (TMS).

90 children have been observed (42 girls and 48 boys) of 5-12 years old. Urodynamic system “ACS 180 Plus” (MENFIS BioMed., USA) was used for uroflowmetry. The psychological state was investigated with Spilberg-Hanin test. TMS was performed using “Neuro MS/D” (Neurosoft) device (induction 2.0 Tl) once per day during 10 days — two such courses of treatment were performed.

As a result of research the authors concluded that TMS (2.0 Tl, 5 Hz), which were performed upon left prefrontal cortex, engendered positive effects upon urodynamic disturbances of low urinary tract in children with neurogenic bladder, and pronouncement of effect of treatment was conversely proportional to the level of patient’s anxiety.

Key words: children, low urinary tract urodynamic, uroflowmetry, anxiety, transcranial magnetic stimulation.

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END-OF-LIFE, UNUSUAL SYNDROMIC SYMPTOMS AND PERIODS OF HIGH PHYSICIAN WORK-LOAD

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Key Points

1. The last 22-weeks of life are marked by rapidly escalating acute medical intervention.

2. Death is a retrospective marker for marginal changes in physician workload.

3. Seasonal variation in death could be expected to account for a 20 to 50% variation in end-of-life related workload.

4. A series of poorly understood, presumed infectious, events lead to roughly 12-month periods of higher deaths, medical admissions, staff sickness absence and bed occupancy.

5. Immune disturbance appears capable of triggering acute events across a wide range of conditions.

6. Physician workload, case mix and complexity therefore fluctuate within a pattern of seasonal and wider infectious events.

1. Introduction

Although some suffer occasionally from sudden death, for most individuals dying is a process. As we age the reserve of all our body systems decline and eventually fail. Because of disease, some systems may cause death by failing prematurely. For example, viral myocarditis might precipitate heart failure and death at an early age, long before the reserve of any other system in the body starts to decline. It could be argued that the viral myocarditis was caused by failure of the immune system, so that it was immune decline rather than cardiac failure that was the primary cause of death. In older age, however, even if one system starts to fail a little earlier than the rest, the others are not far behind, so that a patient's renal failure might soon be followed by respiratory failure, then cardiac failure and death. Indeed, how closely are death and acute admissions aligned?

An audit conducted in Scotland of all patients (elective and emergency) in hospital on the 31st March 2010 established that 29% were dead within one year. This rose to 42% for females aged 85+ and 54% for males aged 85+ [1]. The odds ratio for death of medical inpatients was 3.1-times higher than for surgical inpatients [1]. Some 55% of a person's total hospital bed days occur in the last year of life [5], and in Australia 87% of people are hospitalized at least once in the last year of life [2].

A study in Milton Keynes (England) for persons dying over a 3-year period ending in 2016 established that their hospital bed occupancy remained low from 52 to 22 weeks prior to death, was 5-times higher 9 weeks prior to death and 48-times higher 1 week prior to death [3]. The 22-week 'terminal' period was also observed in a 1990 study in Copenhagen [4]. It is currently assumed that as the population ages the demand for hospital beds will increase. However, this may not be the case. A seven-year cohort study in the late 1990's in Germany concluded that acute hospital bed use does not increase as the population ages [5]. A Swedish study demonstrated that as the age at death increases, the age at first admission after the age of 60 also increases [6], i. e. it is the 22-week terminal period (irrespective of age) that consumes the greatest acute resources.

It goes without saying that younger populations experience fewer deaths, and there is a 5-fold variation between locations relating to the number of deaths per head of population, deaths per general practitioner (GP), and hospital deaths per admission [7]. However, all locations experience fluctuation in medical demand in direct proportion to the changes in local deaths [7]. Hence the question as to which factors most influence the marginal changes in the number of persons dying at any point in time, and hence physician workload?

2. Trends in end-of-life

2.1. Seasonal variation

If we accept the hypothesis that death drives the marginal changes in hospital physician workload, and that acute admissions peak in the last month of life, then seasonal changes in death may explain some of the workload fluctuations. Acute physicians in the Northern hemisphere will be aware that January is usually the busiest month of the year.

Depending on the weather and infectious outbreaks, both December and February are usually the peak months for end-of-life care. Average end-of-life related workload for England and Wales in January is typically 37% higher than in August (the reverse situation occurs in the Southern hemisphere). However, this increase varies considerably (from 25% to 50%) by location in England and Wales (authors analysis of local authority deaths). This wide range is not strongly latitude dependant but probably reflects local weather patterns, inland/coastal gradients, the local mix of urban versus rural residence, and social groups. Common conditions which show higher deaths in the winter compared to the summer are respiratory +98%, cerebrovascular +37%, ischaemic heart +27% and other cardiovascular +24% [8]. One study in Canada demonstrated that 33 out of the 52 most common admission diagnoses were moderately or strongly seasonal [9]. However, given these strong seasonal patterns, plus considerable Poisson scatter associated with smaller monthly totals is it possible that more subtle patterns may lie concealed in the long-term trends.

2.2. Longer-term trends

Given the fact that most medical admissions occur among the 'elderly', Fig. 1 shows the trend in deaths among persons aged 75+ in England and Wales between 1963 and 2015. In 1963 the most common age for death was 78 and only 43% of deaths occurred among those aged 75+, however, by 2015 the most common age for death had risen to 86, and 69% of deaths now occurred among those aged 75 and above.

Note that the increase in deaths occurring from 2012 onward in Fig. 1 was not predicted [7,10-13], and still has no official explanation. Also in Fig. 1 are several spike years (1963, 1968, 1972, 1976, 1985, 1989, 1993, 2003, 2008, 2012, 2015). The spike in 1963 arose from a very extended period of extreme cold at a time when central heating was less common in the UK. Spikes in other years have been typically explained by influenza and other winter infectious outbreaks. Prior to 2000 large seasonal influenza epidemics were common, however, since 2000 the seasonal peaks in influenza have been muted, yet the large peaks in deaths continued to occur [10–13].

3. Step-like changes in deaths

A running (moving) 12-month total is a simple but elegant way of detecting fundamental step-like or on/off changes in the death rate. It removes the complicating

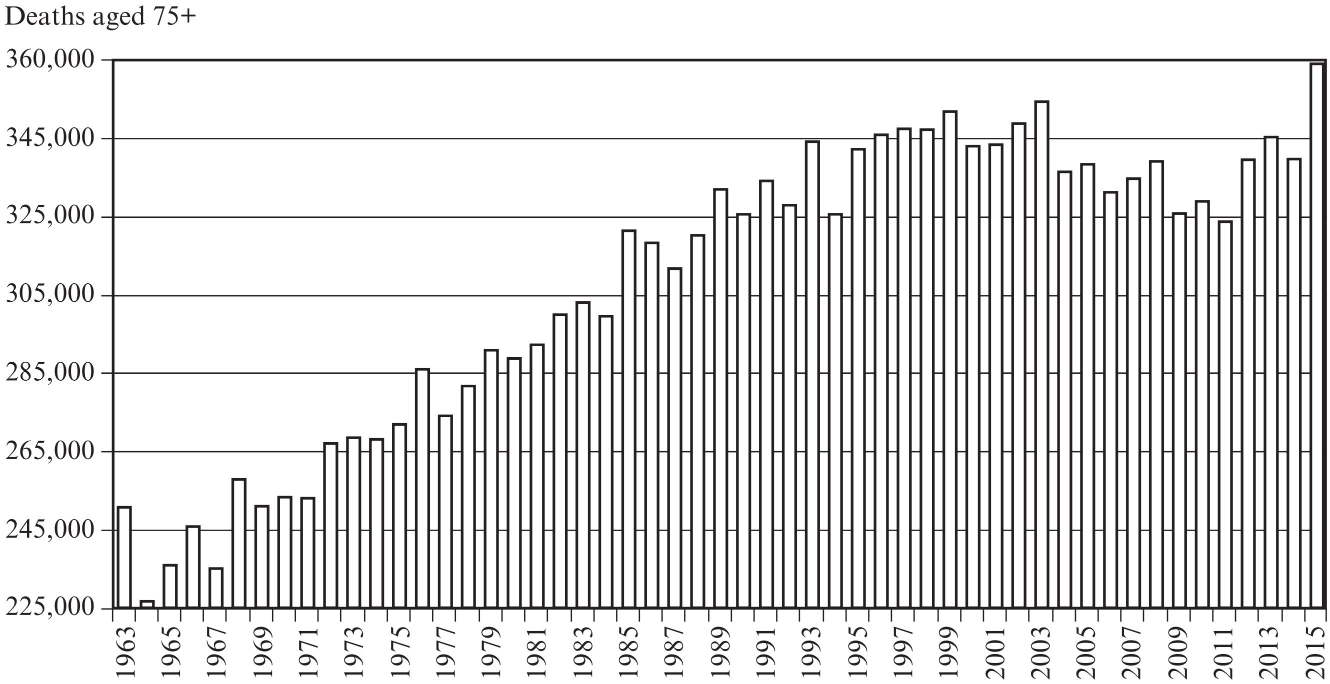

Fig. 1. Annual deaths among persons aged 75+ in England and Wales, 1963 to 2015
Source: Office for National Statistics, deaths by single year of age, https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathregistrationssummarytablesenglandandwalesdeathsbysingleyearofagetables

effects of seasonality, and minimizes the higher monthly Poisson-based variation. Typically, evident in such 12-month running (moving) totals are larger saw-tooth features (Table 1 and Fig. 2) which reflect step-like increases or decreases (on/off changes) in the death rate where deaths stay high for a period of 12-months before switching back to the baseline rate. In a running (moving) 12-month total a sudden shift in death rate creates the upward swing of the saw-tooth, i. e. 11 months of the old and lower rate plus 1 month of the new and higher rate, then 10 months plus 2 months, etc. The actual magnitude of the step-like change is revealed by the absolute difference

Table 1

Magnitude of Recent Step-increase in Medical Bed Occupancy in Several Hospitals and the 12-Month Period Covering This High Bed Demand

Hospital Location	Beds	Step-up, %	12-month ending	Hospital Location	Beds	Step-up, %	12-month ending
Swindon	400	7.2	Dec-15	East Kent	620	10.5	Sep-16
Yeoville	220	8.3	Dec-15	Hampshire	520	3.8	Dec-16
Wirral	470	3.0	Dec-15	Frimley & Slough	860	7.7	Dec-16
Reading	440	6.7	Mar-16	Wye Valley	160	18.1	Dec-16
York	690	5.2	Mar-16	Ipswich	380	14.6	Dec-16
Worcester	450	10.4	Mar-16	Cambridge	570	5.1	Mar-17
Milton Keynes	330	11.1	Mar-16	Kings College (London)	830	5.3	Mar-17
Brighton & Sussex	480	12.1	Jun-16	Wigan	270	7.5	Mar-17
North Tees	420	11.0	Jun-16	East Lancashire	610	3.9	Mar-17
Aintree	500	7.1	Sep-16	Ashford	330	2.7	Mar-17
Dartford & Gravesham	360	8.4	Sep-16	Sheffield	990	3.6	Mar-17

Footnote: Average quarterly occupied beds by specialty for hospitals in England was obtained from NHS England, https://www.england.nhs.uk/statistics/statistical-work-areas/bed-availability-and-occupancy/bed-data-overnight/. Analysis is based on quarterly data which may underestimate the magnitude of the step-increase. Bed availability may also limit the magnitude of the step-increase. The 12-month period occurs at a point in the quarter ending on the month given above. Each hospital will service multiple local government areas, the size of the population will vary roughly with bed numbers. Occupied medical bed numbers are an average over quarters ending March-14 to March-17

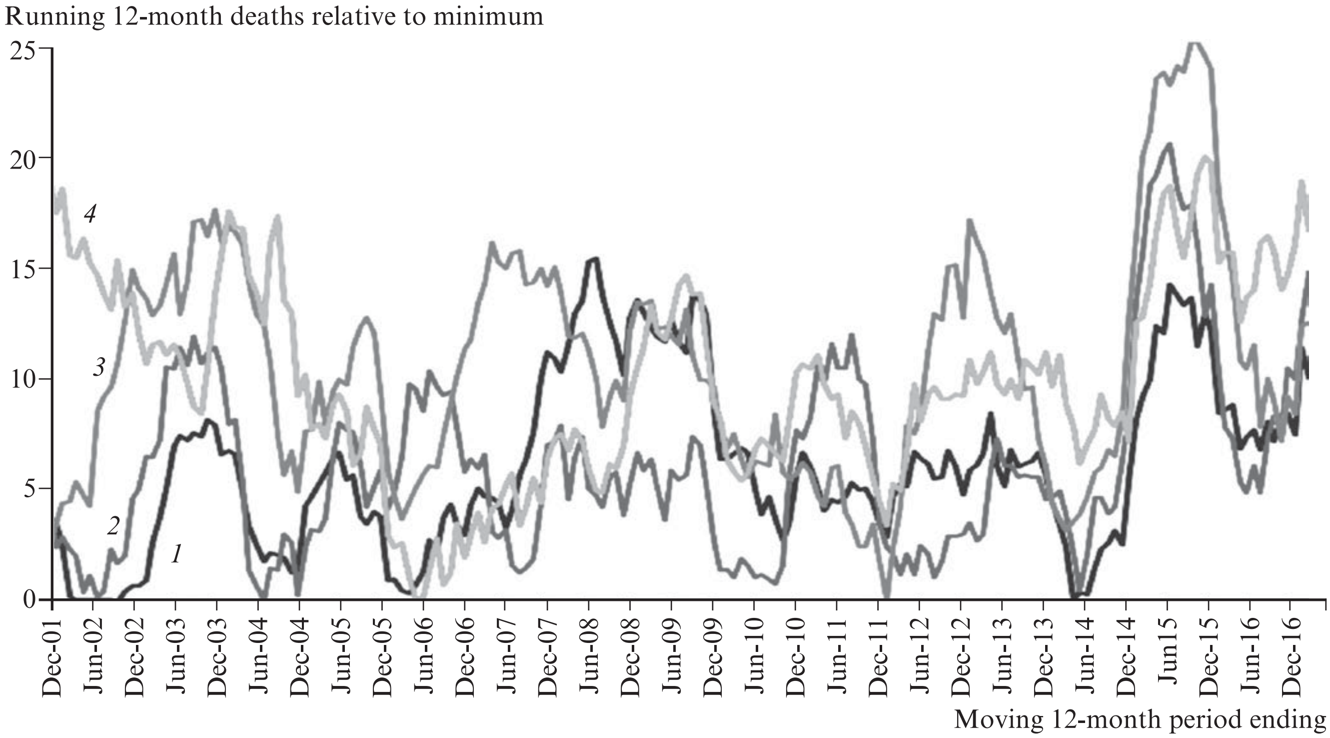

Fig. 2. Running (moving) 12-month total deaths for local authorities in Nottinghamshire, England: *1* — Nottingham; *2* — Broxtowe; *3* — Gedling; *4* — Rushcliffe

Source: Monthly deaths by usual area of residence is from Office for National Statistics. Between 2001 and 2010 there was an overall downward trend in total deaths across the UK and in many local authority areas. This downward trend has been linearized by the application of a second order polynomial (no adjustment has been applied beyond 2010). This allows the saw-tooth behaviour to be more easily visualized.

between peak and trough of the saw-tooth features. The step-like changes only occur in the numbers of medical patients, with obvious effects on work load.

These subtle changes in population deaths have been illustrated in Fig. 2 using four local authority areas in the county of Nottinghamshire (England). These unusual high periods of death endure for around 12-months before reverting to the base-line level of deaths. The 12-month duration is a population average, and as such, may not apply to individuals. This high step-like increase in the apparent death rate seen in Table 1 and Fig. 2 is a composite picture of all the small areas comprising each local authority, hospital or (inter)national geography. The smaller fluctuations seen for each local authority arise from simple Poisson-based variation, hence the larger changes are systematic and not simply due to randomness. Hence, from a medical workload viewpoint the residents of Gedling (Fig. 2) experienced 22% more deaths in the 12-month period ending November 2015 compared to the 12-month period ending March 2014. Likewise, the residents of Nottingham experienced 15% more deaths in the 12-month period ending July 2008 compared to the 12-month period ending May 2006, etc.

One of these step-like events which started during 2014 gave statistically significant increases in death across all UK local government areas, and led to a lower quartile increase of +8.8%, a median increase of +11.5%, and an upper quartile increase of +14.1% [14]. Around 1% of very small areas across England and Wales experience one of these events at any point in time [15], leading to the near simultaneous increase in both deaths and medical admissions. In practice, the increase in deaths lags the increase in medical admissions by around 6–8 weeks [12; 13], as does accompanying staff sickness absence [12]. However, these very small area events aggregate to give larger local and even national events. It is important to stress that local hospitals experience periods of higher death and medical admissions which differ in magnitude and timing (Table 1 and Fig. 1) to the more general national picture, which is a composite across many small areas.

4. What is the cause?

While it would be easy to blame the weather for these curious events, this is not borne out by the facts as these local fluctuations seem to occur in every location and climate so far studied [11], and that there are timing and magnitude differences even between adjacent small areas [15]. In addition, males and females appear to behave separately [15]. During these step-like increases there are 10 additional medical admissions for every extra death [7] and increased staff sickness [12], suggesting that although not generally recognised throughout the whole population, there is an underlying infectious agent or agents. If so, it is not likely to be influenza since it is widely recognised throughout the entire community and kills its older victims within in a relatively short period of time, not over a one-year duration.

It might be possible that a local outbreak of an agent that is innocuous or unnoticed in the general healthy wider population, such as the immune modifying herpes virus cytomegalovirus (CMV), precipitates or aggravates illness in a vulnerable population with multiple co-morbidity [10; 13].

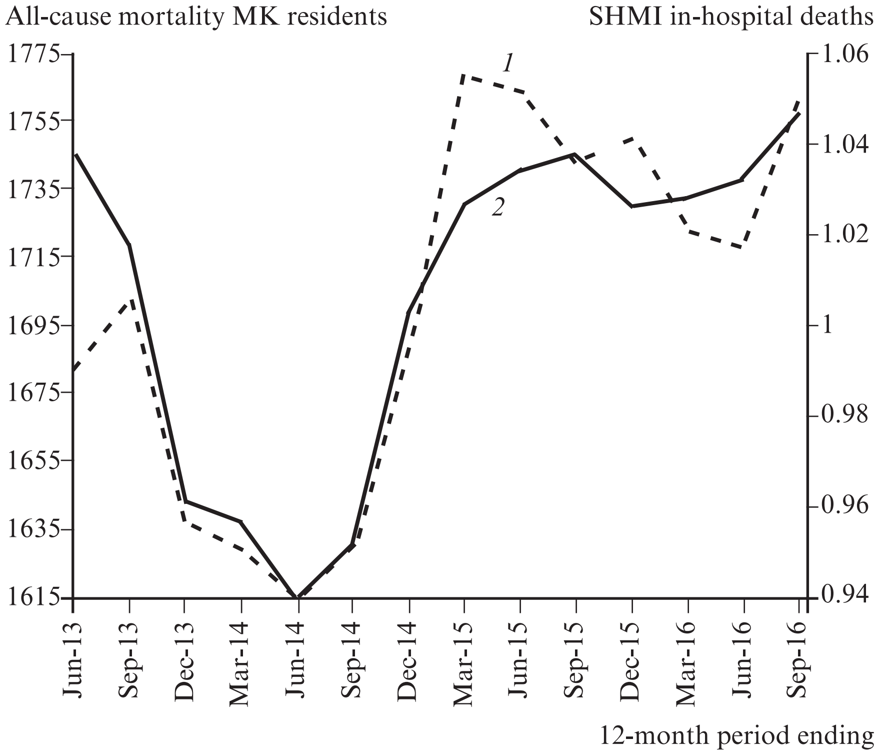

Fig. 3. Moving (running) 12-month total deaths (all-cause mortality) for residents of Milton Keynes local authority, and average SHMI for in-hospital deaths at the Milton Keynes University Hospital (MKUH): *1* — all-cause mortality; *2* — SHMI

Footnote: SHMI data is from NHS Digital, http://content.digital.nhs.uk/SHMI. Monthly deaths for residents of Milton Keynes are from the Office for National Statistics, https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/monthlyfiguresondeathsregisteredbyareaofusualresidence. Note that the MKUH receives patients from adjacent local authority areas and Milton Keynes residents can be admitted to other hospitals. While SHMI has been age, gender and diagnosis group standardized deaths are simply a count of actual numbers and will show higher statistical scatter.

5. Ramifications

Given this dependence on end-of-life and related hospital workload it is important to note that the marginal changes in hospital bed occupancy have been directly linked to marginal changes in the total number of persons dying at any point in time [14]. To make this point clear, it is the count of persons dying (as a proxy for the last year of life) rather than age standardized mortality that drives the changes in medical workload experienced at the individual hospital.

Somewhat surprisingly, the Summary Hospital-level Mortality Indicator (SHMI), a variant of the Hospital Standardized Mortality Rate (HSMR), appears to track the step-lie changes in all-cause mortality in the wider community surrounding a hospital (Fig. 3), suggesting that SHMI/HSMR may not actually be measuring hospital quality of care per se, but wider issues of morbidity and mortality in the surrounding population. The key issue is that neither deaths or SHMI should be behaving in the way demonstrated in Fig. 3.

6. Conclusions

Summer/winter changes in deaths and consequent end-of-life acute admissions reflect strongly in physician workload. Outbreaks of a presumed (persistent) infectious agent add additional 12-month periods of higher admissions/workload whose magnitude and timing depend on location. The usual summer/winter pattern is simply shifted to a higher level.

In persons who are in the terminal phase of life the presenting condition(s) can arise out of general dysregulation in the most susceptible system. This dysregulation appears to be exacerbated (in some individuals) by both small-area mini-outbreaks and larger local and national outbreaks of a presumed infectious agent. While the persistent immune modifying virus CMV has been circumstantially identified as a potential candidate urgent research is required to identify the exact pathogen.

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Ключові слова: завершення життя, робоче навантаження, звичайні діагнози, загальна смерт-

ність, інфекційні спалахи, сезонний, імунітет.

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Родні П. Джонс

ЗАВЕРШЕННЯ ЖИТТЯ, НЕЗВИЧАЙНИЙ СИНДРОМ І ПЕРІОДИ ВИСОКОГО ЛІКАРСЬКОГО НАВАНТАЖЕННЯ

Лікарі у своїй практиці часто стикаються з періодами нез'ясованого високого навантаження і труднощів у роботі з хворими. Близько 55 % часу перебування пацієнтів у лікарні може припадати на їхній останній рік життя, а саме — на останні 22 тиж. життя. Смерть — це ретроспективний маркер зростання кількості втручань для усунення заплутаних, поєднаних патологій. Цей процес впливає на зміни в лікарському навантаженні: кількість хворих, що надійшли до лікарні; відсоток поєднаних патологій, внутрішньолікарняних летальних випадків, використання госпітальних ліжок. До того ж у період сезонних циклів також відмічаються підйоми, можливо викликані поки що неідентифікованими патогенами, які призводять щорічно до підвищення смертності, кількості надходжень хворих до стаціонару, захворюваності тощо.

Ключові слова: завершення життя, робоче навантаження, звичні діагнози, загальна смертність, інфекційні спалахи, сезонний, імунітет.

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Rodney P Jones

END-OF-LIFE, UNUSUAL SYNDROMIC SYMPTOMS, AND PERIODS OF HIGH PHYSICIAN WORKLOAD

Physicians often encounter periods of unexplained higher workload and patient complexity. End-of-life marks a period of declining immune function, increasing frailty and declining cognitive function. Some 55% of a person's lifetime stay in an acute hospital can occur in the last year of life, and more specifically in the last 22 weeks of life. Death is therefore a retrospective marker of escalating acute intervention for a seeming confusing jumble of conditions. Marginal changes in death appear to drive the marginal changes in physician workload in both volume of admissions, apparent case-mix, in-hospital deaths and occupied beds. In addition to the more widely recognised seasonal cycles, there are outbreaks, possibly caused by a yet unidentified infectious pathogen(s), which lead to 12-month periods of higher deaths, medical admissions and health care worker sickness absenteeism.

Key words: end-of-life; workload; common diagnoses; all-cause mortality; infectious outbreaks; seasonal; immune function.