Medical health care utilization cost of patients presenting with psychogenic nonepileptic seizures.

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Key words: Epilepsy monitoring, Psychogenic nonepileptic seizures, Cost effectiveness, Medical care, Status epilepticus

SUMMARY

Objective

To investigate the health care utilization cost of patients presenting with psychogenic nonepileptic seizures (PNES) to a tertiary hospital in Australia.

Methods

This is a retrospective analysis of adult patients with PNES based on video-EEG confirmation over a 5-year period. We used an itemized list to collect detailed health care utilization data. The items included emergency room (ER) visits, hospital ward admissions, intensive care unit (ICU) admissions, outpatient neurology clinic visits, medical interventions, Code Blue and Medical Emergency Team calls for seizures, medications, and investigations. We calculated the cost of each individual item separately for each individual presentation. To investigate the proportional contribution of each covariate towards the total health care utilization cost, an analysis of the relative importance in the linear regression was performed.

Results

There were 39 patients out of which seven (18%) were admitted to the ICU with suspected status epilepticus. The median total health care utilization cost per person until the diagnosis of PNES was established was 26,468 AUD (19,207 USD). In the item breakdown, the highest median cost was incurred by investigations (13,119 AUD = 9,520 USD), followed by hospital ward management (8,890 AUD = 6,451 USD), ICU stay (3,764 AUD = 2,731 USD), outpatient neurology clinics (2,200 AUD = 1,596 USD), and ER visits (570 AUD = 413 USD). Nonepileptic psychogenic status (23%) and the duration of PNES disorder (10%) were the most significant variables contributing to the variance ($R^2$) of the model.

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Significance

A considerable burden of health care utilization cost is caused by PNES. The presence of nonepileptic psychogenic status and a longer duration of the condition predicts a higher cost.

Key words: Epilepsy monitoring, Psychogenic nonepileptic seizures, Cost-effectiveness, Medical care, Status epilepticus

Introduction

Psychogenic nonepileptic seizures (PNES) are among the most challenging diagnostic and management problems in clinical practice. The rate of misdiagnosis of PNES as epilepsy is as high as 30%\(^1\), with an average diagnostic delay of 7-9 years.\(^2,3\) Misdiagnosis and inappropriate interventions lead to adverse outcomes such as increased morbidity and even mortality.\(^4,5\)

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The health care utilization cost incurred as a result of misdiagnosis and delayed diagnosis of PNES has received relatively less emphasis in the literature. Multiple emergency room (ER) visits, hospital admissions, and diagnostic tests resulting in an increased health care utilization cost by patients presenting with PNES has been reported. Establishing the diagnosis of PNES leads to a significant drop in health care utilization including ER visits. This is accompanied by a significant reduction in the health care utilization cost. Some patients with markedly prolonged PNES are misdiagnosed as status epilepticus (nonepileptic psychogenic status=NEPS), and the health care utilization cost of this particular group has not been well characterized.

In the US, the mean incidence of PNES is three per 100,000 people per year, whereas the prevalence has been estimated to be 33 per 100,000 people. The incidence and the prevalence are relevant to understanding the overall burden of health care utilization cost in a country. The lifetime dollar cost per year in the PNES patient cohort ranges from $110 to 920 million in the US setting.

There is no incidence and health care utilization cost data related to PNES published from Australia. Australia has a publicly-funded universal health care system (“Medicare”) providing free health care to all citizens. Hence, a deep understanding of health care utilization cost caused by PNES has important implications for health care planning.

Against this backdrop, we undertook the current study to estimate the health care utilization cost incurred by PNES patients until their diagnosis was established by video-EEG monitoring (VEM) in a tertiary hospital. We adopted a detailed costing evaluation to calculate the most likely cost value per each patient taking into consideration all aspects of health care utilization within the same hospital network.

**Methods**

**Subjects**

This was a retrospective study conducted at Monash Medical Centre, Victoria, Australia. The study was approved by the Human Research Ethics Committee of Monash Health, Australia. We reviewed medical records of all patients who underwent inpatient VEM from May 2009 to June 2014. In the current study, we included adult patients (age ≥18 y) who received a final diagnosis of PNES. The final diagnosis was established by the consensus opinion of at
least two epileptologists based on the history, examination, and investigations including VEM. Patients who had a combination of both epileptic seizures and PNES were excluded from the analysis in keeping with previous research.6,9 Our methodology and protocols of VEM have been published previously.10

Data acquisition

We reviewed all medical records pertaining to ER visits, hospital admissions (including the intensive care unit), and outpatient neurology clinic visits for data collection. In addition to demographic and clinical data, we collated detailed information on health care utilization. We collected data from the first PNES-related presentation to a hospital affiliated with Monash Health Network, until the diagnosis was established with VEM. Emergency room visits, outpatient neurology clinic visits, and hospital admissions due to unrelated medical conditions were excluded.

We used an itemized list to collect health care utilization data in relation to presentations with PNES. This included ER visits (number and duration), hospital ward admissions (number and duration), intensive care unit (ICU) admissions (number and duration), number of outpatient neurology clinic visits, interventions (intubation, ventilation, arterial line etc.), Code Blue and Medical Emergency Team (MET) calls for seizures, medications with total dosages, and investigations (EEG, VEM, ECG, radiology, blood tests).

We calculated the cost of ER visits, ward admissions, interventions, emergency calls, and the ICU stay based on the billing policy obtained from the finance department of the hospital. The cost of outpatient neurology clinic visits and investigations was calculated according to the corresponding Medicare item number specified by the Department of Human Services. Similarly, we calculated the cost of medications based on the medicines price list formulated by the Pharmaceuticals Benefits Scheme of the Department of Health, Australia.

Statistical analysis

We calculated the cost of each individual item separately for each individual presentation in keeping with our model of detailed costing. Then, we categorized costings into five groups; 1. emergency department, 2. hospital ward, 3. intensive care unit, 4. outpatient neurology clinic, and 5. investigations. The costs of interventions, medications, and emergency calls were included in the relevant department (ER, ward, ICU, outpatient neurology clinic), whereas the
cost of all investigations was grouped together under one category. We calculated the median cost of each group and the total cohort. We explored the differences in the health care utilization cost between males and females as well as patients presenting with and without NEPS using Mann-Whitney U test.

Finally, we conducted an analysis of the relative importance of covariates in a linear regression model to investigate the proportionate contribution of variables to the total health care utilization cost. We selected sex, NEPS (yes/no), comorbid anxiety or depression (yes/no), seizure burden (frequency), receiving a disability support pension, and the duration of PNES as covariates, while the total health care utilization cost was the dependent variable. The confidence intervals were estimated by bootstrapping the data 1000 times using “relaimpo” package for R. P values of <0.05 were considered statistically significant. Analyses were conducted using R statistical package (version 3.4.3).

**Results**

A total of 39 patients fulfilled the inclusion criteria. Females constituted 74.4% of the cohort (29 cases). The median age of the cohort was 35 y (range 20-82 y) and the median duration of the condition was 3 years (range 1 to 432 months). Twenty-four patients (61.5%) were found to be diagnosed with anxiety or depression. All patients underwent inpatient VEEG monitoring (range=2 to 13 days; mean 5.7±2.4 days).

Seven patients (18%) had ICU admissions for suspected status epilepticus. This subgroup consisted of five females and two males with ages ranging from 21 to 50 y. Notably, one patient had two ICU admissions. They spent a total of 31 days in the ICU (average=4.4 days). Four patients were intubated and mechanically ventilated subsequently. Medical records revealed that patients were intubated for airway protection due to prolonged reduced conscious state and sometimes due to respiratory depression as a result of overtreatment with benzodiazepines. Arterial lines were inserted in three patients. This subgroup of patients recorded a prolonged stay in the hospital ward as well (total=81, average=11.6 days).

During their stay as inpatients in the hospital, eight patients had Medical Emergency Team (MET) calls for sudden deteriorations of the conscious state. MET calls are activated for rapid assessment and management by a dedicated emergency team in instances of unexpected clinical deterioration of patients. Seizures and decreased conscious state are indications for
MET calls in our hospital. Repeated episodes of altered conscious state were a common feature among these patients and one had nine such episodes prompting MET calls during an admission. Code Blue was activated for suspected cardio-respiratory arrest on one occasion.

Twenty-five patients (64.1%) underwent magnetic resonance imaging (MRI) brain scans and seven patients had multiple scans. One patient had five MRI brain scans while three patients underwent four scans each before confirmation of the diagnosis of PNES. Computed tomography (CT) brain scans were done in 15 patients (38.5%) and nine of them had multiple scans. In all patients, outpatient EEGs had been performed prior to VEM, while eight had multiple outpatient EEGs. CT scans of the cervical spine were performed in six patients (15.4%) for suspected cervical spinal injury due to seizures. Fifteen patients (38.5%) had chest radiographs and seven of those patients were treated in the ICU with suspected status epilepticus. Electrocardiograms were recorded from 21 patients (53.8%). Numerous blood tests including serum biochemistry, full blood count, liver function tests, and serum antiepileptic drug levels were performed across the entire cohort.

The median total health care utilization cost per person until the diagnosis of PNES was established was 26467.63 AUD (interquartile range 14875.00 to 43358.12) (USD equivalent =19,207) (Figure 1). The total cost was calculated by adding the costs of five categories defined above. In the cost breakdown of those five categories, the highest median cost was incurred by investigations (13,118.75 AUD = 9,520 USD), followed by hospital inpatient (ward) management (8,890 AUD = 6,451 USD), ICU stay (3,763.60 AUD = 2,731 USD), outpatient neurology clinics (2,200 AUD = 1,596 USD), and ER visits (570 AUD = 413 USD). Those who presented with NEPS incurred significantly more cost (p=0.002) than other PNES patients (median cost 55226.64 AUD versus 20028.87 AUD; USD equivalent 40,078 versus 14,535). There was no significant difference in health care utilization costs between males and females (p=0.8). In our regression analysis, NEPS (23%; 95% CI=0.07 to 0.41) and the duration of PNES (10%; 95% CI=0.01 to 0.30) were the most important variables contributing to the variance (R²) of the model (Figure 2). The individual characteristics are summarized in table 1. Figure 1 shows a single outlier, a patient who presented with recurrent NEPS. Repeating the analysis with the exclusion of this outlier did not change our results.

Discussion
We investigated the health care utilization cost in patients presenting with PNES to a tertiary hospital in Australia. Importantly, the median total cost per patient until the confirmation of diagnosis was 26,468 Australian Dollars (approximately 19,207 USD). The presence of NEPS and a longer duration of the condition were associated with a higher health care utilization cost. Our findings highlight the importance of early detection of PNES, in particular, NEPS, to minimize health care utilization costs.

Several studies have been conducted on health care resource utilization in PNES without estimating the costs involved.\textsuperscript{12-15} Our literature search yielded only four studies, three conducted in the US and one from Ireland, describing health care utilization costs in PNES (Table 2).\textsuperscript{6, 9, 16, 17} Direct comparisons of those with our study are difficult due to variable methodologies used particularly in relation to the itemization and calculation of various costs, differences in health care delivery systems, and temporal variability of costs.

A study from the US published in 1998 reported 20 patients diagnosed with PNES analyzing the cost of medications, outpatient clinic visits, standard diagnostic tests (EEG, MRI, CT), laboratory blood tests, and ER visits six months before and six months after confirming the diagnosis.\textsuperscript{6} The average pre-diagnosis total cost was 8,156 USD per six months and the cost significantly dropped to 1,306 USD (p<0.003) after establishing the diagnosis. Similar to our study, the highest contribution to the total cost was from investigations (average 4,190 USD). The lower total cost compared with our study (8,156 USD versus 19,207 USD) can be explained on several grounds. First, the US study did not include ICU and hospital ward costs. Second, they calculated the cost for 6 months, whereas we analyzed the total cost from the first presentation to the hospital until the diagnosis was established. Finally, changing health care costs with time may have affected the results as the US study was conducted in 1998.

Another study conducted in the US and published in 2013 reported health care utilization costs of 24 patients 12 months before and after confirmation of the diagnosis.\textsuperscript{9} The costs included ER visits, inpatient stay, and outpatient visits. The mean pre-diagnosis cost was 4,567 USD per 12 months and it was reduced to 2,783.77 USD post-diagnosis. Exclusion of the ICU cost and the differences between two health care systems may account for the cost discrepancy with our study. In comparison, the pre-diagnosis cost of PNES is moderately less than epilepsy-related direct medical costs of uncontrolled epilepsy but much higher than that of well-controlled epilepsy in the US setting.\textsuperscript{18}
Based on 16 patients, a study conducted in the US in 1995 found the pre-diagnosis medical cost to be 15,000 USD per person with PNES. The cost analysis was based on six items: antiepileptic drugs, imaging, EEG, ER visits, physician cost, and hospital cost. The “hospital cost” was the highest contributor averaging 6,000 USD per patient. However, the components contributing to the hospital cost are not specified in the publication. It is unclear whether costs related to ICU, outpatient clinics, and blood tests were considered. Similar to our study, they report the total pre-diagnosis cost per patient and the results can be considered roughly concordant.

A more recent study (2014) from a tertiary hospital in Ireland calculated the health care utilization costs based on ER visits, consultations, antiepileptic drugs, and investigations. Based on their retrospective analysis, authors reported an annual direct medical cost of €5429.30 per patient. This is likely to be an underestimate as authors did not include the cost related to ICU and hospital admissions. Additionally, the indirect economic cost (loss of income tax, social welfare cost) was estimated to be €15,566 per patient.

These studies, along with our results, indicate that the reported health care utilization cost of PNES depends on the health care system and the items included in the analysis. Yet, all studies demonstrate similar trends.

Markedly prolonged PNES, identified as NEPS, remains a poorly understood and challenging entity. It perhaps is an under-recognized condition and among 85 consecutive patients with PNES, 77.6% reported at least one episode of prolonged PNES in one study. A survey among neurologists has revealed many gaps in the diagnosis and treatment of NEPS in the current clinical practice. The potential for unnecessary interventions and subsequent complications including death in NEPS has been well documented in the literature. It is important to note that 18% of the cohort we studied had ICU admissions due to NEPS. This group utilized significantly more health care resources than other PNES patients. More than 50% of those patients received unnecessary interventions such as intubation (sometimes), mechanical ventilation, and arterial line insertion. Beyond the dollar cost, we wish to emphasize the risk of potentially deleterious complications in this group.

Functional neurological symptom disorder/conversion disorder, defined as conditions without any demonstrable structural or pathophysiological abnormalities, represent approximately 10% of the patients seen in the neurology practice. Neurological presentations classified

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under functional disorders include pain, sensory disturbances, weakness, gait abnormality, and seizures (PNES).\textsuperscript{22, 23} There is a considerable burden of psychiatric comorbidity in this group of patients. One study based on 300 consecutive referrals to an outpatient neurology clinic reported depression or anxiety disorders in 67% of patients with functional symptoms as opposed to 38% in other patients with neurological conditions.\textsuperscript{24} Most studies suggest depression and anxiety rates of around 50% in PNES.\textsuperscript{16} The management of psychiatric comorbidities is likely to incur a considerable health care utilization cost in patients with PNES.

Medical comorbidities are common among patients diagnosed with PNES. A retrospective analysis reported a significantly higher frequency of medical comorbidities in PNES (65%) compared with epilepsy (27%).\textsuperscript{25} Furthermore, 5% of PNES population seen in epilepsy monitoring units has coexisting epilepsy.\textsuperscript{26} The management of medical comorbidities is likely to increase the overall health care utilization cost among patients with PNES.

Multiple, repetitive, and often unnecessary investigations were salient findings in our study. Two-thirds of the cohort had MRI scans of the brain and one-third of them had multiple scans. Similarly, 38.5% of patients underwent CT brain scans and many of them had multiple scans. We also found that several patients had chest radiographs and cervical spine CT scans. A study conducted in the US revealed that, on average, 10 radiologic studies were performed per patient over a three-year period before confirming the diagnosis of PNES.\textsuperscript{15} These findings highlight the tendency for excessive investigations in this group of patients and the need for an early diagnosis to reduce the cost of investigations as well as undue morbidity such as radiation exposure.

It would be useful to compare the health care utilization cost of PNES with refractory epilepsy. However, results are comparable only if the same methodology is used. Most studies from the US are based on health insurance claims.\textsuperscript{18} A recent study from Australia, based on hospitalization costs from 2012 to 2016, reported a median health care utilization cost of 16,800 AUD among patients with refractory epilepsy who underwent epilepsy surgery.\textsuperscript{27} Though not directly comparable due to differences in the study methodology, our results suggest that PNES is associated with a high financial burden on the health care system similar to refractory epilepsy.
There is an increasing need for an integrated approach within health care systems to reduce the cost associated with PNES. Early diagnosis and intervention remains the key to prevent undue costs. There is a pressing need to develop evidence-based treatment pathways involving a multidisciplinary approach adapted to the local health care system in order to close the treatment gap and eventually reduce the undue cost.²⁸

We acknowledge some study limitations. First, the sample size was small. However, we believe that our detailed methodology has compensated for this drawback. Second, we believe that our total cost is likely to be an underestimate due to several reasons. In our experience, patients with PNES tend to seek treatment from multiple institutions and providers including hospitals, general practitioners, specialists, psychologists, outpatient clinics, and support services in both private and public sectors. Health care cost data extraction from multiple institutions and providers is difficult without an access to a complex data linkage system. Hence, we decided to limit our study to costs incurred within our hospital network. We did not include the cost of the management of medical and psychiatric comorbidities as we did not have access to data on services provided outside our hospital network.

Third, this was a retrospective study from a single health care network in Australia. Hence, the results may not be generalizable. Fourth, there is no comparator group. It would have been useful to compare the cost of PNES with an epilepsy cohort. Our PNES cohort varied in severity and included patients at different stages (early onset, chronic, NEPS). Finding a comparable epilepsy cohort was hence challenging (e.g. newly diagnosed epilepsy, refractory epilepsy, chronic stable epilepsy, epilepsy surgical series). An alternative would have been to compare the costs before and after the confirmation of PNES diagnosis. However, some patients were lost to follow-up and we did not have sufficient data on post-diagnosis health care utilization cost. Therefore, we opted to study the costs of PNES alone until confirmation of the diagnosis with VEM. Previous studies have demonstrated significantly reduced health care resource utilization after establishing the diagnosis of PNES.⁶

Finally, we highlight the impact of tertiary center bias. It has been well established that there is a long delay in establishing the diagnosis of PNES. However, in a tertiary center, this delay may be less when the patient is seen by an expert at an early stage of the condition. Hence,
the overall health care utilization cost in the PNES population is likely to be much higher than what we have reported.

In conclusion, this is the first health care utilization cost study in PNES from Australia based on detailed cost analysis. Our findings demonstrate similar trends compared with previous studies from the US and Ireland. Longer duration of the condition and the presentation with NEPS are the most important variables associated with an increasing cost of health care utilization. Our results also demonstrate the tendency for repeated investigations and unwarranted ICU admissions as well as unnecessary and potentially dangerous interventions in these patients. Finally, we wish to highlight the financial burden of PNES and emphasize the need for improved medical education to reduce the rate of misdiagnosis and the diagnostic delay.

Key Points

- We conducted a detailed medical cost analysis of PNES
- 18% of patients presented with NEPS
- The highest cost was incurred by investigations
- NEPS and longer duration of PNES predicted a higher cost

Ethical publication statement

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Disclosure of conflict of interest

None of the authors has any conflict of interest to disclose. We did not receive any funding for the study.
Figure legends

Fig 1. The histogram of total health care utilization cost.

Fig 2. The bar diagram showing relative importance of regressors in linear models for total health care utilization cost.

This bar chart illustrates relative contributions of sex, nonepileptic psychogenic status, duration of psychogenic nonepileptic seizure history, history of anxiety, history depression, receipt of disability support pension, and seizure burden to the total variance of the model.

$y = R^2$ Explained (%)

A= Anxiety; B= Depression; C= Disability support; D= Duration of illness; E= Nonepileptic psychogenic status; F= seizure burden; G= Sex
Table 1. Demographic characteristics, clinical associations, and total health care utilization costs of individual subjects.

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*Seizure burden refers to the average frequency of psychogenic nonepileptic seizures during the six-month period preceding the diagnostic confirmation with video-EEG. 1= rarely, 2= monthly, 3= weekly, 4= daily*

**Table 2: A comparison of previous publications on health care utilization cost in psychogenic nonepileptic seizures with the current study**

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<tr>
<th>reference</th>
<th>Country &amp; year of publication</th>
<th>Number of patients</th>
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<th>Total cost (pre-diagnosis)</th>
<th>Cost breakdown (pre-diagnosis)</th>
<th>Total cost (post-diagnosis)</th>
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<td>Martin et al, USA, 1998</td>
<td>20</td>
<td>Retrospective case series</td>
<td>8156 USD (mean/patient/6 months)</td>
<td>Outpatient visits=299.1; ER visits=3407; diagnostic procedures=4010; laboratory test=180; drugs=654.7 (mean/patient/6 months)</td>
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<th>Study</th>
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<td>Binder et al</td>
<td>USA, 2007</td>
<td>16</td>
<td>Retrospective case series</td>
<td>15,000 USD (average/patient)</td>
<td>Drugs=3000; imaging=2000; ER visits=1000; hospital cost=6000, physician cost=900; EEG=600 (average/patient)</td>
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<td>Ahmedani et al</td>
<td>USA, 2013</td>
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<td>Retrospective case series</td>
<td>4567.01 USD (mean/patient/12 months)</td>
<td>ER visits=91.76; inpatient cost=3142.92; neurology costs=3479.67; behavioural health costs=182.80; other services costs=786.67 (mean/patient/12 months)</td>
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<td>Magee et al</td>
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<td>Current study</td>
<td>Australia, 2018</td>
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<td>Retrospective case series</td>
<td>26467.63 AUD (median/patient until diagnosis)</td>
<td>investigations=13118.75; inpatient=8890.00; ICU=3763.60; outpatient neurology clinics=2200.00; ER visits=570.0 (median/patient until diagnosis)</td>
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References


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Author/s:
Seneviratne, U; Low, ZM; Low, ZX; Hehir, A; Paramaswaran, S; Foong, M; Ma, H; Phan, TG

Title:
Medical health care utilization cost of patients presenting with psychogenic nonepileptic seizures

Date:
2019-02-01

Citation:

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