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A comparative cost analysis of functional neurological disorder with other neurological disorders in patients admitted at Universitas Academic Hospital Neurology Ward.

By

Dr Leonriche Leonard Christo Christopher

"Submitted in fulfilment of the requirements in respect of the Master's Degree (MMed) in the Department of Psychiatry in the Faculty of Health Sciences at the University of the Free State."

Supervisor:

Prof PJ Pretorius

Department of Psychiatry

Co-supervisor:

Prof A Moodley

Department of Neurology

11 May 2021

DECLARATION OF AUTHORSHIP

I, Leonriche Leonard Christo Christopher, declare that the coursework Master's Degree mini-dissertation and interrelated publishable article that I herewith submit for the degree in MMed (Psychiatry) at the University of the Free State are my own independent work and that I have not previously submitted it for a qualification at another institution of higher education. Where help was sought, it has been acknowledged.

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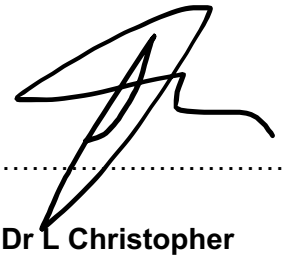

…….. 11 May 2021

Dr L Christopher **Date**

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ABSTRACT

Background: There is a lack of published data about functional neurological disorder and related costs incurred on the health care system in South Africa.

Aim: To compare the health care costs of functional neurological disorder (FND) to those of other neurological conditions admitted in an inpatient setting.

Setting: Universitas Tertiary Academic Hospital, Neurology Department, Free State, South Africa.

Method: Secondary data was collected from Meditech for the period of 1 January 2018 until 31 December 2019. All neurology patient records were reviewed to ensure that patients with FND admitted during the study period were correctly identified. A descriptive data analysis was performed with means and standard deviations calculated for all patients included in the analysis. Categorical variables were summarised by frequencies and percentages. P-values were reported as a measure of significance for the main outcome variable, namely cost.

Results: A total of 530 patients were admitted during the study period. Every 12th patient with a diagnosis other than FND were chosen as the comparator group. Of the 58 patients included in the study, 29/58 (50%) had a diagnosis of FND and 29/58 (50%) were admitted for other neurological disorders. A median age of 28 years IQR (19-36) was reported for the patients diagnosed with FND and 34 years IQR (25-45) for admissions with comparable neurological diagnoses. Both groups had similar gender representations with 11/29 (37.9%) being male, and 18/29 (62.1%) females. The median length of stay was significantly shorter (p value 0.007) for patients diagnosed with FND. Patients with FND most commonly (41.4%) presented with paraplegia. The average cost for the FND patients was significantly less (p value 0.008) than other neurological disorders. The majority (72.4%) of patients admitted for FND was from a low-income category.

Conclusion: Patients admitted at the neurology ward with FND incurred lower costs and had fewer medical comorbidities than patients diagnosed with other neurological disorders.

LIST OF ABBREVIATIONS

ANS	Autonomic Nervous System
CAD	Canadian Dollar
CBT	Cognitive Behavioural Therapy
DSM-5	Diagnostic and Statistical Manual of Mental Disorders Five
FND	Functional Neurological Disorder
GBP	British Pound
HCP's	Health Care Professionals
HPA	Hypothalamic-Pituitary-Adrenal axis
HSREC	Health Sciences Research Ethics Committee
ICD-10	International Statistical Classification of Diseases and Relate Health Problems – 10th revision
IQR	Inter Quartile Range
LEDS	Life Events and Difficulties Schedule
MUS	Medically Unexplained Symptoms
PAG	Periaqueductal Grey Area
PNES	Psychogenic Non-epileptic Seizures
SD	Standard Deviation
SE	Standard Error
SES	Socio-economic Status
SMA	Supplementary Motor Area
TPJ	Temporoparietal Junction

UPFS	Uniform Patient Fees Schedule
USD	United States Dollar
ZAR	South African Rand

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CHAPTER 1

LITERATURE REVIEW

Introduction

Research suggests that the total costs per admission for functional neurological disorders (FND) is higher than for other neurological disorders. Furthermore, there are indications that the costs for FND have increased at a higher rate than that of other neurological disorders over the past decade.[1] Physicians and health systems remain challenged by this patient population as symptoms are often chronic, require extensive specialist workup, and are difficult to treat. The etiology of FND is poorly understood but evidence suggests several contributing factors.[2]

Functional neurological disorders are a collection of neurological symptoms that present with symptoms that are inconsistent and incongruent with the range of manifestations of other neurological disorders.[3,4] Symptoms may include difficulties with gait, limb weakness, cognitive and sensory complaints, and abnormal movements that include seizures and dissociative episodes.[5] Functional neurological disorders are more prevalent in women and affect all age groups, including children.[5]

Up to a third of adult outpatients with neurological disorders are reported to have symptoms that are not at all or only somewhat explained by disease.[5] The majority of these cases are eventually found to have FND in isolation or as a comorbid condition with an existing neurological disorder. Functional neurological disorders represent up to 9% of admissions[6] to neurology wards and 30- 50% of those admitted for monitoring of epilepsy.[7]

It is associated with impaired occupational and social functioning and may cause significant distress in the patient and close relatives .[3] Functional neurological disorder is classified by the American Psychiatric Association in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as part of the somatic symptom and related disorders.[3] The other conditions included in this category are somatic symptom disorder, illness anxiety disorder, factitious disorder, psychological

factors affecting other medical conditions, other somatic symptom and related disorder, as well as unspecified somatic symptom and related disorders.[3]

Sigmund Freud (1856-1939) emphasised the contribution of psychological conflicts in the etiology of "conversion disorder" which corresponds to the current FND diagnosis.[8] He regarded "conversion" is an unconscious mechanism, where emotional reactions to traumatic events were inhibited or repressed because they were unacceptable to the self in some way.[8] The resulting emotional tension is then converted and expressed in physical form.[8] Attention is then shifted away from the subconscious conflict to the physical symptom, resulting in reduced level of anxiety.[8]

Georges Libman Engel (1913-1977) developed the "biopsychosocial" model where the focus shifted onto the individual and his perception.[8] A patient's perception was affected by their beliefs, attitudes, life events and sociocultural background.[8] Perception has the ability to amplify or reduce a minor physical or psychological impairment.[8]

In 1980 the third addition of DSM distinguished between conscious and unconscious production of symptoms.[8] Factitious Disorder was added to this edition, which entailed the conscious falsification of symptoms with the goal of assuming the sick role.[8] This behaviour was precipitated by unconscious conflicts outside the awareness of the patient. On the other hand malingering is the conscious fabrication of symptoms with the purpose of achieving a tangible goal. This was however mostly seen amongst the military and criminals, in an attempt to avoid adverse situations (secondary gain).[8]

There is neuroscientific evidence of a strong association between childhood adversities, negative life events and the development of FND.[9] Childhood abuse is directly proportional to the prevalence and severity of conversion symptoms.[9] Childhood sexual abuse is associated with psychogenic non-epileptic seizures (PNES).[9] Loss of significant persons, bullying, parental neglect or psychopathology were also identified as contributing factors.[9] There was however a significant proportion of patients who did not have a history of childhood adversity or significant life events.[9] This could be due to the fact that many patients do not recall trauma's or did not perceive the experiences as traumatic.[9] In individuals who reported the adverse life event, some stressors might not have been captured by standard trauma measures.[9] One study found that 37% of patients reported physical events or illness

immediately prior to onset of conversion symptoms.[9] Eighty percent of patients reported symptoms three months prior to the onset of conversion symptoms.[9] These events include soft tissue injury, fractures, Bell's palsy, migraine, acute pain, drug reactions, surgery and syncope.[9] Stress has also been implicated, but is more subtle and difficult to identify.[9] A study found identifiable stressors in 91% of patients with FND using the Life Events and Difficulties Schedule (LEDS).[9]

Functional MRI found increased activity in the right supplementary motor area (SMA) and the right temporoparietal junction (TPJ).[9] Those changes were more significant when they were recalling escape events, compared to when they recalled other severe events.[9] Peak responses were elicited in both areas, even though the task was not targeting motor or sensory function.[9] This pattern was also only found in events with escape secondary gain potential.[9] These changes were only found in FND patients and not in healthy controls.[9] The SMA is responsible for execution of motor responses and inhibition of conscious and unconscious prepotent responses.[9] The TPJ is responsible for making sensorimotor predictions, multisensory integration and in the sense of self agency.[9]

Patients with FND are believed to respond differently to psychological stressors.[9] Performing Emotional Stroop tests on patients with psychogenic seizures, demonstrated that threatening faces drew attention away from the task at hand.[9] FND patients took much longer than controls, to name colours that were superimposed with emotional faces.[9] Another study found that children and adolescents with FND were significantly faster at identifying sad faces compared to happy faces.[9] They were found to be more efficient at identifying social cue threats and to be hypersensitive to emotional stimuli.[9]

Some researchers believe that animal threat response behaviours can be used to understand reactions to threat in FND.[9] Fight or flight is not always possible, which may explain other mechanisms, such as tonic immobility thanatosis (where the animal acts dead) and the freeze response.[9] Late in an attack when the opportunity to escape is no longer possible, the animal mimics death.[9] They display hypertonicity, unresponsiveness and motor inhibition to avoid being eaten.[9] This may resemble atonic nonepileptic seizures. The freeze response is mediated by the Periaqueductal Grey Area (PAG).[9] Abnormal response in this area was noted, in patients with motor

FND.[9] Another study found increased connectivity between the amygdala and the PAG.[9]

Biomarker studies have shown evidence for an elevated stress response in FND.[9] Correlations have been found between reaction times to angry faces in Emotional Stroop tests and basal cortisol level.[9] Elevated diurnal basal cortisol levels were found in patients with PNES and motor FND.[9] Salivary amylase was also found to be elevated in FND patients, a protein secreted in response to adrenergic activation.[9] These findings implicate the Hypothalamic-pituitary-adrenal axis (HPA) and a stress pathway in activating rapid adrenal responses.[9] Studies of the autonomic nervous system (ANS), reveal impaired vagal tone.[9] Several heart rate variability indices have been found in children and adults with FND.[9]

There is a lack of evidence for the role of genetics in the development of FND.[9] Some individuals may however be genetically predisposed to react to the environment or stressors in a way that puts them at risk for developing FND.[9] The oxytocin receptor gene is involved with stress regulation.[9] Studies have found increased methylation rates on the promotor of the oxytocin receptor gene.[9]

Medically unexplained symptoms (MUS) make up 30% of neurology consultations, with 16% of the new outpatients being diagnosed with psychological and functional symptoms.[8] Functional diagnosis made up 14% of new visits in neurology outpatients in Scotland.[5] There was a high prevalence of functional disorders in symptom based clinics.[5] FND has an incidence of 4-12/100 000 per year.[5] Motor FND has a incidence of 4 to 5 per 100 000 per year, compared to 1.5 to 4.9 per 100 000 per year for confirmed cases of PNES. The prevalence of FND is estimated to be 50 per 100 000 according to a community registry.[4] Females are affected more than men, and make up 60-75% of this patient population,[4] the female to male ratio being nearly 3:1.[10] Women may have a harder time expressing their emotions, due to certain cultural or political beliefs. It is believed that women tend more readily to somatise their inner conflicts, compared to men.[10] The effected individuals tend to be adolescents and young adults in most studies. The mean age of onset being 10.3 years. The prevalence increases from 0.5% in children, to 10% in adolescents.[10] This is believed to be due to the immaturity of defence mechanisms, and limited resilience during those early years. FND can have a varied presentation, with certain presentations more

frequent in men. Motor symptoms were more common in men, while psychogenic non-epileptic seizures (PNES) and sensory loss were more common in females[10] Patients may present with weakness, abnormal movements, problems swallowing, speech symptoms, seizures, sensory loss or mixed symptoms.[3] It has even been reported that conversion symptoms may even occur at the site of previous organic disease.[10] The disorder is known to occur more frequently in individuals from a lower socioeconomic background.[11] Limited education has been linked to less awareness of physical and mental illness.[11] Countries with value systems that do not allow open emotional expression, are thought to be at risk for higher rates of FND.[11] Remission rates are 21, 5 % at 7,4 years, but 83% of impairments persist at 12,5 years.[5] Patients often see many doctors, in the hope that a non-psychiatric diagnosis would be found or made.[12] It is now being recognised that a patient's outcome is related to their expectations, illness beliefs and satisfaction with treatment.[13]

FND rarely occurs in isolation, with studies showing rates of 31-71% of psychiatric comorbidity.[10] This include mood disorders (64-85%), dissociative disorders (91%), post-traumatic stress disorder (33-49%) and somatoform disorders (89%).[10] The most common comorbid disorders were depressive disorders, somatization disorder, panic disorder and drug abuse.[10]

Various treatment options have been explored in the management of FND, including antidepressants. All antidepressant treatments were shown to have similar efficacy. Antidepressants showed a 32% improvement in medically unexplained symptoms, compared to placebo.[12] Some authors have postulated a connection between personality disorders and FND.[10] Both stem from ineffective coping mechanisms under stress. Histrionic, dependant, borderline and narcissistic personality disorder are commonly associated with FND.[10] The rate of suicide attempts is between 19.6 to 34.2% amongst patients with FND.[14] Suicidal behaviour is important because of the often delayed diagnosis of FND.[14] Suicide attempt rates were higher in those with a severe comorbid dissociative disorder.[14] Risky alcohol use, emotional abuse and number of hospitalizations were other predictors of suicide attempts.[14]

The diagnosis is made by identifying features in the patient's history and physical examination, that are incongruent with organic neurological disorders.[15] The diagnosis of FND can now reliably be made by finding positive signs on clinical examination.[15]

The presence of psychological factors is no longer a requirement for the diagnosis of FND.[15] Updated criteria to diagnose FND in the recent DSM-5, excludes the requirement of a psychological stressor and feigning.[15] The reliability of existing positive signs as the Hoover's sign and the entrainment test has been established as clinical signs for diagnosis of FND.[15,16] Such signs have reasonable sensitivity and specificity, but also acceptable inter-rater reliability.[15] More studies are being described, such as accelerometry for functional head tremor and using reaction time to assess functional dystonia.[15] The rate of misdiagnosis is only 4% after a mean of 5 years.[4] These patients often find interactions with health care professionals (HCP) difficult and distressing.[13] They feel misunderstood by HCP's and lack confidence in the abilities of the doctors to help them. On the other side of the spectrum, doctors see such patients as being difficult, with many doctors feeling that their symptoms are feigned. Research has highlighted a number of limitations in service provision for such patients due to the stigma attached to such a diagnosis.[13]

Patients who suffer from functional neurological disorder are often unable to understand their inner conflicts. Once they are able to make the connection between psychological conflict and their symptoms, there is improvement or resolution of their symptoms. Psychotherapy forms the cornerstone of treatment, and its efficacy depends greatly on the therapeutic alliance. Cognitive Behavioural Therapy (CBT) has shown the most efficacy in treating PNES. CBT aims at elucidating the emotional bases for the patient's symptoms. There is also a focus on improving self-esteem, increasing the capacity for emotional expression and communication. Physiotherapy helps patients overcome their physical symptoms, but also prevents secondary complications such as stiffness and weakness. The physiotherapists builds on the patient's motor abilities, as the exercises get progressively more challenging. Conversion symptoms can also be improved or resolved by treating comorbid psychiatric conditions. Medications such as anxiolytics and antidepressants have been found to be effective. Regular follow up with a psychiatrist or neurologist limits emergency visits and unnecessary special investigations. The prognosis is better in patients who have a good premorbid functioning, no psychiatric comorbidity, short duration of symptoms, sudden onset of symptoms and who are not involved in ongoing litigation.[17]

FND serves as an important determinant of medical care utilization. This leads to increased incurred costs on the health system of any country. In a study conducted in a hospital in Italy 273 patients with unexplained medical symptoms were analysed retrospectively over a period of 10 years. The study reported an overall estimated incurred cost of 475 409,73€. The neurology ward incurred the most cost at a total of 328 192€ followed by the internal medicine incurring costs of 147 976€. The average cost per year treating these patients was reported as 47 504,9€. The examination costs overall (blood tests and instrumental examination) for these patients was 119 926.34€.[18]

In another study by Arthur J in the United Kingdom, somatization patients utilized the outpatient and inpatient medical care twice as much of the non-somatization patients. The annual medical care costs in this patient group was double that of the non-somatization patient. The somatising patient had more primary care visits with a mean visit of 4.9 times (SE 0.32) while the non-somatization patient had a mean visit of 3.43 times (SE 0.11). These patients also had more emergency department visits and hospital admissions. More visits mean more costs are incurred for this patient population which may place a burden on the health system.[19]

A study conducted in New Zealand in 2013 examined 49 patients and estimated the direct health costs associated with the frequency and type of medically unexplained symptoms. The total cost incurred was GBP 89, 636. Inpatient admissions made up the largest proportion (43.4%) of the expenditure. Emergency care was 32.4% and investigations were only 11.6% of the total health care costs.[20]

In a review article looking at the economics of medically unexplained symptoms (MUS) they found a mean annual health care cost ranging from 1 584 to 6 424 USD. The range of excess costs was from 432 to 5353 USD. Two studies found a large part of the total direct costs was from inpatient costs. Diagnostic procedures contributed 40% toward the total direct cost. While medical treatment and drugs made up 57% and 11% respectively of the total direct cost, mental treatment only made up 32% of total direct cost.[21]

In a study in Ontario, Canada, 33 272 patients with a diagnosis of somatic symptom and related disorder were examined. The median age was 20 years, females made up 52.3% of the sample population. Majority of patients were between the ages of 18-

24 years (66.5%), compared to 13 to 17 years (21.9%) and 4 to 12 years (11.6%). Most of the diagnosis was made at their index visit to outpatients (53.8%), and only 6.2% were diagnosed in the inpatient settings. During their inpatient stays, 35.3% of patients did not receive mental health care from a mental health doctor. Readmissions within 1 year of previously being admitted was 37.7%. Mean (SD) 2-year patient costs were CAD$9 845 ($39 725). Hospitalized patients had a 2-year mean (SD) cost of $51 424 ($100 416).[22]

For this study we hypothesize that the FND patients at Universitas Tertiary Academic Hospital in the Free State province incur less cost to the health system than the non FND patients.

Identification of research gaps

In South Africa there is a lack of published data on the subject of somatization and costs incurred on the health system. However, globally it is evident that the somatised patient incurs more costs on the health system. Cost saving may be evident if the management of this patient population is researched and optimized. Establishing the cost of FND is important with the approaching National Health Insurance. Once costs are established, cost reduction strategies can be implemented.

Aim

The aim of the study is to establish the inpatient cost of managing a patient with functional neurological disorder compared with the inpatient cost of Non-FND patients admitted to the neurology department at Universitas academic hospital.

Objectives

- To compare the cost of managing a patient with FND, with the cost of managing a Non-FND neurology patient.
- To describe the demographics of inpatients diagnosed with FND at the Neurology department at Universitas Academic Hospital for the period 1 January 2018 till 31 December 2019.

- To calculate the inpatient prevalence of FND at the Neurology Department at Universitas hospital for the period 1 January 2018 till 31 December 2019.

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CHAPTER 2

A COMPARATIVE COST ANALYSIS OF FUNCTIONAL NEUROLOGICAL DISORDER WITH OTHER NEUROLOGICAL DISORDERS IN PATIENTS ADMITTED AT UNIVERSITAS ACADEMIC HOSPITAL NEUROLOGY WARD

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1. Researchers

The principal investigator for this research study is Dr L Christopher, from the Free State Psychiatric Complex. The supervisor is Prof PJ Pretorius, from the Department of Psychiatry of Free State Psychiatric Complex. The co-supervisor is Prof A Moodley, from the Neurology department of Universitas Academic Hospital.

2. Introduction

Functional Neurological Disorder (FND) is a debilitating condition which has long been recognised as a disorder of unknown etiology. Physicians and health systems remain challenged by this patient population as symptoms are often chronic, require extensive specialist workup, and are difficult to treat. Furthermore, there are indications that the costs for FND have increased at a higher rate than that of other neurological disorders over the past decade.[1] The Diagnostic and Statistical Manual Fifth (DSM-5) defines FND as one or more symptoms that affect the motor or the sensory systems of the patient, and where these symptoms cannot be explained by a neurological or other medical condition or another mental health disorder. These symptoms can cause significant distress or social problems. It may affect the patient's capabilities at work or other areas in daily life.[2]

3. Literature review

Functional neurological disorder previously known as conversion disorder (DSM IV) was thought to be primarily in the domain of psychiatry. Recent abnormal findings on functional brain imaging studies have shifted the concept of FND as a purely psychiatric condition, to that of a neurological condition with biological underpinnings. Jean Martin Charcot developed the term “hysteria” and the concept of a “psychodynamic lesion” producing the symptoms. Joseph Babinski believed that some symptoms were produced by suggestion, and they could therefore be eliminated by suggestion and persuasion leading to abusive therapies being used on soldiers during World War I.[3]

Sigmund Freud differentiated hysteria from simulation, and emphasised the unconscious nature of “conversion”. “Conversion” is an unconscious mechanism, where emotional reactions to traumatic events were inhibited or repressed because they were unacceptable to the self in some way. This leads to build up of emotional tension, which the brain manages by converting it to physical symptoms. The subconscious emotional conflict becomes represented by the physical symptoms that functions as a distraction from the underlying emotional conflict.[3]

Georges Engel developed the “biopsychosocial” model where the focus shifted onto the individual and his perception. Perception has the ability to adjust physical or psychological impairment.[3]

In 1980 the DSM III made the distinction between conscious and unconscious production of symptoms. Factitious Disorder was included, which was the conscious production of symptoms, but the motivation for this behaviour remains in the unconscious. [3]

There is neuroscientific evidence of a strong association between childhood adversities, recent life events and the development of FND. Childhood abuse is directly proportional to the amount of conversion symptoms and their severity.[4] One study found that 37% of patients reported physical events or illness

immediately prior to onset of conversion symptoms. Eighty percent of patients reported symptoms three months prior to onset of conversion symptoms.

These events include soft tissue injury, fractures, Bell's palsy, migraine, acute pain, drug reactions, surgery and syncope.[4]

FND patients had increased activity in the supplementary motor area and the right temporoparietal junction (TPJ), regions in the brain responsible for motor execution and inhibition. The right TPJ is responsible for self-agency, which is hypothesised to be defective in FND. These patients are thought to be sensitive to emotional stimuli and respond faster to what they perceive as social cue threats.[4]

Studies have also indicated the involvement of the hypothalamus pituitary adrenal axis in FND. It was found that these patients had elevated diurnal cortisol levels and increased amylase levels; a protein secreted in response to adrenergic activation. This correlates with impaired vagal tone also found in the FND patients.[4]

There is not much evidence for the role of genetics in the development of FND. Some individuals may however be more vulnerable than others, based on temperament or modelling behaviour. [4]

These medically unexplained symptoms (MUS) make up 30% of neurology consults, with 16% of the new patients being diagnosed with functional symptoms.[5] Functional neurological disorder has an incidence of 4-12/100 000 per year.[6] Females are affected more than men at a ratio of 3:1 and make up 60-75% of this patient population.[6] Being from a lower socioeconomic background is a risk factor for developing FND.[7] Remission rates are 21,5 % at 7,4 years, but 83% of impairments persist at 12,5 years.[5] Functional neurological disorder rarely occurs in isolation, there is a strong psychiatric comorbidity of between 31-71% of patients.[8] The most common psychiatric diagnosis made in patients with FND is Panic disorder followed by Mood disorders, Anxiety disorders and substance abuse.[2] Suicide rates are also much higher than the general population.[9]

Functional neurological disorder is no longer a diagnosis of exclusion.[10] The diagnosis can be made when finding positive signs on clinical examination.[11] The diagnosis of FND is often difficult to make, even by specialists in the field. The rate of misdiagnosis is 4%.[6] Patients go for years with impairing symptoms that

negatively affect their quality of life. These patients are often seen as being difficult, with a lot of doctors feeling that their symptoms are feigned. Patients are left unsatisfied with their symptoms being attributed to emotional distress.[12]

FND which forms part of somatoform disorders serves as an important determinant of medical care utilization. This leads to increased incurred costs on the health system of any country. In a study conducted in a hospital in Italy 273 patients with unexplained medical symptoms were analysed retrospectively over a period of 10 years. The study reported an overall estimated incurred cost of 475 409,73€. The neurology ward incurred the most cost at a total of 328 192€ followed by the internal medicine ward incurring costs of 147 976€. The average cost per year treating these patients was reported as 47 504,9€. The examination costs overall (blood tests and instrumental examination) for these patients was 119 926,34€.[13]

In another study by Arthur J in the United Kingdom, somatization patients utilized the outpatient and inpatient medical care twice as much of the non-somatization patients. The annual medical care costs in this patient group was double that of the non-somatization patient. The somatising patient had more primary care visits with a mean visit of 4.9 times (SE 0.32) while the non-somatization patient had a mean visit of 3.43 times (SE 0.11). These patients also had more emergency department visits and hospital admissions. More visits means more costs are incurred for this patient population which may place a burden on the health system.[14]

A study conducted in New Zealand in 2013 examined 49 patients and estimated the direct health costs associated with the frequency and type of medically unexplained symptoms. The total cost incurred was GBP 89, 636 where the most significant expenditure was at inpatient care and emergency care. The study reports that the incurred cost was substantial and comparable to the cost of chronic medical conditions with identifiable pathology.[15]

In South Africa there is a lack of published data on the subject of somatization and costs incurred on the health system. However, globally, it is evident that the somatised patient incurs more costs on the health system that may be reduced if the management of this patient population is researched and optimized.

Establishing the cost of FND is important with the approaching National Health Insurance.

Objectives

- To describe the demographics of inpatients diagnosed with FND at the Neurology department at Universitas Academic Hospital for the period 1 January 2018 till 31 December 2019 .
- To compare the cost of neurology inpatients with FND, and those with other neurological disorders .
- To establish the prevalence of FND among inpatients admitted at the Neurology Department at Universitas Tertiary Academic hospital for the period 1 January 2018 to 31 December 2019.

Method

Study population

The study population included all neurology inpatients aged 14 and above from 1 January 2018 till 31 December 2019.

- **Inclusion criteria**
  - Patients diagnosed with FND who were admitted in the Neurology department ward for the period 1 January 2018 till 31 December 2019.
  - Patients with other neurological conditions besides FND, to be used as comparator group.
  - Patients 14 years and above.
- **Exclusion criteria**
  - Patient records which do not contain all the required variables namely:
    - Age, gender, race, clinical presentation, length of stay, medical co-morbidities, psychiatric co-morbidities, blood investigations, cerebrospinal fluid investigations, radiological investigations, neurophysiological

investigations, medications administered, allied health services received.

- Patients seen at Neurology Outpatient Department at Universitas Academic Hospital, that were not admitted during the study.

Data collection and data analysis

Data collection

Secondary data was collected from patient notes on Meditec. Meditec is a electronic data base that contains clinical information about all patients admitted at Universitas hospital. The total number of admissions to the Neurology Department for the period 1 January 2018 till 31 December 2019 was recorded, and all records were reviewed to ensure all patients with FND were identified. The ICD 10 codes F44.9 and F44.9 was used to search Meditec. The patient accounts which contains all costs was retrieved from the revenue section of Universitas Academic Hospital. All demographic, clinical data and financial data was entered electronically by the investigator onto a Excel data collection spread sheet, designed for the purpose of this study.

Measurements

Variables:

- Age
- Gender
- Length of stay
- Medical co-morbidities
- Psychiatric co-morbidities
- Blood investigations
- Cerebrospinal fluid investigations
- Radiologic investigations
- Neurophysiological investigations
- Medications administered
- Allied Health services receive
- H classification

Outcome variable: **Cost**

- The Uniform Patient Fees Schedule (UPFS) is used for billing all patients
- The patient contribution is determined by the patient H-classification. H0 to H4 (lower to higher income)
- The UPFS is done by the Revenue section of Universitas Academic Hospital
- The UPFS contains **all costs** incurred to the hospital
    - Ward fee and ward professional fee
    - Laboratory fees
    - Imaging fees and imaging professional fees
    - Pharmacy fee and medication fees
    - Allied health service fees
    - The amount the patient owes the hospital and the amount written off according to patient classification

Data analysis

Descriptive data analysis was performed by the Department of Biostatistics at the University of the Free State. Means were reported with the standard deviation for the average patient cost of FND. Categorical variables were summarised by frequencies and percentages. 95% Confidence intervals were calculated for main outcomes.

The prevalence of functional neurological disorder was calculated, using the numerator as the functional neurological disorder patients admitted to the neurology department for the period of 01 January 2018 until 31 December 2019. The denominator was all patients admitted to the neurology department for the same period, who were 14 years of age and older.

Data Storage

Data was stored safely and securely on a password protected computer. The researcher password-protected the data on Excel using the password protected option. Data was stored until the completion and submission of the researchers MMed thesis. Data will be retained for five years post awarding of the MMed thesis to facilitate availability of data for subsequent follow up studies and as per HSREC regulations. After five years data records will be destroyed by the researcher.

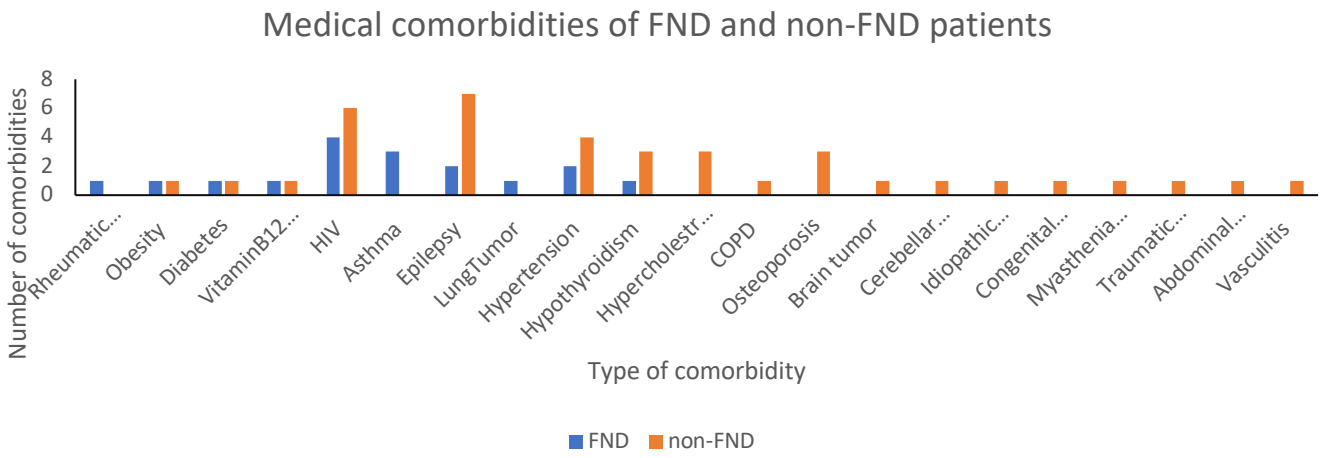
Results

Table 1: Demographic characteristics of Functional Neurological Disorder vs patients with Other Neurological Disorders. n=58

	FND n/N (%)	non-FND n/N (%)	p-value
Characteristics			
Age			
14-29	16/27 (60.3)	11/27 (40.7)	0.485
30-49	12/25 (48.0)	13/25 (52.0)	1
>50	1/6 (16.7)	5/6 (83.3)	0.316
Gender			
Male	11/29 (37.9)	11/29 (37.9)	1
Female	18/29 (62.1)	18/29 (62.1)	
Length of stay in days: median (IQR)	4 (2-7)	8 (4-11)	0.007*

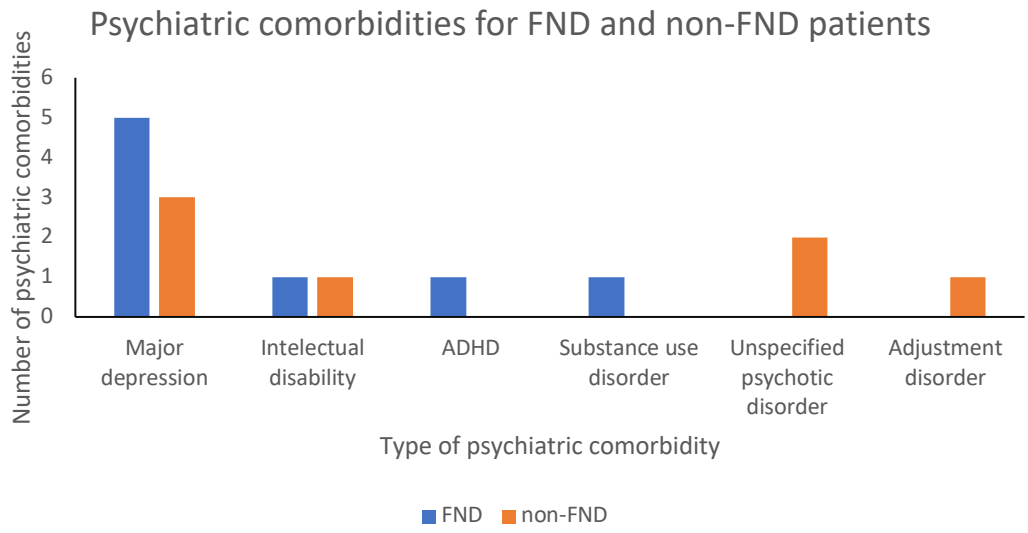
The median age reported for the FND patients was 28 IQR (19-36) while the median age reported for the Non-FND patients was 34 IQR (25-45). No significant statistical differences were observed for the age categories between the patients with functional neurological disorder and patients with other comparable neurological conditions. No significant differences in terms of gender were found. The average length of stay was significantly shorter (p-value = 0.007) for patients diagnosed with FND.

Graph 1: Medical comorbidities in patients with Functional Neurological Disorder vs patients with Other Neurological Disorders. n=58



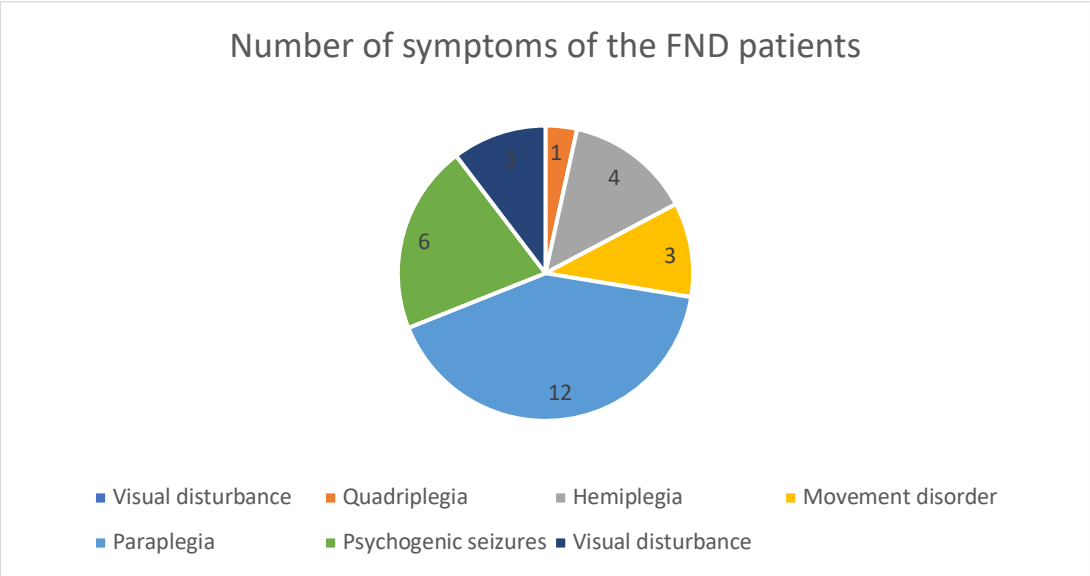
The comparator group tended toward more medical comorbidities, but the difference failed to reach statistical significance. The most common medical comorbidity among patients with FND was HIV 4/29 (13.8%), while epilepsy 7/29 (24.1%) was the most common medical comorbidity among the comparator group.

Graph 2: Psychiatric comorbidities in patients with Functional Neurological Disorder vs patients with Other Neurological Disorders. n=58



High rates of depression were reported in both groups 5/29 (17.2%) FND, and 3/29 (10.3%) non FND, of patients being diagnosed with other neurological disorders.

Graph 3: Clinical presentation of patients with Functional Neurological Disorder. n=29



The most common clinical presentation among patients with functional neurological disorder was paraplegia 12 (41.4%) followed by psychogenic seizures 6 (20.7%).

Table 2: Average cost in South African Rands (ZAR) of patients with functional neurological disorder compared to other neurological disorders. n=58

	FND	Non-FND	p-value
Cost categories(mean, ±SD)			
• Laboratory Investigations	2117.8 (1713.9)	2574.7 (2205.1)	0.382
• Imaging	4215.1 (7366.3)	5616.6 (6203.7)	0.436
• Ward Admission and medical practitioner fees	9964.9 (6687.1)	20036.6 (19238.7)	0.01
• Pharmacy	321.7 (877.5)	3541.1 (10189.6)	0.095
• Occupational Therapy	62.7 (208.7)	23.6 (83.2)	0.352
Total^	16682.2 (3336.4)	31792.6 (6358.5)	0.008

^=Total and the reported mean

The total average cost for patients with other neurological disorders was significantly higher ($p<0.05$), than for the study group. The average total cost for the comparator group was R 31 792,60 and R16 682,20 for those with FND (see table 5). The ward admission and medical practitioner fees were significantly less in the study group. This difference is probably explained by the significantly shorter average length of stay in the study group (4 vs 8 days).

Table 3: Patient H-classification and amount contributed by the patient H-classification patient type. n=58

Patient classification according to income	FND n (%)	Non-FND n (%)
H1	21 (72.4)	25 (86.2)
H2	1 (3.5)	0
H3	1 (3.5)	1 (3.4)
H4	1 (3.5)	2 (7.0)
H0	5 (17.2)	1 (3.4)
Prescribed patient contribution in Rands per income category		
H1	266.4 (102.3)*	217.2 (40.1)
H2	12752.13	0
H3	9119.08	2792.2
H4	1947.8	495.5 (700.7)
H0	0	0

Prescribed patient contribution according to income. * Denotes the average amounts and standard deviation owed by patient classification type.

H1: Income 0-R70 000 per annum

H2: Income R70 000-R250 000 per annum

H3: Income more than R250 000 per annum

H4: Patient with medical aid

H0: Pensioners

The majority of patients in the study population were classified in the low income category fell into the H1 patient classification category for both functional neurological disorder and patients with other than neurological disorders; 21/29 (72.4%) and 25/29 (86.2%), respectively.

Prevalence of functional neurological disorder

A total of 530 patients were admitted to the neurology ward for the period 1 January 2018 until 31 December 2019. Twenty nine patients who had functional neurological disorder were identified. Every 12th patient who did not have FND were chosen as the comparator group. Therefore the inpatient prevalence of functional neurological of the neurology department at Universitas is 5.4%.

Discussion

The estimates in our study suggest a significant lower expenditure on the inpatient care of patients diagnosed with FND, when compared to other neurological conditions. The difference in expenditure between the two groups was significantly less (p=0.01) in the study group for cost of hospitalisation and professional fees. Expenditure was similar in the two groups in terms of expenditure on laboratory, imaging medication and occupational therapy costs. Our finding contrasts with the previous research that reported hospitalisation and laboratory investigations as the substantial cost-drivers in this patient population.[16,17,18] Comorbidities did not contribute to the cost difference between the groups in our study population. However, there are studies that suggest that the FND patient incurs increased cost on the health system because of a myriad of investigations before a definitive diagnosis and even after the diagnosis is made.[19,20] In another study by Konnkopa et al in Germany, the FND patient incurred an excess cost ranging from 432 to 5 353 USD when compared to other care intensive neurological disorders.[16]

In our study, the patients with FND were younger when compared to those with other neurological disorders. Saunders et al reported similar results with a significantly high proportion of FND patients to be of younger age (<30y).[20] However, another study by Tomasson et al found a mean age of 37 years.[17] This indicates wide age-ranges in patients with FND. Thus interventions for early recognition of this patient population is imperative.[19] It also indicates that FND may set in at a young age and go undiagnosed for a significant period in a majority of patients. This does not appear to be the case in our study.

As with other studies, more women were represented in the FND group. Kuloglu et al reported a female to male ratio of 3:1 and this gender difference is also supported by other studies.[8,21,22] Thus, some authors hold the view that FND may be inferred as a defence mechanism utilized more frequently by women.[10] As a result, it is postulated that women living in male dominant societies are unable to express their feeling efficiently resulting in expression of emotional conflict as physical symptoms.[8,23]

The most common symptoms experienced by the FND population in our study was paraplegia. It is well known that paraplegia is one of the most common symptoms in FND. This finding is consistent with other studies on characteristics of the FND patient.[24]

A study conducted by Stephen et al found that the FND patient also has a shorter length of stay if they were admitted to the Emergency Department first.[25] This may be the case at UAH but our study did not explore costs incurred before admisssion. This is a shortcoming of this study. Although unrelated to our study but consistent to our finding, the FND patient has a shorter length of stay which also relates to the total cost of the FND patient being less than that of the non-FND patient

Majority of patients from both the FND and Non-FND groups were H1 classification. As there is a lack of published literature on patient classification in South Africa, the majority H1-classified individuals are working class with low socioeconomic status (SES). A low SES is a well-known risk for poor health outcomes and this may be the reason why a large proportion of our patients were classified as H1.[26]

In conclusion, although FND patients present with less medical comorbidities and cost less on the healthcare system compared to the non-FND patient, it is imperative to expand the undergraduate training of neurology for medical students. This would allow FND to be detected at an early stage and more frequently at primary health care level thus negating referral to tertiary levels and reducing the costs involved with diagnosing the FND patient.

Recommendations

- At a tertiary level, when a patient is suspected of having FND after history and clinical examination special investigations should be limited and tailored for individual patients.
- FND patients have a better prognosis when multi-disciplinary approach is implemented. This approach involves the inclusion of physiotherapy, occupational therapy and psychiatry.
- Undergraduate neurology training should include a lecture on FND.

Limitations

- The period for data collection could have been longer.
- Neurophysiological investigation data was not complete.
- Allied health data was also incomplete.
- Because of the stigma attached to functional disorders, health care workers may be reluctant to make the diagnosis of functional neurological disorder. It is therefore suspected that there are more patients with functional neurological disorder than was reflected.
- Pre and post admission costs were not taken into account. It is likely that many patients in our study population, had already undergone extensive investigations before admission. Our study did not include the costs of the services rendered by psychiatry.

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Appendices

Appendix 1: HSREC Approval

UNIVERSITY OF THE FREE STATE
UNIVERSITEIT VAN DIE VRYSTAAT
YUNIVESITHI YA FREISTATA

UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

Health Sciences Research Ethics Committee

01-Sep-2020

Dear **Dr Leonriche Christopher**

Ethics Clearance: **A comparative cost analysis of functional neurological disorders with other neurological disorders in patients admitted at Universitas Academic Hospital neurology ward.**

Principal Investigator: **Dr Leonriche Christopher**

Department: **Psychiatry Department (Bloemfontein Campus)**

APPLICATION APPROVED

Please ensure that you read the whole document

With reference to your application for ethical clearance with the Faculty of Health Sciences, I am pleased to inform you on behalf of the Health Sciences Research Ethics Committee that you have been granted ethical clearance for your project.

Your ethical clearance number, to be used in all correspondence is:**UFS-HSD2020/0342/2909**

The ethical clearance number is valid for research conducted for one year from issuance. Should you require more time to complete this research, please apply for an extension.

We request that any changes that may take place during the course of your research project be submitted to the HSREC for approval to ensure we are kept up to date with your progress and any ethical implications that may arise. This includes any serious adverse events and/or termination of the study.

A progress report should be submitted within one year of approval, and annually for long term studies. A final report should be submitted at the completion of the study.

The HSREC functions in compliance with, but not limited to, the following documents and guidelines: The SA National Health Act. No. 61 of 2003; Ethics in Health Research: Principles, Structures and Processes (2015); SA GCP(2006); Declaration of Helsinki; The Belmont Report; The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services- (HHS), 21 CFR 50, 21 CFR 56; CIOMS; ICH-GCP-E6 Sections 1-4; The International Conference on Harmonization and Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Tripartite), Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines, Constitution of the HSREC of the Faculty of Health Sciences.

For any questions or concerns, please feel free to contact HSREC Administration: 051-4017794/5 or email EthicsFHS@ufs.ac.za.

Thank you for submitting this proposal for ethical clearance and we wish you every success with your research.

Yours Sincerely

Dr. SM Le Grange
Chair : Health Sciences Research Ethics Committee

Health Sciences Research Ethics Committee
Office of the Dean: Health Sciences
T: +27 (0)51 401 7795/7794 | E: ethicsfhs@ufs.ac.za
IRB 00011992; REC 230408-011; IORG 0010096; FWA 00027947
Block D, Dean's Division, Room D104 | P.O. Box/Posbus 339 (Internal Post Box G40) | Bloemfontein 9300 | South Africa

Appendix 2: FSDOH Approval

health
Department of Health
FREE STATE PROVINCE

10 August 2020

Dr L Christopher
Dept. of Psychiatry
UFS

Dear Dr L Christopher

Subject: A comparative cost analysis of functional neurological disorder at Universitas Academic Hospital.

- Please ensure that you read the whole document, Permission is hereby granted for the above – mentioned research on the following conditions:
- Serious Adverse events to be reported to the Free State department of health and/ or termination of the study
- Ascertain that your data collection exercise neither interferes with the day to day running of **Universitas Hospital** nor the performance of duties by the respondents or health care workers.
- Confidentiality of information will be ensured and please do not obtain information regarding the identity of the participants.
- **Research results and a complete report should be made available to the Free State Department of Health on completion of the study (a hard copy plus a soft copy).**
- Progress report must be presented not later than one year after approval of the project to the Ethics Committee of the University of the Free State and to Free State Department of Health.
- Any amendments, extension or other modifications to the protocol or investigators must be submitted to the Ethics Committee of the University of the Free State and to Free State Department of Health.
- **Conditions stated in your Ethical Approval letter should be adhered to and a final copy of the Ethics Clearance Certificate should be submitted to** sebeclats@fshealth.gov.za / makenamr@fshealth.gov.za **before you commence with the study**
- No financial liability will be placed on the Free State Department of Health
- **Please discuss your study with Institution Manager on commencement for logistical arrangements see 2nd page for contact details.**
- Department of Health to be fully indemnified from any harm that participants and staff experiences in the study
- Researchers will be required to enter in to a formal agreement with the Free State department of health regulating and formalizing the research relationship (document will follow)
- **As part of feedback you will be required to present your study findings/results at the Free State Provincial health research day**

Trust you find the above in order.

Kind Regards

Dr D Motau
HEAD: HEALTH
Date: 12/8/2020

Head : Health
PO Box 227, Bloemfotein, 9300
4th Floor, Executive Suite, Bophelo House, cnr Maitland and, Harvey Road, Bloemfotein
Tel: (051) 408 1646 Fax: (051) 408 1556 e-mail khusem@fshealth.gov.za@fshealth.gov.za/dhikobvup@fshealth.gov.za

Appendix 3: Approval from HOD Neurology

UNIVERSITY OF THE FREE STATE
UNIVERSITEIT VAN DIE VRYSTAAT
YUNIVESITHI YA FREISTATA
UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

DEPARTMENT OF NEUROLOGY

5 May 2020

Health sciences research ethics committee
University of the Free State

Principal investigator: Dr L Christopher
Study title: A comparative cost analysis of functional neurological disorders with other neurological disorders in patients admitted at Universitas Academic Hospital neurology ward.

This serves to confirm that Dr Christopher has been given approval to conduct the above study in the department of neurology at Universitas Academic Hospital.

Kind regards

Anand Moodley
Associate professor and head of neurology
Universitas Academic Hospital and University of the Free State
moodleyAA@ufs.ac.za

Department of Neurology: School of Medicine/Departement Neurologie: Skool vir Geneeskunde
T: +27 (0)51 4053550 | F: +27(0)51 401 9804 | E: dupreezac@ufs.ac.za
205 Nelson Mandela Drive/Rylaan |Parkwes | Bloemfontein 9301 | South Africa / Suid Afrika
PO Box /Posbus 339 (G63) | Bloemfontein 9300 | South Africa/Suid-Afrika | www.ufs.ac.za

Appendix 4: Protocol

University of Free State
Faculty of Health Sciences
Department of Psychiatry

A comparative cost analysis of functional neurological disorder with other neurological disorders in patients admitted at Universitas Academic Hospital Neurology Ward.

Researcher: Dr Leonriche Christopher

Student number: 2005086935

Contact details:
Address: 74A Calliope Street, Pentagon Park, Bloemfontein, South Africa
Tel: +27 51 405 3545
Cell: +27 82 353 0968
Email address: lenchristopher88@gmail.com
@ufs4life.ac.za

Supervisor: Prof PJ Pretorius

Co-supervisor: Prof A Moodley

Content

1. Researchers

The principal investigator for this research study is Dr L Christopher, from the Free State Psychiatric Complex. The supervisor is Prof PJ Pretorius, from the Free State Psychiatric Hospital. The co-supervisor is Prof A Moodley, from the Neurology Department of Universitas Academic Hospital.

2. Introduction

Functional Neurological Disorder (FND) is a debilitating condition which has long been recognised as a psychiatric disorder. The Diagnostic and Statistical Manual Five (DSM-5) defines FND as one or more symptoms that affect the motor or the sensory systems of the patient, and where these symptoms cannot be explained by a neurological or other medical condition or another mental health disorder. These symptoms can cause significant distress or social problems. It may affect the patient's capabilities at work or other areas in daily life.[1]

3. Literature review

FND previously known as Conversion Disorder (DSM IV) was thought to be primarily in the domain of psychiatry. There has been a shift toward the condition being considered a neurological condition as well. Jean Martin Charcot developed the term "hysteria" and the concept of a "psychodynamic lesion" producing the symptoms. Joseph Babinski believed that some symptoms were produced by suggestion, and they could therefore be eliminated by suggestion and persuasion leading to abusive therapies being used on soldiers during World War I.[2]

Sigmund Freud differentiated hysteria from simulation, and emphasised the unconscious nature of "conversion". "Conversion" is an unconscious mechanism, where emotional reactions to traumatic events were inhibited or repressed because they were unacceptable to the self in some way. This leads to build up of emotional tension, which the brain manages by converting it to physical symptoms. The emotional tension becomes represented by the symptoms, without the person being aware of it.[2]

Georges Engel developed the “biopsychosocial” model where the focus shifted onto the individual and his perception. Perception has the ability to adjust physical or psychological impairment.[2]

In 1980 the DSM III made the distinction between conscious and unconscious production of symptoms. Factitious Disorder was included, which was the conscious production of symptoms. [2]

There is neuroscientific evidence of a strong association between childhood adversities, recent life events and the development of FND. Childhood abuse is directly proportional to the amount of conversion symptoms and their severity.[3] One study found that 37% of patients reported physical events or illness immediately prior to onset of conversion symptoms. Eighty percent of patients reported symptoms three months prior to onset of conversion symptoms. These events include soft tissue injury, fractures, Bell’s palsy, migraine, acute pain, drug reactions, surgery and syncope.[3]

FND patients had increased activity in the supplementary motor area and the right temporoparietal junction (TPJ), regions in the brain responsible for motor execution and inhibition. The right TPJ is responsible for self-agency, which is hypothesised to be defective in FND. These patients are thought to be sensitive to emotional stimuli and respond faster to what they perceive as social cue threats.[3]

Studies have also indicated the involvement of the hypothalamus pituitary adrenal axis in FND. It was found that these patients had elevated diurnal cortisol levels and increased amylase levels; a protein secreted in response to adrenergic activation. This correlates with impaired vagal tone also found in the FND patients.[3]

There is not much evidence for the role of genetics in the development of FND. Some individuals may however be more vulnerable than others, based on temperament or modelling behaviour. [3]

These medically unexplained symptoms (MUS) make up 30% of neurology consults, with 16% of the new patients being diagnosed with functional symptoms.[4] FND has an incidence of 4-12/100 000 per year.[5] Females are affected more than men at a ratio of 3:1 and make up 60-75% of this patient population.[5] Being from a lower socioeconomic background is a risk factor for developing FND.[6] Remission

rates are 21, 5 % at 7,4 years, but 83% of impairments persist at 12,5 years.[4] FND rarely occurs in isolation, there is a strong psychiatric comorbidity of between 31-71% of patients.[8] The most common psychiatric diagnosis made in patients with FND is Panic disorder followed by Mood disorders, Anxiety disorders and substance abuse.[1] Suicide rates are also much higher than the general population.[9]

FND is no longer a diagnosis of exclusion.[10] The diagnosis can be made when finding positive signs on clinical examination.[11] The diagnosis of FND is often difficult to make, even by specialists in the field. The rate of misdiagnosis is 4%.[5] Patients go for years with impairing symptoms that negatively affect their quality of life. These patients are often seen as being difficult, with a lot of doctors feeling that their symptoms are feigned. Patients are left unsatisfied with their symptoms being attributed to emotional distress.[12]

FND which forms part of somatoform disorders serves as an important determinant of medical care utilization. This leads to increased incurred costs on the health system of any country. In a study conducted in a hospital in Italy 273 patients with unexplained medical symptoms were analysed retrospectively over a period of 10 years. The study reported an overall estimated incurred cost of 475, 409.73€. The neurology ward incurred the most cost at a total of 328, 192€ followed by the internal medicine incurring costs of 147,976€. The average cost per year treating these patients was reported as 47, 504.9€. The examination costs overall (blood tests and instrumental examination) for these patients was 119, 926.34€. [13]

In another study by Arthur J in the United Kingdom, somatization patients utilized the outpatient and inpatient medical care twice as much of the non-somatization patients. The annual medical care costs in this patient group was double that of the non-somatization patient. The somatising patient had more primary care visits with a mean visit of 4.9 times (SE 0.32) while the non-somatization patient had a mean visit of 3.43 times (SE 0.11). These patients also had more emergency department visits and hospital admissions. More visits means more costs are incurred for this patient population which may place somewhat of a burden on the health system.[14]

A study conducted in New Zealand in 2013 examined 49 patients and estimated the direct health costs associated with the frequency and type of medically unexplained symptoms. The total cost incurred was GBP 89, 636 where the most significant expenditure was at inpatient care and emergency care. The study reports that the incurred cost was substantial and comparable to the cost of chronic medical conditions with identifiable pathology.[15]

In South Africa there is a lack of published data on the subject of somatization and costs incurred on the health system. However, globally, it is evident that the somatised patient incurs more costs on the health system that may be reduced if the management of this patient population is researched and optimized. Establishing the cost of FND is important with the approaching National Health Insurance.

4. Method

Study design

The research conducted will be a retrospective comparative study. The intent of the retrospective research is to produce a comparative cost analysis whereby the outcome may lead to important recommendations.

Aim

The aim of the study is to establish the inpatient cost of managing a patient with functional neurological disorder compared with the inpatient cost of Non-FND patients admitted to the neurology department at Universitas academic hospital.

Objectives

- To compare the cost of managing a patient with FND, with the cost of managing a Non-FND neurology patient
- To describe the demographics of inpatients diagnosed with FND at the Neurology department at Universitas Academic Hospital for the period 1 January 2018 till 31 December 2019
- To calculate the inpatient prevalence of FND at the Neurology Department at Universitas hospital for the period 1 January 2018 till 31 December 2019

Study population

The study population for the FND group will be all inpatients aged 14 years and above who were diagnosed with FND from 1 January 2018 till 31 December 2019. The population is estimated to be 40 patients. The comparative group will be selected from all inpatients aged 14 years and above admitted to the neurology department with any diagnosis other than FND. The comparative group will be 40 patients. Every 12th patient will be chosen as part of the comparative group. On average the admission for the period of 1 January 2018 until 31 December 2019, 509 patients were admitted to the neurology department at Universitas academic hospital.

Inclusion criteria

All patients 14 years of age and above admitted to the inpatients Neurology ward (6B) at Universitas hospital for the period 1 January 2018 till 31 December 2019 are eligible for inclusion. All patients diagnosed with FND during this period will be included in the study. Every 12th patient admitted with another diagnosis (other than FND) will be selected for inclusion and analysis for the comparator group.

Exclusion criteria

Patient records, which do not contain all the information, required to complete the data capture sheet. These include:

Age, gender, race, clinical presentation, length of stay, medical co-morbidities, psychiatric co-morbidities, inadequate documentation on required special investigations. These include blood investigations, cerebrospinal fluid investigations, radiological investigations, neurophysiological investigations, medications administered, allied health services received.

Financial statements will be checked against the clinical file for completeness of billing information. Patients with incomplete billing information will be excluded from the data analysis.

Patients seen at Neurology Outpatient Department at Universitas Academic Hospital will be excluded from the study.

Outliers with costs more than double the average, or less than 50% of the average in each group will be excluded from the data analysis.

5. Data collection and data analysis

a. Data collection

Secondary data will be collected from patient notes on Meditech. The total number of admissions to the Neurology Department for the period 1 January 2018 till 31 December 2019 will be recorded, and all records reviewed to ensure all patients with FND are found. The ICD 10 code F44.9 and F44.9 will also be used to search Meditec. 40 patients from the same period with any other neurological condition will also be chosen from Meditec. Billing of those 80 patients, will be obtained from the revenue section of Universitas Academic Hospital. All demographic, clinical data and financial data for both groups will be entered onto the data collection tool.

b. Measurements

Variables:

- Age
- Gender
- Race
- Length of stay
- Medical co-morbidities
- Psychiatric co-morbidities
- Blood investigations
- Cerebrospinal fluid investigations
- Radiologic investigation
- Neurophysiological investigations
- Medications administered

- Allied Health services receive
- H classification

Outcome variable: Cost

i. The Uniform Patient Fees Schedule (UPFS) is used for billing all patients
ii. The bill that is owed, will be determined by the patients classification H0, H1, H2, H3
iii. The UPFS is done by the Revenue section of Universitas Academic Hospital
iv. The UPFS contains **all costs** incurred to the hospital:
    - Ward fee and ward professional fee
    - Laboratory fees
    - Imaging fees and imaging professional fees
    - Pharmacy fee and medication fees
    - Allied health service fees
    - The amount the patient owes the hospital and the amount written off according to patient classification

6. Data analysis

Descriptive data analysis will be performed by the Department of Biostatistics at the University of the Free State. Means will be reported with the standard deviation for the average patient cost of FND and Non-FND patients. Categorical variables will be summarised by frequencies and percentages. 95% Confidence intervals will be calculated for main outcomes. Results will be compared using 95% confidence intervals for differences in medians or means, with appropriate hypothesis testing.

The prevalence of functional neurological disorder will be calculated, using the numerator as the functional neurological disorder patients admitted to the neurology department for the period of 01 January 2018 until 31 December 2019. The denominator will be all patients admitted to the neurology department for the same period, who were 14 years of age and older.

7. Data Storage

Data will be stored safely and securely on a password protected computer. The researcher will password-protect the data on Excel using the password option. Data will be stored until the completion and submission of the researchers MMed thesis. Data will be retained for five years post awarding of the MMed thesis to facilitate availability of data for subsequent follow up studies and as per HSREC regulations. After five years data records will be destroyed by the researcher.

8. Pilot study

Data will be extracted from the first 10 patients, 5 from each group who meet the inclusion criteria for this study, after all approval has been received. The demographic data and costs will be added to the data collection tool. Any problems with methodology, the data collection tool or determination of costs will be detected during the Pilot study. These cases will be included in the main study if no changes are required to the methodology.

9. Implementation of findings

The findings of this study will be submitted for publication in a peer reviewed journal. The findings of this study could help the department of health to draw up more cost effective protocols of investigating and managing patients with FND.

10. Budget

Item	**Cost**
Printing paper	R500
Stationery	R500
Transport	R1 000
Telephone/Cellphone use	R500
Printing & binding of research report	R750
Language Editor	R3000
Total	R 6250

The researcher will cover all cost pertaining to the budget as stipulated above.

11. Time schedule

	Expected start date	Expected completion date
Protocol	January 2020	February 2020
Biostats approval	February 2020	February 2020
Ethics submission	March 2020	Unknown
Approval from DoH	June 2020	June 2020
Pilot study to start	July 2020	July 2020
Data collection	July 2020	October 2020
Development of Excel database	October 2020	November 2020
Data analysis	November 2020	December 2020
Compiling the research report/manuscript	January 2021	May 2021

12. Ethical considerations

Approval will be obtained from the following:

- The Health Sciences Research Ethics Committee of the University of the Free State
- Head of Department of Health of the Free State Dr David Motau
- Head of Department of Neurology Prof A Moodley
- Head of Revenue section of Universitas Academic Hospital Mr Kwame Kwakwa

12. Confidentiality

For confidentiality purposes only the principal researcher and the researcher's supervisor will have access to the data. Data will be treated with the strictest confidentiality where all patient identifiers will be removed and replaced by a study number e.g. FNDP00.

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Appendix 5: Data Collection Tool

#Patient_study_no.	Age	Gender	FND y/n ?	Clinical Presentation	Medical comorb y/n/u?	If yes specify	Psych comorb y/n/u?	If yes specify	Lab invest y/n?	Lab cost	Imaging y/n?	If yes specify	Imaging fee	Imag Prof fee	Imag mat fee	Total imag cost	No. days admitted	No of admis	Ward fee	Ward prof fee	Total ward cost	Pharmacy fee	Pharmacy script	Total Pharmacy	Physio y/n?	Physio cost	Occup therapy y/n?	OT Cost	Speech Therapy y/n?	ST Cost	NPI y/n	If yes specify	NPI cost	Grand total	PI Classifcation	Amount owed by pt	Amount paid by UAH

Appendix 6: Authors Guidelines

South African Psychiatric Journal

Original Research Article

An original article provides an overview of innovative research in a particular field within or related to the focus and scope of the journal, presented according to a clear and well-structured format. Systematic reviews should follow the same basic structure as other original research articles. The aim and objectives should focus on a clinical question that will be addressed in the review. The methods section should describe in detail the search strategy, criteria used to select or reject articles, attempts made to obtain all important and relevant studies and deal with publication bias (including grey and unpublished literature), how the quality of included studies was appraised, the methodology used to extract and/or analyse data. Results should describe the homogeneity of the different findings, clearly present the overall results and any meta-analysis.

Word limit	3000-4000 words (excluding the structured abstract and references)
Structured abstract	250 words to include a Background, Aim, Setting, Methods, Results and Conclusion
References	60 or less
Tables/Figures	no more than 7 Tables/Figure
Ethical statement	should be included in the manuscript
Compulsory supplementary file	ethical clearance letter/certificate

Cover Letter

The authorship, disclosure statements, copyright, and license agreement form is our compulsory cover letter which needs to form part of your submission. Kindly download and complete, in English, the provided **form**.

Anyone that has made a significant contribution to the research and the paper must be listed as an author in your cover letter. Contributions that fall short of meeting the criteria as stipulated in our policy should rather be mentioned in the 'Acknowledgements' section of the manuscript. Read our **authorship** guidelines and **author contribution** statement policies.

Original Research Article full structure

Title: The article's full title should contain a maximum of 95 characters (including spaces).

Abstract: The abstract, written in English, should be no longer than 250 words and must be written in the past tense. The abstract should give a succinct account of the objectives, methods, results and significance of the matter. The structured abstract for an Original Research article should

consist of six paragraphs labelled Background, Aim, Setting, Methods, Results and Conclusion.

- Background: Summarise the social value (importance, relevance) and scientific value (knowledge gap) that your study addresses.
- Aim: State the overall aim of the study.
- Setting: State the setting for the study.
- Methods: Clearly express the basic design of the study, and name or briefly describe the methods used without going into excessive detail.
- Results: State the main findings.
- Conclusion: State your conclusion and any key implications or recommendations.

Do not cite references and do not use abbreviations excessively in the abstract.

Introduction: The introduction must contain your argument for the social and scientific value of the study, as well as the aim and objectives:

- Social value: The first part of the introduction should make a clear and logical argument for the importance or relevance of the study. Your argument should be supported by use of evidence from the literature.
- Scientific value: The second part of the introduction should make a clear and logical argument for the originality of the study. This should include a summary of what is already known about the research question or specific topic, and should clarify the knowledge gap that this study will address. Your argument should be supported by use of evidence from the literature.
- Conceptual framework: In some research articles it will also be important to describe the underlying theoretical basis for the research and how these theories are linked together in a conceptual framework. The theoretical evidence used to construct the conceptual framework should be referenced from the literature.
- Aim and objectives: The introduction should conclude with a clear summary of the aim and objectives of this study.

Research methods and design: This must address the following:

- Study design: An outline of the type of study design.
- Setting: A description of the setting for the study; for example, the type of community from which the participants came or the nature of the health system and services in which the study is conducted.
- Study population and sampling strategy: Describe the study population and any inclusion or exclusion criteria. Describe the intended sample size and your sample size calculation or justification. Describe the sampling strategy used. Describe in practical terms how this was implemented.
- Intervention (if appropriate): If there were intervention and comparison groups, describe the intervention in detail and what happened to the comparison groups.
- Data collection: Define the data collection tools that were used and their validity. Describe in practical terms how data were collected and any key issues involved, e.g. language barriers.
- Data analysis: Describe how data were captured, checked and cleaned. Describe the analysis process, for example, the statistical tests used orsteps followed in qualitative data analysis.
- Ethical considerations: Approval must have been obtained for all studies from the author's institution or other relevant ethics committee and the institution’s name and permit numbers should be stated here.

Results: Present the results of your study in a logical sequence that addresses the aim and objectives of your study. Use tables and figures as required to present your findings. Use quotations as required to establish

your interpretation of qualitative data. All units should conform to the **SI convention** and be abbreviated accordingly. Metric units and their international symbols are used throughout, as is the decimal point (not the decimal comma).

Discussion: The discussion section should address the following four elements:

- Key findings: Summarise the key findings without reiterating details of the results.
- Discussion of key findings: Explain how the key findings relate to previous research or to existing knowledge, practice or policy.
- Strengths and limitations: Describe the strengths and limitations of your methods and what the reader should take into account when interpreting your results.
- Implications or recommendations: State the implications of your study or recommendations for future research (questions that remain unanswered), policy or practice. Make sure that the recommendations flow directly from your findings.

Conclusion: Provide a brief conclusion that summarises the results and their meaning or significance in relation to each objective of the study.

Acknowledgements: Those who contributed to the work but do not meet our authorship criteria should be listed in the Acknowledgments with a description of the contribution. Authors are responsible for ensuring that anyone named in the Acknowledgments agrees to be named. Refer to the acknowledgement structure guide on our *Formatting Requirements* page.

Also provide the following, each under their own heading:

- Competing interests: This section should list specific competing interests associated with any of the authors. If authors declare that no competing interests exist, the article will include a statement to this effect: *The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.* Read our **policy on competing interests**.
- Author contributions: All authors must meet the criteria for authorship as outlined in the **authorship** policy and **author contribution** statement policies.
- Funding: Provide information on funding if relevant
- Data availability: All research articles are encouraged to have a data availability statement.
- Disclaimer: A statement that the views expressed in the submitted article are his or her own and not an official position of the institution or funder.

References: Authors should provide direct references to original research sources whenever possible. References should not be used by authors, editors, or peer reviewers to promote self-interests. Refer to the journal referencing style downloadable on our *Formatting Requirements* page.

Style and format

File format

- Manuscript files can be in the following formats: DOC, DOCX, or RTF. Microsoft Word documents should not be locked or protected.
- LaTeX documents (.tex) should be converted into Microsoft Word (.doc) before submission online.
- Rich Text Format (RTF): Users of other word processing packages should save or convert their files to RTF before uploading. Many free tools are available that will make this process easier.

Length

Manuscripts should adhere to the author guidelines of the journal. There are restrictions on word count, number of figures, or amount of supporting information.

Font

Use a standard font size and any standard font family.

Special characters

Do not use the font named 'Symbol'. To add symbols to the manuscript, use the Insert → Symbol function in your word processor or paste in the appropriate Unicode character. Refer to our AOSIS house style guide on mathematical and Unicode font guidelines.

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Ensure that formatting for headings is consistent in the manuscript. Limit manuscript sections and sub-sections to four heading levels. To avoid confusion during the review and production process, ensure that the different heading levels used in your work are visually distinct from one another. The simplest way to achieve this is to use different font sizes and/or a combination of bold/italics for different heading levels.

Keywords

Identify eight keywords that represent the content of your manuscript and are specific to your field or sub-field. Test your keywords: when you enter your keywords into the various journal and academic databases like Google Scholar, do the results include papers similar to your topic? If not, revise the terms until they do.

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Manuscript text should have a 1.5 line spacing.

Page and line numbers
Include page numbers and line numbers in the manuscript file. Use continuous line numbers (do not restart the numbering on each page).

Footnotes
Footnotes are not ideal. If your manuscript contains footnotes, move the information into the main text or the reference list, depending on the content.

Language
Manuscripts must be written in British English, according to the Oxford English Dictionary (avoid Americanisms [e.g. use 's' and not 'z' spellings], and set your version of Microsoft Word default language to UK English). Refer to the AOSIS house style guide for more information.

Abbreviations
Define abbreviations upon first appearance in the text. Do not use non-standard abbreviations unless they appear at least three times in the text. Keep abbreviations to a minimum.

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Illustrations fall into two categories:

- Figures: Photographs, drawings, diagrams, graphs, flowcharts, maps, etc.
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The manuscript must adhere to the **AOSIS house style guide**.

References

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Check the contract with the other publisher to see whether, and under what conditions, the material can be reused in this AOSIS publication. If in any doubt, permission must be obtained.

Images of, or information about, identifiable individuals
It is your responsibility to obtain consent from patients and other individuals for the use of information, images, audio files, and video clips from which they may be identified. Bear in mind the following points:

- Masking a person's eyes is not an adequate or acceptable means of rendering an image anonymous.
- People may still be recognizable to individuals or their families, even if head/shoulders are not included.
- People may recognize themselves from clinical descriptions or case reports.

Modification/adaptation of figures and tables
Use the original figure as first published where appropriate. However:

- No clearance is required if you create figures or tables using factual data from copyrighted material.
- No clearance is required if, after you have created a single figure or table using data from two or more figures or tables, no single source comprises more than 75% of the new figure or table.
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For prose, permission is required for single quotations of over 400 words or multiple quotations from the same source that cumulatively total more than 800 words. But note that, even if below these limits, permissions must be cleared for quotations that represent the 'heart of the work' or a substantial portion of the overall original source material.

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Permissions must be cleared before the final version of your manuscript is submitted for publication. If permission cannot be obtained, you should find an alternative or remove the material. Provide electronic copies of all consent forms obtained when you submit your final manuscript, numbered and named accordingly.

Acknowledgements structure

Acknowledgements

The acknowledgement section follows the conclusions section and addresses formal, required statements of gratitude and required disclosures. It includes listing those who contributed to the work but did not meet authorship criteria, with the corresponding description of the contribution. Acknowledge anyone who provided intellectual assistance, technical help (including with writing and editing), or special equipment and/or materials. Authors are responsible for ensuring that anyone named in the Acknowledgements agrees to be named.

Also provide the following, each under their own subheading:

- Competing interests
- Author contributions
- Funding information
- Data availability statement
- Disclaimer

Competing interests

This section should list specific competing interests associated with any of the authors. If authors declare that no competing interests exist, the article will include a statement to this effect. Read our **policy on competing interests**.

The following are examples of competing interest statements. If you use one of the examples, you should modify it to fit your specific relationship.

Scenario	Suggested competing interest statements
Example 1	The author(s) declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.

Author contributions
All authors must meet the criteria for authorship as outlined in the **authorship** policy and **author contribution** statement policies.

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Scenario	Suggested author contribution statements
Example 1	A.B. and B.C. conceived of the presented idea. A.B. developed the theory and performed the computations. C.D. and D.E. verified the analytical methods. B.C. encouraged A.B. to investigate [a specific aspect] and supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

Funding information
All research articles should have a funding acknowledgement statement included in the manuscript in the form of a sentence under a separate heading entitled 'Funding information'. The funding agency should be written out in full, followed by the grant number in square brackets.

The following are examples of a funding statement. If you use one of the examples, you should modify it to fit your specific relationship.

Scenario	Suggested funding statements
Example 1	The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Medical Research Council [grant number xxx].

Example 2	This work was supported by the Trust [grant numbers xxxx, yyyy]; the Natural Environment Research Council [grant number zzzz]; and the Economic and Social Research Council [grant number aaaa].
Example 3	The author(s) received no financial support for the research, authorship, and/or publication of this article.

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All research articles should have a data availability statement included in the manuscript in the form of a sentence under a separate heading entitled 'Data availability statement'.

The following are examples of a data availability statement. If you use one of the examples, you should modify it to fit your specific relationship.

Availability of data	**Suggested data availability statements**
Data openly available in a public repository that issues datasets with DOIs	The data that support the findings of this study are openly available in [repository name e.g 'figshare'] at http://doi.org/[doi], reference number [reference number].
Data openly available in a public repository that does not issue DOIs	The data that support the findings of this study are openly available in [repository name] at [URL], reference number [reference number].
Data derived from public domain resources	The data that support the findings of this study are available in [repository name] at [URL/DOI], reference number [reference number]. These data were derived from the following resources available in the public domain: [list resources and URLs]
Data available within the article or its supplementary materials	The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

Data generated at a central, large-scale facility, available upon request	Raw data were generated at [facility name]. Derived data supporting the findings of this study are available from the corresponding author [initials] on request.
Embargo on data due to commercial restrictions	The data that support the findings will be available in [repository name] at [URL / DOI link] following a [6 month] embargo from the date of publication to allow for the commercialisation of research findings.
Data available on request due to privacy/ethical restrictions	The data that support the findings of this study are available on request from the corresponding author, [initials]. The data are not publicly available due to [restrictions, e.g. their containing information that could compromise the privacy of research participants].
Data subject to third party restrictions	The data that support the findings of this study are available [from] [third party]. Restrictions apply to the availability of these data, which were used under licence for this study. Data are available [from the authors / at URL] with the permission of [third party].
Data available on request from the authors	The data that support the findings of this study are available from the corresponding author, [author initials], upon reasonable request.
Data sharing not applicable – no new data generated	Data sharing is not applicable to this article, as no new data were created or analysed in this study.

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