Economic Cost of Functional Neurologic Disorders

A Systematic Review

Brian O'Mahony, MB BCh, BAO, Glenn Nielsen, BSc, PhD, Sallie Baxendale, PhD,
Mark J. Edwards, MBBS, BSc, PhD, FRCP, FEAN, and Mahinda Yogarajah, MD

Correspondence
Dr. Yogarajah
mahinda.yogarajah@nhs.net

Abstract

Background and Objectives

Functional neurologic disorder (FND) represents genuine involuntary neurologic symptoms and signs including seizures, weakness, and sensory disturbance, which have characteristic clinical features, and represent a problem of voluntary control and perception despite normal basic structure of the nervous system. The historical view of FND as a diagnosis of exclusion can lead to unnecessary health care resource utilization and high direct and indirect economic costs. A systematic review was performed using Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to assess these economic costs and to assess for any cost-effective treatments.

Methods

We searched electronic databases (PubMed, PsycInfo, MEDLINE, EMBASE, and the National Health Service Economic Evaluations Database of the University of York) for original, primary research publications between inception of the databases and April 8, 2022. A hand search of conference abstracts was also conducted. Key search terms included "functional neurologic disorder," "conversion disorder," and "functional seizures." Reviews, case reports, case series, and qualitative studies were excluded. We performed a descriptive and qualitative thematic analysis of the resulting studies.

Results

The search resulted in a total of 3,244 studies. Sixteen studies were included after screening and exclusion of duplicates. These included the following: cost-of-illness (COI) studies that were conducted alongside cohort studies without intervention and those that included a comparator group, for example, another neurologic disorder (n = 4); COI studies that were conducted alongside cohort studies without intervention and those that did not include a comparator group (n = 4); economic evaluations of interventions that were either pre-post cohort studies (n = 6) or randomized controlled trials (n = 2). Of these, 5 studies assessed active interventions, and 3 studies assessed costs before and after a definitive diagnosis of FND. Studies showed an excess annual cost associated with FND (range $4,964–$86,722 2021 US dollars), which consisted of both direct and large indirect costs. Studies showed promise that interventions, including provision of a definitive diagnosis, could reduce this cost (range 9%–90.7%). No cost-effective treatments were identified. Study comparison was limited by study design and location heterogeneity.

Discussion

FND is associated with a significant use of health care resources, resulting in economic costs to both the patient and the taxpayer and intangible losses. Interventions, including accurate diagnosis, seem to offer an avenue toward reducing these costs.

Glossary

CBT = cognitive behavioral therapy; **COI** = cost of illness; **FMD** = functional movement disorder; **FND** = functional neurologic disorder; **FS** = functional seizure; **GDP** = gross domestic product; *ICD-9/10* = *International Classification of Diseases, Ninth/Tenth Revision*; **NICE** = National Institute for Health and Care Excellence; **PNES** = psychogenic nonepileptic seizure; **PPP** = purchasing power parity; **QALY** = quality-adjusted life year; **QoL** = quality of life; **RCT** = randomized controlled trial; **SMC** = standard medical care; **USD** = US dollar; **vEEG** = video EEG.

Functional neurologic disorders (FNDs) represent genuine involuntary neurologic symptoms and signs that have characteristic clinical features and represent a problem of voluntary control and perception despite normal basic structure of the nervous system.[1] Manifestations of FND are varied and include the following in isolation or combination: abnormal movements; weakness or paralysis; sensory loss or abnormal sensory symptoms; swallowing or speech symptoms; and epileptic-like episodes (i.e., functional seizures [FSs]).[1] FNDs carry a significant impact on the patient's quality of life (QoL),[2,3] and patients often present with comorbid psychiatric conditions, with both depression and anxiety occurring in up to 40% of patients with FND.[4,5]

FND has a prevalence of up to 50/100,000 and an incidence of up to 12/100,000 per year. Psychogenic nonepileptic seizure (PNES) contributes a further 1.5–4.9 per 100,000 population per year, with a prevalence of 2–33 per 100,000 population.[6] Patients with FND make up 9% of neurology admissions,[7,8] 16% of neurology clinic referrals,[9] and 10%–25% of patients referred to epilepsy specialist centres.[10] Patients with FND often require multiple consultations over several years before receiving a diagnosis of FND[11] and then frequently re-present to emergency departments after receiving such a diagnosis.[12] Delayed diagnosis leads to worse outcomes for patients[4] and preventable costs, such as missed work, general practitioner and specialist appointments, and investigations. Diagnostic uncertainty amid ongoing symptoms can also lead to intangible costs, such as decreased QoL.

These costs carry a burden to patients, clinicians, and health care systems and to the economy. Indeed, patients with FND have been found to be more likely to not be working for health reasons and more likely to be receiving disability-related state financial benefits than people with other neurologic disorders.[13]

Various treatments such as physiotherapy[14] or cognitive behavioral therapy (CBT)[15] can lead to improvement of these symptoms and QoL. Of importance, an intervention of simply providing the patient with an accurate diagnosis, and thus explanation of their symptoms, can also improve mood and QoL[16] and decrease health care resource utilization.[17]

The costs of FND (and other medical conditions) can be believed of as direct and indirect costs. Direct costs represent resources used for health care (e.g., cost of investigations or the time spent on assessment by a doctor), while indirect costs represent productivity losses arising from morbidity-related sickness absence (e.g., loss of employment, benefits, or the cost of childcare while hospitalized). Direct and indirect costs together constitute the economic burden of FND, which can be quantified through cost-of-illness (COI) studies. A COI study can use a top-down or a bottom-up approach. Bottom-up methods estimate costs based on data from records (or observed usage) at the service provider level, whereas top-down approaches use administrative registers of costs.[18]

Other studies of health care utilization focus on economic evaluation (EE). There are different types of EEs: cost-minimization analyses address the question of whether an intervention would result in lower health care costs. Cost-effectiveness analyses combine costs and clinical parameters, such as gained life years or recovered cases, to assess whether the intervention is cost-effective.[19] Cost-utility analyses use quality-adjusted life years (QALYs) as their measure of effectiveness. QALYs attempt to quantify the impact of the patient's condition on the quality and quantity of life lived. Typically, cost-effectiveness analyses use the incremental cost-effectiveness ratio, which is a measure of the additional cost per unit of health gained. Whereas COI presents information only on the economic burden of a disease, EE can assist decision makers to decide toward which interventions to prioritize resources.

Given the reportedly high burden FND places on patients and society, we aimed to systematically review the health economic literature on FND. Our objectives were as follows:

1. to investigate the direct and indirect costs of FNDs and
2. to investigate whether any interventions to treat FNDs are cost-effective.

Methods

Criteria for Considering Studies for the Review

This study followed the methodology and guidelines set out by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist for systematic reviews[20] (eAppendix 1, links.lww.com/WNL/C833). Studies were included if they reported original cost or cost-effectiveness data for FN Ds. The references of any studies whose text was read in full were screened to identify further studies. Reviews, qualitative studies, studies reporting results of other studies, qualitative studies, and any studies that were not available in English were excluded. Case reports and series were also excluded. Article were screened for inclusion by B.O.M. and M.Y., and all data were

Figure PRISMA Flowchart of Study Identification
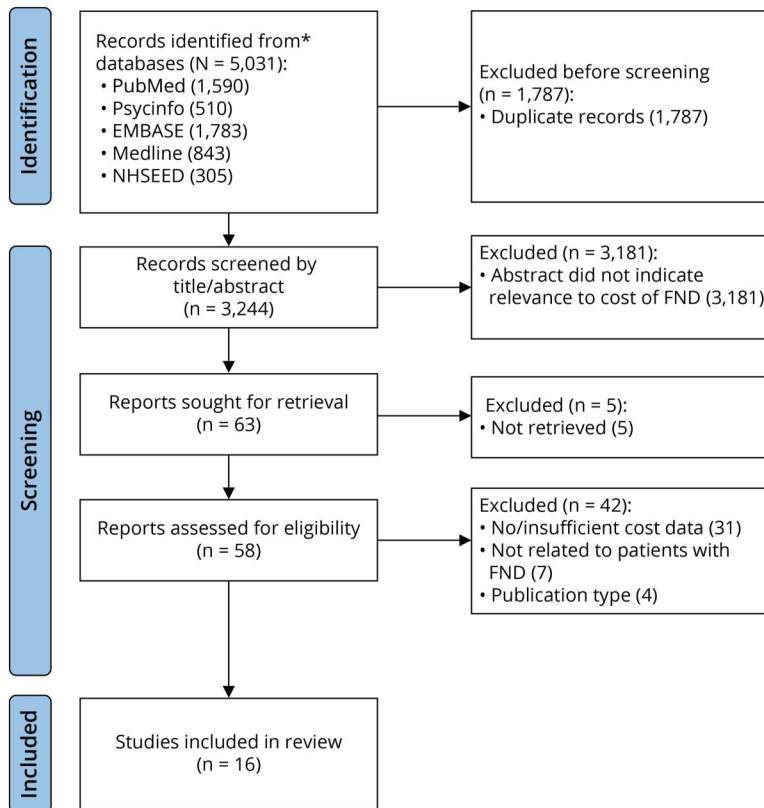
FND = functional neurologic disorder; NHSEED = National Health Service Economic Evaluation Database; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

extracted by B.O.M. When a single study was published in several articles, the article reporting the largest group was used. No restrictions on age, sex, or treatment level were applied.

Outcome Measures

The primary outcome measures were the monetary and nonmonetary costs of FND to patients and the economy.

Search Methods for Identification of Studies

Searches were made in April 2022 from inception of the databases to April 8, 2022, in the following electronic databases: PubMed, EMBASE, MEDLINE, PsycINFO, and the National Health Service Economic Evaluations Database of the University of York and in the reference lists of identified studies. These databases contain a comprehensive list of medical literature and reports.

The following search string was used (in titles and abstracts): ("conversion disorder" OR "conversion reaction" OR psychogen* OR nonepileptic OR nonepileptic OR hysteri* OR "functional neurologic" OR "functional movement" OR "functional motor" OR "functional tremor" OR "functional sensory" OR nonorgan* OR nonorgan* OR Astasia-Abasia OR "Astasia Abasia") AND (QALY OR "quality adjusted life year$" OR "disability adjusted life year$" OR DALY OR cost OR expense OR expenditure OR out-of-pocket OR economic OR

budget OR monetary OR resource* OR consumption OR informal care).

The subject heading of conversion disorder was exploded on the Ovid platforms (Psycinfo, MEDLINE, and EMBASE). The following conference proceedings during the past 5 years were hand searched: Society of Biological Psychiatry, American Psychiatric Association, The British Neuropsychiatry Association, Royal College of Psychiatrists, Association of British Neurology, and American Academy of Neurology. Abstracts that were identified as meeting the inclusion criteria for the review had their full texts sought for assessment. B.O.M. contacted the lead author of any papers found through this method.

Data Collection and Analysis

A record of included and excluded studies (and reasons for exclusion) was kept. Data were extracted using the DistillerSR software[21] by B.O.M. and included study characteristics, demographics, and as economic costs such as direct health care and nonhealthcare costs, indirect costs, and QALY measurements.

A meta-analysis was not deemed appropriate, given the significant heterogeneity in the studies' cohorts, location (differing health care systems), costs included, and cost-data sources. To compare results for the noncomparator studies, costs per patient were transformed using purchasing power parities (PPPs) for gross domestic product (GDP) to US

dollars (USD).[22] The cost data of studies using year of price level before 2021 were inflated by 1% annually to calculate a common end value for the year 2021. If mean values and/or standard deviations were not reported, freely available software was used (Window Ruler) to calculate these measures from the provided graphs.

Assessment of Paper Quality

Assessment of the overall methodological quality of EEs was informed by application of the Scottish Intercollegiate Guidelines Network Methodology checklist[23] (eAppendix 2, links.lww.com/WNL/C834) and a checklist of methods (eAppendix 3, links.lww.com/WNL/C835). Distiller SR was used to produce quality figures based on our assessment as low, acceptable, or high quality.

Standard Protocol Approvals, Registrations, and Patient Consents

The study protocol was registered on PROSPERO on April 8, 2022, registration number CRD42022322142. Ethics was not sought because any data collected was obtained from publicly accessible documents.

Data Availability

Individual researchers may request collected data from the corresponding author.

Results

Search results are shown in the Figure. Fifty-eight studies were reviewed in full text, of which 16 studies were included. Four conference abstracts were identified, and their data requested from their respective authors, of which 1 responded. Forty-two studies were excluded for reasons detailed in the Figure.

Study Quality

Of the included studies, 4 (Stephen et al.,[24] Goldstein et al.,[25] Jennum et al.,[26] and Luthy et al.[27]) were deemed to be of high quality, 10 were deemed to be of acceptable quality (Deleuran et al.,[28] Nelson-Sice et al.,[29] Tinazzi et al.,[30] Seneviratne et al.,[31] Martin et al.,[32] Ahmedani et al.,[33] Russell et al.,[34] Magee et al.,[35] Nielsen et al.,[36] Reuber et al.[37]), and 2 were deemed to be of low quality (Chemmanam et al.,[38] Goyal et al.[39]).

Study Characteristics

General study characteristics are summarized in Tables 1–3. The earliest study was published in 1998, the most recent in 2021. Of the included studies on COI of FND, 81% (n = 13) were published in the year 2013 or later, which perhaps indicates that the COI of FND is a topic of recent and increasing interest. Sample sizes varied from 11 to 64,138. Five studies were conducted in the United States, 4 in Great Britain, 2 in Denmark, and 1 in each of Italy, Ireland, Australia, Canada, and India. Ten studies focused on FS, 4 studies focused on FND/conversion disorder, and 2 studies focused on functional movement disorder (FMD).

Studies were also heterogenous for diagnostic criteria. Of the 6 studies of FND/FMD, 1 used *International Classification of Diseases, Ninth/Tenth Revision* (*ICD-9/10*) (Stephen et al.[24]), 1 used Gupta and Lang Criteria (Tinazzi et al.[30]), 1 used Fahn Williams criteria (Nielsen et al.[36]), and 3 used consensus diagnosis (Nelson-Sice et al.,[29] Goyal et al.,[39] Reuber et al.[37]). Of the studies of FS, 6 used the gold standard of video EEG (vEEG) (Goldstein et al.,[25] Deleuran et al.,[28] Russell et al.,[34] Chemmanam et al.,[38] Seneviratne et al.,[31] Martin et al.[32]), 2 used *ICD-9/10* (Jennum et al.,[26] Luthy[27]), 1 used both *ICD-10* and vEEG (Ahmedani et al.[33]), and diagnostic criteria of 1 study were unclear (Magee et al.[35]).

Study designs were made up of 3 types:

1. COI studies that were conducted alongside cohort studies without intervention, which included a comparator group, that is, another neurologic disorder (n = 4).[24,26,27,39]
2. COI studies that were conducted alongside cohort studies without intervention, which did not include a comparator group (n = 4).[29-31,35]
3. EEs of interventions that were either pre-post cohort studies (n = 6)[28,32-34,37,38] or randomized controlled trials (RCTs, n = 2).[25,36] Of these, 5 studies assessed active interventions, and 3 studies assessed costs before and after a definitive diagnosis of FND.

eAppendix 4 (links.lww.com/WNL/C836) displays the cost categories considered. Studies varied regarding the detail of their breakdown of costs. Eight studies assessed only hospital costs (inpatient and specialist outpatient services), with 7 of these studies focused only on hospital in-patient costs. Only 4 studies assessed medication costs outside of hospital. Three studies assessed productivity losses to the patient and informal carers resulting from their FND, while Jennum et al.[26] assessed productivity loss regarding cost to the state. Studies also varied regarding their reporting of cost data. Although authors reported including different types of costs in their analysis, some did not give exact figures for these individual costs. eAppendix 5 (links.lww.com/WNL/C837) details what costs were explicitly reported, by paper. Two articles gave only the total overall cost per patient.

Population Demographics

Thirteen studies investigated the costs of adults only, and 2 studies (Stephen et al.[24] and Jennum et al.[26]) included both adults and minors with FND. Luthy et al.[27] investigated the costs at a pediatric hospital. Adult patients' mean/median age in studies ranged between 35[25,31] and 45.48 years,[24] and every study that noted sex ratio reported mostly female patients, ranging from 57%[34] to 86%.[28]

Economic Costs

Findings are summarized in Tables 1–3. Several summary results can be derived from the economic data presented in the selected studies.

First, 8 studies assessed costs before/after an intervention, where intervention was defined as psychological-based

Table 1 Economic Characteristics: Studies That Assessed Costs Before and After an Intervention (Including Diagnosis)

Author/year/country	Population	Condition	No. of patients	FND defined by	Costing method/source of cost data/currency	Costs included	Intervention	Cost per patient before intervention	Cost per patient after intervention	% Change from preintervention to postintervention[a]
Goldstein et al.[25] 2021 United Kingdom	Adults with dissociative seizures in the previous 8 wk and no epileptic seizures in the previous year	FS	368 total SMC alone, n = 182; CBT + SMC, n = 186	vEEG and/or clinical consensus	Bottom-up CSRI questionnaire NHS records Average wage rates for value lost work and care provided by family/friends Medication costs: British National Formulary	Community services Medication costs Hospital-based services Informal care Productivity loss	CBT + SMC	6 mo before: £29,066	6 mo after: £29,320 12 mo after: £52,933	6 mo: 1% 12 mo: −9%
					QALYs: EQ-5D-5L, SFQ-6 2017/18 Great British pound sterling		SMC	6 mo before: £33,261	6 mo after: £22,828 12 mo after: £55,503	6 mo: −31.4% 12 mo: −16.6%
Deleuran et al.[28] 2019 Denmark	Patients with PNES offered psychotherapy by the specialized MDT at the Epilepsy Clinic, Rigshosptalet-Glostrup in Denmark, from 2010 to 2016	FS	242 39 included in final analysis	Neurologist diagnosis +/− vEEG	Bottom-up Diagnosis-related group tariffs from the Danish Ministry of Health (provides data on average costs of health care services) Danish Krones, converted to Euro	ED visits, outpatient visits, and hospital admissions	CBT-based or ACT-based interventions	Months before Tx: Mean (SD) 24–13: €2,324 (4,214) 12–0: €5,807 (6,401)	Months after Tx: Mean (SD) 0–12: €1,763 (4,285) 13–24: €1,264 (3,393), (median €64 [highly skewed])	1 y before/after −69.6%
Russell et al.[34] 2016 Canada	Health Canada and the Public Health Agency of Canada databases	FS	28	Neurologist diagnosis and vEEG	Top-down Population Health Research Unit database Physician cost estimates: Calculated using $125 per hour for psychiatrist and family physicians $50 per hour for psychiatry residents, other students and health professionals Canadian dollars	Hospital and physician cost and utilization data 1 y before and up to 3 y after ISTDP treatment	ISTDP	$22,939.10	Year 1: $3,380.6 Year 2: $2,136 Year 3: $4,462.6	Year 1: −85.3% Year 2: −90.7% Year 3: −80.5%
Ahmedani et al.[33] 2013 USA	Patients with a diagnosis of FS, who received services in the EMU, at Henry Ford Hospital from January 2006 to December 2008	FS	103. 24 members of HMO: allowed full collection of medical care costs—included in analysis	ICD-9	Top-down Southeastern Michigan HMO US dollars	Inpatient stays included psychiatric hospital admissions. Outpatient visits included neurology, BHSs, and other services (primary care or other specialty care)	Diagnosis with vEEG	Mean (SD): $4,567.01 (4,329.02) in 12 mo before diagnosis	Mean (SD): $2,783.77 (3,404.86) in 12 mo after diagnosis	−39.10%

Continued

Table 1 Economic Characteristics: Studies That Assessed Costs Before and After an Intervention (Including Diagnosis) *(continued)*

Author/year/ country	Population	Condition	No. of patients	FND defined by	Costing method/ source of cost data/ currency	Costs included	Intervention	Cost per patient before intervention	Cost per patient after intervention	% Change from preintervention to postintervention[a]
Chemmanam et al.[38] **2009 India**	Patients who underwent inpatient vEEG during a 10-mo period from September 2004 to July 2005 at Sree Chitra Tirunal Institute for Medical Sciences and Technology	FS	11 with comorbid epilepsy/FS 8 with only FS	Consensus diagnosis and vEEG	Bottom-up Medication: Local prices in INR Direct nonmedical costs: Patient interview Other data: unclear INR	Direct medical costs: cost of AED therapy, diagnostic investigation, physician and hospital visits, and hospitalizations Direct nonmedical costs: transportation charges to attend medical facilities for the patient and 1 caregiver	Diagnosis with vEEG	INR 6,985.70 ($174.60) in 12 mo before diagnosis	INR 964.3 ($2.43) in 12 mo after diagnosis	−86.20%
Martin et al.[32] **1998 USA**	Patients diagnosed by the attending epileptologist on the UAB seizure monitoring unit at University of Alabama at Birmingham Epilepsy Centre	FS	20	Unclear	Bottom-up Medication: Average price from pharmacy Outpatient clinic: Outpatient clinic administrative office Diagnostic testing and ER visits: Hospital business administrative office US dollars	Medication usage, outpatient clinic visits, standard diagnostic testing (EEG, MRI, CT), laboratory testing (blood serum levels, AED levels), and emergency department visits	Diagnosis with vEEG (cost of 6,832 per patient)	$8,156 in 6 mo before diagnosis	$1,306 in 6 mo after diagnosis	−84%
Nielsen et al.[36] **2017 United Kingdom**	New patients attending an outpatient neurology clinic specializing in movement disorders and FMS	FMD	29 in intervention 25 in control	Fahn-Williams criteria	Bottom-up EQ-5D-5L	QALY (EQ-5D-5L utility score)	Physiotherapy	0.55	0.64	Mean QALYs 0.34 (95% CI 0.31–0.37)[b] (cost per QALY = GBP £12,087)
	Symptoms >6 mo causing impairment				Great British pound sterling		SMC	0.4	0.44	Mean QALYs 0.26 (95% CI 0.22–0.30)[b]
Reuber et al.[37] **2007 United Kingdom**	New patients referred to outpatient psychotherapy with a specialized service within the neurology departments of the Royal Hallamshire Hospital and the Barnsley District General Hospital between October 2003 and May 2006	FND	63	Consultant diagnosis	Bottom-up SF-6D Great British pound sterling	QALY (SF-6D score)	Brief psychodynamic interpersonal therapy adapted for functional symptoms	0.53	0.57	Mean QALYs 0.04[b] (cost per QALY = GBP £5,328)[b]

Abbreviations: ACT = acceptance and commitment therapy; AED = antiepileptic drug; BHS = behavioral health service; CBT = cognitive behavioral therapy; CSRI = Client Service Receipt Inventory; ED = emergency department; EMU = epilepsy monitoring unit; EQ-5D-5L = European Quality of Life 5 Dimensions 5-Level version; FMD = functional movement disorder; FMS = functional movement screen; FND = functional neurologic disorder; FS = functional seizure; HMO = Health Maintenance Organization; *ICD-9 = International Classification of Diseases, Ninth Revision*; INR = Indian rupee; ISTDP = intensive short-term dynamic psychotherapy; MDT = multidisciplinary team; PNES = psychogenic nonepileptic seizure; NHS = National Health Service; QALY = quality-adjusted life year; SF-6D = Short-Form 6-Dimension; SFQ-6 = 6-item Short-Form Questionnaire; SMC = standard medical care; Tx = treatment; UAB = University of Alabama at Birmingham; vEEG = video EEG.

[a] Percentage change refers to the increase/decrease in costs from the period before the intervention to the period after the intervention.

[b] Figures refer to the mean quality-of-life measures before and after intervention and derived QALYs per patient added by the intervention (change preintervention to postintervention).

Table 2 Economic Characteristics: Studies That Compared Costs With a Control Group

Author/ year/ country	Population	Condition	No. of patients	FND defined by	Costing method/ source of cost data/ currency	Costs included	Comparator	Overall cost	Overall cost per patient	Cost of comparator per patient	FND: Comparator cost ratio
Stephen et al.[24] 2020 USA	Adults: 2008 to 2017 discharge data from the National Inpatient Sample	FND	Admissions: 22,895 adult	*ICD-10* and *ICD-9*	Top-down NIS	Billed services but not professional (physician) fees Expense of the ED or admission presentation to the hospital but not actual societal health care spending by payers or patients	AHCD, DD, RE	1,200,000,000 annually Adult inpatient (2017) $1,066 million (95% CI, $971-$1,160 million)	Adult inpatient (2017) Mean (SD): $61,700 (800)	Adult inpatient (2017) AHCD: $75,000 DD: $55,100 RE: $68,900	Per patient ratio: AHCD: 0.823 DD: 1.12 RE: 0.896
	Children: 2003, 2016 discharge data from the KID		Admissions: 1,264 paediatric		KID			Paediatric inpatient (2012) $75 million; 95% CI $57–$92 million	Paediatric inpatient (2012) Mean (SD): $28,400 (2,100)	Paediatric inpatient (2012) AHCD: $92,200 DD: $73,100 RE: $66,100	Per patient ratio: AHCD: 0.308 DD: 0.0.39 RE: 0.43
	ED: 2008–2017 ED visits from NEDS		ED visits: 36,359 adult, 3,800 pediatric		NEDS US dollars			ED (2017) $163 million; 95% CI, $144-$182 million	Could not calculate	ED (2017) AHCD: $84 million DD: $1,310 million RE: $134.9: million	Total cost ratio: AHCD: 1.94 DD: 0.124 RE: 1.21
Luthy et al.[27] 2018 USA	Patients identified using PHIS, an administrative database of 49 North American children's hospitals	FS	399 FS 13,241 Epilepsy	*ICD-9*	Top-down Multiplied hospital charge, adjusted for hospital location, by the relevant cost-to-charge ratio 2016 US dollars	Diagnostic studies: Lumbar puncture, brain, spine, and chest imaging, and laboratory tests, ECG, and echocardiogram Attending physicians, social work, therapists	Epilepsy	N/A	$4,724 (95% CI $4,413–$5,057)	$5326	0.887
Goyal et al.[39] 2015 USA	IV-rtPA treated patients who presented to 1 of 4 primary stroke centres	Conversion disorder	538 total 17 with FND	Diagnostic consensus among 3 physicians, including 2 vascular neurologists	Bottom-up Hospital billing department US dollars	Direct costs: medications, food, consultations, treatments, devices, supplies, and clinical studies Indirect costs: utilities and labor	TIA	N/A	$7,117	$6714	1.06

Table 2 Economic Characteristics: Studies That Compared Costs With a Control Group *(continued)*

Author/year/country	Population	Condition	No. of patients	FND defined by	Costing method/source of cost data/currency	Costs included	Comparator	Overall cost	Overall cost per patient	Cost of comparator per patient	FND: Comparator cost ratio
Jennum et al.[26] 2019 Denmark	People who received a first diagnosis of PNES between 2011 and 2016	FS	873 FS 1,746 controls	ICD-10	Top-down Danish National Patient Registry, Danish Ministry of Health, National Health Security database Danish Medicine Agency databases Danish Income Statistics 2016 Danish Krone: Converted to euro	Direct costs: medications, food, consultations, treatments, devices, supplies, and clinical studies Indirect costs: utilities and labor	Age and location matched controls	N/A	Adults: €41,114 p/a Costs to partners: €20,042 p/a	Adults: €9,879 p/a Costs to partners: €7,495 p/a	Adult patients: 4.16 Partners of FND patients: 2.67

Abbreviations: AHCD = anterior horn cell disease; DD = demyelinating disease; ED = emergency department; FND = functional neurologic disorder; FS = functional seizure; ICD-9/10 = International Classification of Diseases, Ninth/Tenth Revision; IV-rtPA = IV recombinant tissue plasminogen activator; KID = Kids' Inpatient Database; N/A= not available; NEDS = Nationwide Emergency Department Sample; NIS = National (Nationwide) Inpatient Sample; p/a = per annum; PHIS = Pediatric Health Information System; PNES = psychogenic nonepileptic seizure; RE = refractory epilepsy; TIA = transient ischemic attack.

treatments or making and communicating a robust diagnosis. Each of these 8 studies showed cost reduction, or improved QALYs, in the period after the intervention. The only study[25] which conducted a full cost-benefit analysis was calculated the incremental cost of CBT and standard medical care (SMC) as £120,658 per QALY compared with SMC alone. This fell above the threshold for cost-effectiveness required by the National Institute for Health and Care Excellence (NICE) of under £20,000–£30,000 per QALY.[40] Nielsen et al.'s[36] pilot RCT of a physiotherapy intervention for patients with FMD reported a mean incremental cost per QALY gained of £12,087,[36] while Reuber et al.'s[37] uncontrolled pilot study reported a mean incremental cost per QALY gained of £5,328 (if QoL improvements lasted 1 year) for a brief psychodynamic intervention in patients with mixed functional neurologic symptoms.[37]

Second, in those studies that compared FND costs with those for other chronic neurologic diseases, costs were similar. Both Luthy et al.[27] and Stephen et al.[24] showed a lesser cost burden of PNES compared with epilepsy, although the latter study showed greater cost in emergency settings, despite the fact that Stephen et al.[24] included only refractory epilepsy as a comparator. The only study that compared the economic costs of patients with FND with those of healthy controls (Jennum et al.[26]) showed a marked increase in costs to both patients with FND and their carers.

Third, in those studies that gave estimates of total costs to the taxpayer, Stephen et al.,[24] Tinazzi et al.,[30] and Magee et al.[35] gave estimates of the total COI to their countries of $1,200,000,000 USD (hospital charge costs for all FND subtypes and all ages), €34,500,000 (direct health costs for functional motor symptoms in people older than 16 years), and €19,525,629 and €48,289,190 (direct and indirect costs for FSs in adults per annum, respectively).

Finally, overall costs varied significantly because of the studies' methodological and geographical heterogeneity; after costs were adjusted to PPPs for GDP, mean annual costs per patient of PNES ranged from $4,964 2021 USD (Luthy et al.)[27] to $83,884 2021 USD (Goldstein et al.),[25] while those of FN Ds ranged from $21,433 2021 USD (Tinazzi et al.)[30] to $86,722 2021 USD (Nelson-Sice et al.).[29]

Discussion

This systematic review of health economic studies for FND indicates the significant cost of the disorder, and the possibility to mitigate this cost. Our findings indicate 2 trends: first, that FND causes costs per patient, comparable with, or in excess of, other chronic neurologic disorders with similar symptoms (e.g., FS vs epilepsy). Second, that interventions (including making and delivering a robust diagnosis) have the potential to improve patients' health status (measured in both QALYs and symptom relief) and reliance on health care resources, with a subsequent reduction of costs. However, the heterogeneity of studies provides challenges in interpreting and comparing results.

Table 3 Economic Characteristics: Studies That Did Not Use a Comparator

Author/ year/ country	Population	Condition	Number of patients	FND defined by	Costing method/ source of cost data/ currency	Costs included	Overall cost	Overall cost per patient	Estimated cost in US dollars (PPP)	Estimated cost in 2021 US dollars
Magee et al.[35] 2014 Ireland	Patients diagnosed with NEAD at Beaumont Hospital	FS	Unclear	Unclear	Bottom-up Department of Finance in Beaumont Hospital Euro	Medical costs: Annual recurring direct medical costs, Single-incident direct medical costs, and costs associated with diagnosis and treatment Indirect costs: loss of income tax and PRSI, and the costs of social welfare	€19,525,629 to €48,289,190 per annum	€20,995.30	$22,845	$24,115
Tinazzi et al.[30] 2021 Italy	Patients with a definite diagnosis of FMD, referred to the Parkinson Disease and Movement Disorders Unit of Verona	FMD	40	Gupta and Laing	Bottom up Italian Ministry of Health for inpatients services Veneto Region Tariff Nomenclator for Specialist Outpatient Services Euro	Costs for specialist visits, diagnostic tests, emergency department visits, hospital admissions, and rehabilitation services in a period of up to 5 y before diagnosis	Annual direct health care cost for undiagnosed patients with FMDs of the Italian population is €34.5 million (22.5 covered by NHS and 11.5 by patients)	€2,302 per patient per year (€1,524 covered by the NHS) €13,812 per patient (€9,144 incurred to the NHS) until diagnosis	$21,433	$21,433
Nelson-Sice et al.[29] 2019 United Kingdom	Outpatients at St George's Hospital Neurology and Neuropsychiatry FND clinic	FND	71	Consensus diagnosis	Bottom-up CSRI, EQ5D, "Unit costs of Health and Social Care 2016 Curtis L." Loss of employment based on national average salaries. Informal care £18 per hour Great British pound sterling	Direct costs: General Practitioner visits, hospital appointments, investigations (MRI, CT, and EEG) and medications. Out-of-pocket costs to the patient. Indirect costs to patient and family/carers	N/A	Over 6-mo period £2,564 direct costs. £2,374.64 out-of-pocket. £23,108 lost income over 6-mo period. £28,110 total	$42,080	$43,361
Seneviratne et al.[31] 2018 Australia	Patients in Monash Medical Center, Victoria, Australia who underwent inpatient VEM from May 2009 to June 2014	FS	39	Consensus diagnosis +/− vEEG	Bottom up Finance department of the hospital Pharmaceuticals Benefits Scheme of the Department of Health, Australia Australian dollars	Emergency department visits, inpatient admissions, outpatient visits, interventions, MET calls for seizures, medications, and investigations (EEG, VEM, electrocardiogram, radiology, and blood tests)	N/A	Median: 26,467.63 Australian dollars until diagnosis	$18,004	$18,549

Abbreviations: CSRI = Client Service Receipt Inventory; EQ5D = European Quality of Life 5 Dimensions; FMD = functional movement disorder; FND = functional neurologic disorder; FS = functional seizure; MET = medical emergency team; N/A = not available; NEAD = non epileptic attack disorder; NHS = National Health Service; PPP = purchasing power parity; PRSI = Pay-Related Social Insurance; vEEG = video EEG; VEM = vEEG monitoring.

There was significant variation in reported costs, possibly resulting from heterogeneity in diagnostic practices, differences in types of costs included, cost data sources, and study location. After costs were adjusted to PPPs for GDP, mean annual costs ranged from $4,964 2021 2021 USD (Luthy et al.)[27] to $86,722 2021 USD (Nelson-Sice et al.).[29] This heterogeneity of costs is also reflected in systematic reviews of the economic costs of Medically Unexplained Symptoms (mean annual costs ranging from $1,584 to $6,424 2006 USD from 1986 to 2004),[41] multiple sclerosis (mean annual costs ranging from $13,721 to $82,080 2012 USD from 1995 to 2012),[42] Epilepsy (mean annual direct costs ranging from £611 to €4,292 from 1992 to 2013),[43] and Treatment-Resistant Depression (mean annual costs ranging from $3,800 to $49,000 2006 USD from 2004 to 2014).[44]

This heterogeneity limits not only comparisons of studies included in this review but also the comparison of the economic cost of FND with the economic costs of other chronic, neurologic, and psychiatric disorders. However, 2 high-quality studies included in this review (Stephen et al.[24] and Luthy et al.[27]) reported FND and FS, respectively, as having a similar mean direct cost per patient as epilepsy. Stephen et al.[24] also reported a similar mean direct cost per adult patient admitted with FND as with demyelinating disorders. Given that patients with FND have levels of physical disability equivalent to people with multiple sclerosis or epilepsy and higher frequencies of psychological comorbidities than those 2 disorders,[13] one might expect similar or greater indirect and intangible costs. This provides powerful insight into the economic impact of a disorder, which has relatively limited awareness in the medical community.[45,46]

Given the high prevalence of comorbidities which occur in patients with FND,[4,5] it is possible that these comorbidities might have contributed to the costs calculated by the articles included in this review. This lack of adjustment would have led to inflated costs being calculated for the FND cohort.[47] Luthy et al. attempted to isolate the pure economic cost of FND through the use of an extensive exclusion criterion (of both medical and psychiatric comorbidities). The authors acknowledged that study of such a cohort likely lessened the external validity of their findings, given that the successful treatment of many chronic neurologic disorders, and especially FND, requires a holistic approach.

In those studies that assessed economic effectiveness of interventions using QALYs, there was significant variability. Part of this is due to differences in the patient population and interventions. However, in 2 studies, the patient population and intervention were similar, namely patients with FS undergoing psychological-based treatments. Despite this, there were significant differences in QALY costs. Goldstein et al.[25] reported an incremental cost of CBT and SMC as £120,658 per QALY compared with SMC alone, while Reuber et al.[37] reported the mean incremental cost per QALY gained as £5,328. A number of factors are likely to contribute to these widely differing figures. Reuber et al.[37] (n = 63) reported a unit cost of treatment as £213.15, while Goldstein et al.[25] (n = 293) reported a unit cost of £1,064. Furthermore, Reuber et al.[37] based their analysis on clinical outcomes at 6 months, which they assumed would be the same at 12 months. If Goldstein et al.[25] were to use clinical outcomes at 6 instead of 12 months, the cost per QALY gained would be lower because there was a greater QoL difference at that time point and a significant difference in the primary outcome measure of seizures. Finally, as Reuber et al.[37] acknowledge, the lack of a control group in their study means that the cost-effectiveness of intervention cannot be regarded as proven in view of confounders such as placebo or regression to the mean effects. Moreover, the control arm in the study conducted by Goldstein et al.[25] was not treatment as usual, but enhanced "standardized medical care," a package of care greater than what is typically provided for patients with FS, involving education and counseling from neurologists and psychiatrists. This in turn would have led to a smaller difference in QALY effects in the group and therefore an underestimation of the cost-effectiveness of the intervention.

In studies without comparators, total costs varied from $18,549 to $43,661 2021 USD. Any conclusions reached from these studies is limited by their lack of a comparison group, and it is thus difficult to contextualize their reported findings.

A comprehensive COI study should include all direct and indirect health care costs and intangible costs. Most of the studies in this review included only hospital-related costs. Such studies would underestimate the true economic cost of FND. A direct comparison of inpatient admissions costs was also limited by the difference in specific costs included in the studies, for example, diagnostic imaging, medication, or multidisciplinary team consultations.

Another complication of comparing costs from studies is their setting in different countries and therefore different health care systems. Different countries have varying degrees of public health care systems, with patients carrying extra costs in more private systems. Such differences alter resource allocation by clinicians, and differences in health care systems have been shown to alter patients' use of health care resources.[48]

Countries with more extensive social supports might also affect indirect costs. Jennum et al.[26] identified that, compared with controls, a greater proportion of people with FS and their partners received social service benefits, such as sick pay or disability pension and housing benefits. The authors reported that because of these public services, early retirement may be more common. Studies that assessed productivity loss[20,25,29,35] reported that these costs dwarfed those of direct costs. Productivity loss is likely to vary across countries and thus affect differently on the overall economic cost of FND.

The studies in this review demonstrated the high cost of undiagnosed FND and the reduction of this cost with diagnosis. This highlights the importance of establishing an early

diagnosis of FND. The possible reasons for this are 2-fold; minimization of excessive investigations and inappropriate medications,[9] lessening the direct and indirect economic costs associated with both, while also minimizing harm to the patient; improvement of their prognosis after careful communication of a clear and robust diagnosis.[e1] However, none of the studies reviewed have been able to discriminate between these 2 possibilities. The studies identified in this study suggest that this particularly applied to those patients with FS who receive a gold standard diagnosis by way of vEEG. In those studies that assessed treatment interventions, costs were significantly reduced after the treatment intervention, but the evidence for the cost-effectiveness of those interventions is currently more limited.

Future research in this area should ideally include a comprehensive list of direct and indirect costs to ascertain the full extent of the economic burden of FND. More studies from middle-income and low-income countries along with the inclusion of appropriate comparison groups would enable a comprehensive understanding of the global economic burden of FND.

To date, there has been no large study showing cost-effectiveness of a treatment for FND, defined by NICE as a cost per QALY below $35,000–$45,000 2009 USD across countries.[e2] To our knowledge, only Goldstein et al. have thus far performed a comprehensive cost-effectiveness study, though costs were above NICE thresholds. Thus, rigorous cost-effectiveness studies should also be undertaken to investigate cost-effective treatments for FND. Similarly, studies should seek to distinguish the relative contributions to reduced costs after a diagnosis of FND, of the robustness of diagnostic communication, reduced inappropriate medical interventions, or improved prognosis.

As with other health economic systematic reviews, our review is faced with the limitation that studies that use top-down cost calculations would underestimate privately paid health care goods, while those using hospital charge data would, on average, overestimate the true economic cost of the disorder 2-fold.[e3]

This review highlighted a relative paucity of research into this topic. Four studies assessed indirect costs to the patient, and only 3 studies[25,36,37] included intangible costs. Productivity loss and intangible costs, such as cost associated with stigma, have been shown to make up a significant portion of the cost of epilepsy,[e4] and their exclusion from most of the studies in this review limits any estimate of the true burden of FND. The tertiary location of several studies meant that their population represented a severe subset of patients with FND and thus may limit the external validity of their findings. FND is a heterogeneous disorder, even in patients with the same symptoms. Treatment approaches based primarily on the presenting symptom without consideration of other comorbid problems may therefore dilute or even obscure treatment benefit for a subset of patients. This may in turn increase the associated costs per QALY of the intervention. Finally, most of the comparator studies in this review used control groups with chronic neurologic diseases (e.g., motor neuron disease, multiple sclerosis). Only a minority of such studies matched FND symptoms across groups, which should be an aim of future studies to understand relative costs more robustly (e.g., comparison of costs of FMDs with Parkinson disease).

FNDs are associated with the significant use of health care resources, resulting in economic costs to patient and the taxpayer and intangible losses. Given that FND is a medical condition similar to any other, we do not suggest that there should be zero cost associated with it. Rather, in this review, we have tried to explore how these costs can be moderated effectively with timely diagnosis and treatment. Interventions, including simply making a robust diagnosis, seem to offer an avenue toward reducing these costs. Significant heterogeneity exists between studies in this area, and we found a relative lack of research on indirect and intangible costs. Such costs seem to be high in FNDs and offer a focus for further research, as do longer-term studies.

Study Funding

Disclosure

Publication History

Appendix Authors

Name	Location	Contribution
Brian O'Mahony, MB BCh, BAO	Institute of Psychiatry, Psychology & Neuroscience, King's College London, United Kingdom	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data

Appendix (continued)

Name	Location	Contribution
Glenn Nielsen, BSc, PhD	Molecular and Clinical Sciences Research Institute, St. George's University of London, United Kingdom	Drafting/revision of the article for content, including medical writing for content
Sallie Baxendale, PhD	Department of Clinical and Experimental Epilepsy, University College London, Institute of Neurology; Department of Neurology, National Hospital for Neurology and Neurosurgery; Epilepsy Society, Chalfont Centre for Epilepsy, United Kingdom	Drafting/revision of the article for content, including medical writing for content
Mark J. Edwards, MBBS, BSc, PhD, FRCP, FEAN	Molecular and Clinical Sciences Research Institute, St. George's University of London; Neurology Department, Atkinson Morley Regional Neuroscience Centre, St. George's University Hospitals, London, United Kingdom	Drafting/revision of the article for content, including medical writing for content
Mahinda Yogarajah, MD	Department of Clinical and Experimental Epilepsy, University College London, Institute of Neurology; Department of Neurology, National Hospital for Neurology and Neurosurgery; Epilepsy Society, Chalfont Centre for Epilepsy, United Kingdom	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; and study concept or design

References

1. Espay AJ, Aybek S, Carson A, et al. Current concepts in diagnosis and treatment of functional neurological disorders. *JAMA Neurol*. 2018;75(9):1132-1141. doi:10.1001/jamaneurol.2018.1264
2. Věchetová G, Slovák M, Kemlink D, et al. The impact of non-motor symptoms on the health-related quality of life in patients with functional movement disorders. *J Psychosom Res*. 2018;115:32-37. doi:10.1016/j.jpsychores.2018.10.001
3. Gelauff JM, Kingma E, Kalkman J, et al. Fatigue, not self-rated motor symptom severity, affects quality of life in functional motor disorders. *J Neurol*. 2018;265(8):1803-1809. doi:10.1007/s00415-018-8915-7
4. Gelauff J, Stone J, Edwards M, Carson A. The prognosis of functional (psychogenic) motor symptoms: a systematic review. *J Neurol Neurosurg Psychiatry*. 2014;85(2):220-226. doi:10.1136/jnnp-2013-305321
5. Feinstein A, Stergiopoulos V, Fine J, Lang A. Psychiatric outcome in patients with a psychogenic movement disorder: a prospective study. *Cogn Behav Neurol*. 2001;14(3):169-176.
6. Carson A, Lehn A. Chapter 5: epidemiology. In: Hallett M, Stone J, Carson A, eds. *Handbook of Clinical Neurology*. Elsevier; 2016:47-60.
7. Lempert T, Dieterich M, Huppert D, Brandt T. Psychogenic disorders in neurology: frequency and clinical spectrum. *Acta Neurol Scand*. 1990;82(5):335-340. doi:10.1111/j.1600-0404.1990.tb03312.x
8. Beharry J, Palmer D, Wu T, et al. Functional neurological disorders presenting as emergencies to secondary care. *Eur J Neurol*. 2021;28(5):1441-1445. doi:10.1111/ene.14728
9. Stone J, Carson A, Duncan R, et al. Who is referred to neurology clinics? The diagnoses made in 3781 new patients. *Clin Neurol Neurosurg*. 2010;112(9):747-751. doi:10.1016/j.clineuro.2010.05.011
10. Bodde NM, Brooks JL, Baker GA, Boon PA, Hendriksen JG, Aldenkamp AP. Psychogenic non-epileptic seizures: diagnostic issues: a critical review. *Clin Neurol Neurosurg*. 2009;111(1):1-9. doi:10.1016/j.clineuro.2008.09.028
11. Butler M, Shipston-Sharman O, Seynaeve M, et al. International online survey of 1048 individuals with functional neurological disorder. *Eur J Neurol*. 2021;28(11):3591-3602. doi:10.1111/ene.15018
12. Merkler AE, Parikh NS, Chaudhry S, et al. Hospital revisit rate after a diagnosis of conversion disorder. *J Neurol Neurosurg Psychiatry*. 2016;87(4):363-366. doi:10.1136/jnnp-2014-310181
13. Carson A, Stone J, Hibberd C, et al. Disability, distress and unemployment in neurology outpatients with symptoms 'unexplained by organic disease' *J Neurol Neurosurg Psychiatry*. 2011;82(7):810-813. doi:10.1136/jnnp.2010.220640
14. Nielsen G, Stone J, Edwards MJ. Physiotherapy for functional (psychogenic) motor symptoms: a systematic review. *J Psychosom Res*. 2013;75(2):93-102. doi:10.1016/j.jpsychores.2013.05.006
15. LaFrance WC Jr, Miller IW, Ryan CE, et al. Cognitive behavioral therapy for psychogenic nonepileptic seizures. *Epilepsy Behav*. 2009;14(4):591-596. doi:10.1016/j.yebeh.2009.02.016
16. Walther K, Volbers B, Erdmann L, et al. Psychosocial long-term outcome in patients with psychogenic non-epileptic seizures. *Seizure*. 2020;83:187-192. doi:10.1016/j.seizure.2020.09.014
17. Nunez-Wallace KR, Murphey DK, Proto D, et al. Health resource utilization among US veterans with psychogenic nonepileptic seizures: a comparison before and after video-EEG monitoring. *Epilepsy Res*. 2015;114:114-121. doi:10.1016/j.eplepsyres.2015.05.002
18. Batura N, Pulkki-Brännström A-M, Agrawal P, et al. Collecting and analysing cost data for complex public health trials: reflections on practice. *Glob Health Action*. 2014;7(1):23257. doi:10.3402/gha.v7.23257
19. Levin HM, McEwan PJ. *Cost-Effectiveness Analysis: Methods and Applications*. Vol. 4. Sage; 2000.
20. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. 2009;151(4):264-269. doi:10.7326/0003-4819-151-4-200908180-00135
21. Distiller SR. Accessed June 12, 2022. evidencepartners.com/products/distillersr-systematic-review-software.
22. OECD. PPPs and exchange rates. 2022. Accessed June 12, 2022. stats.oecd.org/Index.
23. Culyer AJ. *Scottish Intercollegiate Guidelines Network. The Dictionary of Health Economics*, 3rd ed. Edward Elgar Publishing Ltd.; 2014.
24. Stephen CD, Fung V, Lungu CI, Espay AJ. Assessment of emergency department and inpatient use and costs in adult and pediatric functional neurological disorders. *JAMA Neurol*. 2021;78(1):88-101. doi:10.1001/jamaneurol.2020.3753
25. Goldstein LH, Robinson EJ, Pilecka I, et al. Cognitive-behavioural therapy compared with standardised medical care for adults with dissociative non-epileptic seizures: the CODES RCT. *Health Technol Assess*. 2021;25(43):1-144. doi:10.3310/hta25430
26. Jennum P, Ibsen R, Kjellberg J. Welfare consequences for people diagnosed with nonepileptic seizures: a matched nationwide study in Denmark. *Epilepsy Behav*. 2019;98:59-65. doi:10.1016/j.yebeh.2019.06.024
27. Luthy SK, Moss AF, Torok MR, McLeod L, Wilson KM. Characteristics of children hospitalized for psychogenic nonepileptic seizures due to conversion disorder versus epilepsy. *Hosp Pediatr*. 2018;8(6):321-329. doi:10.1542/hpeds.2017-0103
28. Deleuran M, Nørgaard K, Andersen NB, Sabers A. Psychogenic nonepileptic seizures treated with psychotherapy: long-term outcome on seizures and healthcare utilization. *Epilepsy Behav*. 2019;98:195-200. doi:10.1016/j.yebeh.2019.05.007
29. Nelson-Sice R, Edwards M, Yogarajah M. A cross-sectional evaluation of health resource use in patients with functional neurological disorders referred to both a tertiary neurology centre and a neuropsychiatry clinic. *J Neurol Sci*. 2019;405:59-60. doi:10.1016/j.jns.2019.10.1671
30. Tinazzi M, Gandolfi M, Landi S, Leardini C. Economic costs of delayed diagnosis of functional motor disorders: preliminary results from a cohort of patients of a specialized clinic. *Front Neurol*. 2021;12:786126. doi:10.3389/fneur.2021.786126
31. Seneviratne U, Low ZM, Low ZX, et al. Medical health care utilization cost of patients presenting with psychogenic nonepileptic seizures. *Epilepsia*. 2019;60(2):349-357. doi:10.1111/epi.14625
32. Martin RC, Gilliam FG, Kilgore M, Faught E, Kuzniecky R. Improved health care resource utilization following video-EEG-confirmed diagnosis of nonepileptic psychogenic seizures. *Seizure*. 1998;7(5):385-390. doi:10.1016/s1059-1311(05)80007-x
33. Ahmedani BK, Osborne J, Nerenz DR, et al. Diagnosis, costs, and utilization for psychogenic non-epileptic seizures in a US health care setting. *Psychosomatics*. 2013;54(1):28-34. doi:10.1016/j.psym.2012.08.005
34. Russell LA, Abbass AA, Allder SJ, Kisely S, Pohlmann-Eden B, Town JM. A pilot study of reduction in healthcare costs following the application of intensive short-term dynamic psychotherapy for psychogenic nonepileptic seizures. *Epilepsy Behav*. 2016;63:17-19. doi:10.1016/j.yebeh.2016.07.017
35. Magee JA, Burke T, Delanty N, Pender N, Fortune GM. The economic cost of nonepileptic attack disorder in Ireland. *Epilepsy Behav*. 2014;33:45-48. doi:10.1016/j.yebeh.2014.02.010
36. Nielsen G, Buszewicz M, Stevenson F, et al. Randomised feasibility study of physiotherapy for patients with functional motor symptoms. *J Neurol Neurosurg Psychiatry*. 2017;88(6):484-490. doi:10.1136/jnnp-2016-314408
37. Reuber M, Burness C, Howlett S, Brazier J, Grünewald R. Tailored psychotherapy for patients with functional neurological symptoms: a pilot study. *J Psychosom Res*. 2007;63(6):625-632. doi:10.1016/j.jpsychores.2007.06.013
38. Chemmanam T, Radhakrishnan A, Sarma SP, Radhakrishnan K. A prospective study on the cost-effective utilization of long-term inpatient video-EEG monitoring in a developing country. *J Clin Neurophysiol*. 2009;26(2):123-128. doi:10.1097/wnp.0b013e31819d8030
39. Goyal N, Male S, Al Wafai A, Bellamkonda S, Zand R. Cost burden of stroke mimics and transient ischemic attack after intravenous tissue plasminogen activator treatment. *J Stroke Cerebrovasc Dis*. 2015;24(4):828-833. doi:10.1016/j.jstrokecerebrovasdis.2014.11.023

40. Rawlins MD, Culyer AJ. National Institute for Clinical Excellence and its value judgments. *BMJ*. 2004;329(7459):224-227. doi:10.1136/bmj.329.7459.224

41. Konnopka A, Schaefert R, Heinrich S, et al. Economics of medically unexplained symptoms: a systematic review of the literature. *Psychother Psychosom*. 2012;81(5): 265-275. doi:10.1159/000337349

42. Ernstsson O, Gyllensten H, Alexanderson K, Tinghög P, Friberg E, Norlund A. Cost of illness of multiple sclerosis-a systematic review. *PLoS One*. 2016;11(7):e0159129. doi:10.1371/journal.pone.0159129

43. Allers K, Essue BM, Hackett ML, et al. The economic impact of epilepsy: a systematic review. *BMC Neurol*. 2015;15(1):245. doi:10.1186/s12883-015-0494-y

44. Johnston KM, Powell LC, Anderson IM, Szabo S, Cline S. The burden of treatment-resistant depression: a systematic review of the economic and quality of life literature. *J Affect Disord*. 2019;242:195-210. doi:10.1016/j.jad.2018.06.045

45. Tinazzi M, Fiorio M, Berardelli A, et al. Opinion, knowledge, and clinical experience with functional neurological disorders among Italian neurologists: results from an online survey. *J Neurol*. 2022;269(5):2549-2559. doi:10.1007/s00415-021-10840-y

46. Lehn A, Navaratnam D, Broughton M, et al. Functional neurological disorders: effective teaching for health professionals. *BMJ Neurol Open*. 2020;2(1)e000065. doi:10.1136/bmjno-2020-000065

47. Tarricone R. Cost-of-illness analysis: what room in health economics? *Health Policy*. 2006;77(1):51-63. doi:10.1016/j.healthpol.2005.07.016

48. Commonwealth Fund. *2016 Commonwealth Fund International Health Policy Survey of Adults*. Commonwealth Fund; 2020.

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