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## **Title**

# **Functional Neurological Disorder in Children and Young People: Incidence, Clinical Features and Prognosis**

## **Short title**

### **Functional Neurological Disorder in Children**

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## Functional Neurological Disorder in Children

### Abstract

**AIM** – To report incidence, demographic and clinical characteristics, and symptom outcome of functional neurological disorder (FND) in children.

**METHOD** – Children diagnosed with FND at a regional children’s hospital were prospectively recruited by weekly active surveillance for 36 months. Demographic, clinical and follow-up data were retrospectively extracted by review of electronic records. Descriptive statistical analyses were used.

**RESULTS** – Ninety-seven children (range 5-15 years (51% 13 or above)) met the case definition of FND (annual incidence = 18.3/100,000 children). Children with FND were likely to be female (n=68 (70% female) and older (median 13 years) with no difference in the Scottish Index of Multiple Deprivation (marker of socioeconomic status) compared to the general childhood population. Functional motor (41%) and sensory (41%) symptoms were most common; other somatic symptoms such as headache (31%) and pain (27%) were frequent. Self-reported psychiatric symptoms and infection/inflammation were commonest predisposing and precipitating factors respectively. At a median of 15 months follow-up, 49% of 75 children reported improvement or resolution of FND symptoms with no prognostic factors found.

**INTERPRETATION** – At this regional centre, FND in children had a higher incidence than previously reported and a less optimistic outcome than in some other studies.

## **What this paper adds**

- FND is common with a higher incidence (18.3/100,000 children) than previously reported.
- FND is typically complex with multiple symptoms, predisposing psychosocial and precipitating factors.
- Short-term outcome of FND may be less favourable than often thought.

## Background/Rationale

Functional neurological disorder (FND) refers to symptoms of altered voluntary motor or sensory function where there is clinical evidence of incompatibility with recognised neurological conditions, and significant distress and functional impairment<sup>[1]</sup>. FND symptoms are experienced as involuntary and commonly grouped into three categories: i) motor symptoms, such as limb weakness and gait disturbance; ii) sensory symptoms, such as numbness or visual loss; and iii) functional seizures. The diagnosis of FND should be made using positive clinical signs that demonstrate internal inconsistencies, such as Hoover's sign and tremor entrainment, and not as a diagnosis of exclusion<sup>[2]</sup>.

There is a substantial body of work on FND in adults whereas, in comparison, less is known about FND in children and young people under the age of 16, for which we use the word 'children' in this article<sup>[3]</sup>. The incidence of FND in children is estimated at 1.3-6.0/100,000<sup>[4-6]</sup> although this may be rising with better diagnosis<sup>[7]</sup>. It increases with age through the teenage years and is more common in females<sup>[4,5]</sup>. Children with FND often have multiple somatic symptoms such as pain, fatigue and abdominal symptoms<sup>[4,5]</sup>. The aetiology of FND is typically formulated around predisposing, precipitating and perpetuating factors with a wide range of factors described in the literature<sup>[8]</sup>. Children with FND have high service use<sup>[9]</sup>; although a generally good prognosis has often been reported<sup>[6,10,11]</sup>. Some recent small treatment studies suggest that therapy may be effective<sup>[12,13]</sup>. Children with FND, especially those whose FND symptoms do not improve, are, subsequent to the diagnosis, more likely to have worse quality of life with more difficulties with education, mental health disorders and other persistent physical symptoms<sup>[14]</sup>.

Most of what is known about FND in children comes from national surveillance studies<sup>[4,5,7]</sup>, and case series reported by specialist units, including psychiatric services<sup>[11,14]</sup>. Data from these studies are

potentially skewed towards complex/severe cases with consequent under-estimation of the incidence and over-reporting of predisposing/precipitating factors. This study, therefore, aimed to examine the epidemiology of FND in an unselected population of children from within a specific geographical area presenting to a regional Paediatric service without a tertiary FND clinic. Our specific objectives were to estimate the incidence of FND in children; characterise demographic and socioeconomic profile; describe symptoms, potential predisposing and precipitating factors; investigate differences in sex or age for the presence of potential predisposing and precipitating factors; and report FND symptom outcome, including change in diagnosis, and explore factors that might predict favourable outcome.

## **Methods**

### **Study design**

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guideline<sup>[15]</sup>. We present routinely collected anonymised data with Caldicott Guardian approval.

### **Setting and recruitment**

The Royal Hospital for Children and Young People (RHCYP) is the sole provider of general and subspeciality paediatric inpatient and outpatient services for a Scottish region with a population of 116,720 children<sup>[16]</sup>. Active prospective surveillance of children diagnosed with FND was conducted between 1 January 2018 and 31 December 2020. Weekly emails were sent to clinicians in General Paediatrics, Paediatric Neurology and Paediatric Psychology and Liaison Service requesting Community Health Index numbers, a number that can be linked to centrally-held health data<sup>[17]</sup>.

## **Participants**

Children were included if they had FND according to DSM-5 diagnostic criteria<sup>[1]</sup>, including if it occurred with another comorbidity, but excluded if symptoms were wholly accounted for by another medical or mental disorder. The diagnosis of FND was determined by Paediatric Neurologists and/or General Paediatricians with particular emphasis on criterion B – demonstration of clinical incompatibility with other recognised conditions. In practice, this meant identifying positive features of FND and not just exclusion of disease<sup>[2]</sup>.

## **Variables**

We recruited individuals prospectively and collected data from electronic records documented as part of routine clinical care (Box 1). The Scottish Index of Multiple Deprivation (SIMD) is a relative measure of socioeconomic status, according to geographic area of residence, based on seven domains – income, employment, education, health, access to services, crime, and housing; it ranks areas from most deprived (first) quintile to least deprived (fifth) quintile<sup>[18]</sup>. FND symptom outcome was determined from clinician reports – children did not undergo standardised, formal treatment or standardised outcome measurement. Predisposing and precipitating factors were not defined a priori but we relied on clinicians recording factors that they considered to be relevant during the first assessment prior to diagnosis of FND. Data from all clinical contact between first FND presentation and a census date of 31 July 2021 were treated in a summative manner. Data post-FND presentation were considered follow-up data.

## **Statistical methods**

Annual incidence was calculated using children diagnosed for the first time ever with FND as the numerator and the mid-2019 regional child population<sup>[16]</sup> as the denominator. Complete case analysis

was carried out. Cases with multiple or new FND symptoms on follow-up were counted as single cases. Incident cases were stratified into <11 years-old and 11-15 years-old to reflect primary and secondary school ages in Scotland and age-stratified incidences calculated using corresponding child populations as denominators.

Statistical analyses were conducted using IBM SPSS Statistics 28 (United States). Descriptive statistical analyses were used for sex (Chi-squared analysis), age (median and inter-quartile range (IQR)) and SIMD quintiles (Chi-squared analysis). The relationships of sex and age with potential predisposing and precipitating factors were investigated using Chi-squared analysis and Mann-Whitney U analysis.

Sex and age differences between cases with and without follow-up data were compared using Yates' Continuity Correction and Fisher's Exact Test, and Student's t-test respectively. Logistic regression was used to compare factors – (1) sex, (2) age, (3) SIMD quintile, (4) number of FND and somatic symptoms (combined), (5) presence of predisposing and (6) precipitating factors, (7) whether any investigations had been undertaken and (8) any therapies/treatments dispensed – associated with FND symptom outcome (good vs. poor, Box 1).

## **Results**

### **Participants**

A hundred and eight notifications were received (Figure 1). After five duplicate notifications were removed, 103 electronic records were reviewed and 97 cases were included in this study. Of the six that were excluded, five did not meet the case definition. The remaining case was the only misdiagnosis identified over the time course of this study. This was a child with a limp who was initially



diagnosed with a functional gait disorder but found to have Slipped Upper Femoral Epiphysis four months later, which with hindsight, explained the original presentation.

Most cases were notified by paediatric neurologists (77/97, 79%) with the remainder notified by general paediatricians and psychologists. Of the latter, 16 (16%) had Paediatric Neurology input. Some children in this case series had no investigations undertaken (11/97, 11%), all of whom had Paediatric Neurology input. Of those who had investigations undertaken, nearly two-thirds (56/86, 65%) had more than one form of investigation other than history and examination including blood tests (46/97, 47%), cerebrospinal fluid tests (1/97, 1%), electrophysiological (29/97, 30%) studies and neuroimaging (60/97, 62%).

Sixty-four (66%) children of the 97 eligible cases were incident cases. Of these, 42 (66%) were 11-15 years-old (Figure 2). The mid-year populations of the region were 116,720 children under 16 years; 82,326 children under 11 years; and 34,394 children 11-15 years-old<sup>[16]</sup>. Annual incidence rate was 18.3/100,000 (95% confidence interval (95% CI) 13.8-22.8/100,000) children under 16 years. Incidence was less among children under 11 years (8.9/100,000, 95% CI 5.2-12.6/100,000) compared to those aged 11-15 years (40.7/100,000, 95% CI 28.4-53.0/100,000) (difference between incidences=31.8/100,000, 95% CI 18.9-44.7/100,000).

Of the total 97 children, there were more females (n=68, 70%,  $\chi^2=15.7$ ,  $p<0.001$ ). The median age was 13 years (IQR 9-13 years, range 5-15 years; Figure 2). Amongst the 75 children residing in the region, there were more children from the *least* deprived (fifth) SIMD quintile (Figure 3). However, observed and expected quintile proportions for 2019<sup>[18]</sup> were calculated and no difference was found between the proportions of SIMD quintiles in this case series and the baseline population ( $\chi^2=6.70$ ,  $df=4$ ,

$p=0.153$ ). Thus, there was no evidence of an excess of children from the least deprived quintile in this case series.

The most common FND symptoms were functional motor (40/97, 41%) and sensory symptoms (40/97, 41%). The most common somatic symptom was headache (30/97, 31%) followed by pain (26/97, 27%) (Table 1). Most children presented with more than one symptom (69/97, 71%) and in those who presented with more than one symptom, headache and pain were still their commonest symptoms.

Three-quarters of children and their families reported potential predisposing factors (76/97, 78%). Table 2 lists all potential predisposing/precipitating factors that were identified; they were not mutually exclusive so a child with multiple factors could be counted more than once for each predisposing/precipitating factor. The most common predisposing factor was self-reported psychiatric symptoms followed by pressure from academic/sporting achievement. Children with self-reported psychiatric symptoms (34/97, 35%) consisted of those with formal diagnoses of psychiatric conditions pre-FND onset (8/97, 8%) and those who self-reported anxiety, low mood or suicidal ideation pre-FND onset (26/97, 27%). Of those who self-reported psychiatric symptoms, half (13/26, 50%) went on to receive formal diagnoses of psychiatric conditions and three children (3/26, 12%) were diagnosed with Autistic Spectrum Disorder after the diagnosis of FND. Female children, independent of age, were more likely to have predisposing factors ( $\chi^2=4.02$ ,  $df=1$ ,  $p=0.045$ ).

Precipitating factors were reported in 36 (37%) children, most commonly infection/inflammation and physical trauma/injury. Older children, independent of sex, were more likely to report precipitating factors ( $U=816$ ,  $p=0.033$ ). Commonly reported precipitating factors included physical injury leading to functional weakness and tremor, and migraine leading to functional seizures.

Therapies ranged, in order of decreasing frequency, from psychotherapy using a cognitive behavioural therapy framework (44/97, 45%), physical therapy (32/97, 33%) to pharmacotherapy (22/97, 23%). A minority of children (23/97, 24%) were admitted as inpatients; the median length of admission was three days (IQR 2-4 days, range 1-28 days). Some children (36/97, 37%) did not receive any treatment; five (22%) of them were admitted.

Data for FND symptom outcome was available in 75 (77%) out of 97 children. There were no differences in sex and age between children with and without outcome data. The median length of follow-up was 15 months (IQR 7-22.5, range 1-40 months). Where data for symptom outcome was unavailable, this was due to absence of follow-up – either intentionally discharged or not brought to follow-up appointment – with no re-presentation to RHCYP over the duration of this study. Thirty-eight children (51%) had poor symptom outcome – four (5%) had worsening of symptoms, 27 (36%) had no change in symptoms and seven (9%) had new FND symptoms; thirty-seven children (49%) had good symptom outcome – 21 (28%) had improvement and 16 (21%) had resolution of symptoms. Fifty-nine children (79%) had ongoing symptoms at last follow-up. The following variables studied were not associated with FND symptom outcome: (1) sex, (2) age, (3) SIMD quintile, (4) number of FND and somatic symptoms (combined), (5) presence of predisposing and (6) precipitating factors, (7) whether any investigations had been undertaken and (8) any therapies/treatments dispensed.

## **Discussion**

The main findings from this study were: annual incidence of FND in children was 18.3/100,000 which is much higher than previously reported; it was especially common in females and children aged 11-15 years but no association with socioeconomic status was found; self-reported psychiatric symptoms

and pressure related to academic/sporting achievement were common predisposing factors whilst infection/inflammation and injury were common precipitating factors; most children had continued symptoms 15 months after diagnosis but half showed improvement or resolution of FND symptoms with no prognostic factor emerging from those assessed. Table 3 summarises our findings in comparison to similar studies with comparable reported variables.

Our incidence estimate is 14 times higher than a UK surveillance study<sup>[4]</sup> and three times higher than another recent British regional study on FND in children<sup>[6]</sup>. Our higher incidence could relate to better study methodology, increasing recognition of FND or both. As a whole, previous studies on FND in children have relied on surveillance with poor response proportions (66-93%<sup>[4,5]</sup>) or on coding and databases<sup>[7]</sup>, or have collected data retrospectively (Table 3). Our study however, collected cases prospectively with active surveillance on a weekly basis amongst a tight-knit group of clinicians. The year-on-year increase in the incidence rate of functional seizures seen in Denmark between 1996 and 2014 was thought to be due to recognition bias rather than a true rise in cases<sup>[7]</sup>. Even though our incidence is higher than previously reported, it is likely to be an underestimate since not all children with FND may present to hospital and we could have missed children who were seen in General Practice.

Our study found similar demographic, socioeconomic and symptom profiles of children with FND as previously reported (Table 3)<sup>[4-7,19]</sup>, thus reinforcing that female and older children are more likely to have FND. Although most of our children were predominantly from the least deprived areas, we found no evidence that socioeconomic status was associated with increased risk of FND, which is similar to that observed in an American study<sup>[9]</sup>. We also reported a higher occurrence of functional sensory symptoms compared to other studies<sup>[4-6,19]</sup>. Functional sensory symptoms are inherently less debilitating than functional seizures and motor symptoms and may have a better long-term

outcome<sup>[3]</sup>. This may explain why children with functional sensory symptoms are not represented as much in selected cohorts published by specialist centres.

Similarly, our findings of the commonest predisposing/precipitating risk factors are consistent with previous studies<sup>[4,5,9,19,20]</sup>. Self-reported psychiatric symptoms pre-FND diagnosis (34%) was the commonest predisposing factor although it is perhaps just as notable that in two-thirds of cases, it was not mentioned. We observed a high prevalence of academic-/sporting achievement-related pressure (34%) which has been studied in different guises such as academic difficulties (24%)<sup>[19]</sup> and examination issues (40%)<sup>[21]</sup>, but is probably related to recognised predisposing factors such as stress and perfectionism. Eight per cent of our sample had a co-occurring neurodevelopmental condition, something that has only rarely been studied as a predisposing factor in paediatric FND: A Danish study found a frequency of 12% in 384 children diagnosed with functional seizures; this increased to 18% after two-years follow-up<sup>[7]</sup>. Our finding that three per cent had abuse as a predisposing factor is based on reported abuse and is consistent with other studies in which the prevalence of reported abuse in children with FND has been shown repetitively to be low<sup>[4,5,19]</sup>. Despite this, child protection concerns remain paramount and should not be overlooked as some abuse can go unreported<sup>[22]</sup>.

This study reported a poorer outcome overall of FND than most other studies (Table 3) with half either the same or worse at follow-up. This may be related to the waxing and waning nature of FND where children often improve early on with a minority relapsing and developing chronic FND over time, and/or differences in study follow-up period. Multiple studies, with follow-up durations of up to two and a half years, reported 72-82% of children with functional seizures only and not any other FND symptom, becoming seizure-free<sup>[23-25]</sup>; this decreases to 45-66% at up to four-and-a-half-years follow-up<sup>[26,27]</sup>. Similarly, 75-100% of children with FND reported improvement in their symptoms at up to four-years follow-up<sup>[4,28]</sup> but 23% reported ongoing symptoms at eight-years follow-up<sup>[6]</sup>. Our finding

that 78% of children have persistent symptoms at 15 months follow-up is comparable to a tertiary London centre study (84% persistent symptoms at 24 months follow-up)<sup>[29]</sup>. Our negative findings, however, are affected by attrition bias as some children were not actively followed-up following diagnosis or was not brought to their follow-up appointment; all data points over the time course of this study were treated in a summative manner to minimise this effect.

We did not identify any factors predicting favourable outcome, similar to a study in Newcastle, another regional paediatric neuroscience centre in the UK<sup>[6]</sup>. In other studies, early diagnosis and good premorbid adjustment – both of which were not studied here – have been reported to be associated with favourable outcome<sup>[28,30]</sup>. In this study, the low rate of misdiagnosis, also corroborated elsewhere<sup>[31]</sup>, indicates that FND in children can be reliably diagnosed, and should be considered a specific condition, and not a “catch-all diagnosis” for unexplained neurological symptoms.

### **Limitations**

Our methodology introduces a number of different sources of bias: data collection was based on review of electronic records rather than interview with standardised measures, and predisposing/precipitating factors were not defined a priori. Consequently, recorded data were subject to clinician biases on what they think were relevant or important when eliciting the history. Certain predisposing factors such as psychosocial factors and academic-/sporting achievement-related pressure could, therefore, have been under- or over-reported respectively. Similarly, FND symptoms themselves were not characterised systematically but subject to documentation.

Only 77% of cases had outcome data which were determined by researchers reviewing the treating clinician records rather than using standardised outcome measures. Although we did not find

demographic difference between children with and without outcome data, we did not measure their disability or distress; children who had further contact with secondary care may have had more severe FND presentations and therefore, contributed to our negative outcome data. In addition, although we did not find that exposure to treatment affected outcome, we were unable to take into account case severity or treatment modalities.

This study was carried out in a single institution that provides sole paediatric hospital services for the region; thus, the results could be considered representative of the general population. Results from this unselected population of children can be extrapolated to other regional children's hospitals with Paediatric Neurology and Psychology services serving a predominantly White British population but may not be applicable to other populations.

### **Interpretation**

FND is a common condition in the paediatric setting with a much higher incidence than previously reported. Children with FND are typically complex, presenting with more than one symptom and an interplay of predisposing psychosocial and precipitating factors. The short-term outcome of FND may not be as good as some other studies suggest and some children do go on to develop chronic FND. We did not identify any factors that could predict outcome.

Future research should focus on the outcome of children diagnosed with FND by means of long-term prospective studies; these studies should look, not just at the persistence of FND symptoms, but also meaningful outcome markers such as education, employment and social participation in adulthood. Cohort studies should be conducted to determine new and confirm previously reported factors

associated with favourable outcome followed by randomised-controlled trials to investigate multidisciplinary interventions.

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### **Conflict of interest**

None declared

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*Box 1: Variables recorded for each child with FND*

- 1) First ever diagnosis of FND during surveillance period or not
- 2) Sex
- 3) Age at FND diagnosis
- 4) Home postcode – home postcode was used to determine the Scottish Index of Multiple Deprivation (SIMD) quintile as a marker of socioeconomic status<sup>[18]</sup>.
- 5) FND symptoms (motor symptoms (weakness/paralysis; movement disorder such as tremor/dystonia/jerks/tics; gait disorder), sensory symptoms (somatosensory, visual, auditory) and seizures)
- 6) Other somatic symptoms not fully explained by a recognised condition (including headache, fatigue, pain, gastrointestinal symptoms, dizziness, sleep, memory and dissociative symptoms). ‘Presence of multiple symptoms’ was defined as a binary variable identifying the occurrence of more than one FND or other somatic symptom
- 7) Potential predisposing factors identified from the medical or psychosocial history and/or used by clinicians seeing the child in the formulation of the diagnosis and/or management of FND as extracted from the initial assessment electronic record. These include but are not limited to self-reported psychiatric symptoms (recorded either as a psychiatric diagnosis or subjective report of low mood or anxiety with note of whether these were prior or after the onset of FND), adverse experiences such as abuse or neglect, pressure related to academic or sporting achievement, social stressors such as bullying, and other recognised chronic physical illness<sup>[8,32]</sup>. Predisposing factors were not defined a priori but we relied on clinicians recording factors that they considered to be relevant
- 8) Potential precipitating factors – physical or emotional events occurring at the time of FND symptom onset such as a physical injury to a limb prior to functional weakness in the same limb or a faint triggering the first occurrence of a functional seizure<sup>[20,33]</sup> – as extracted from the initial assessment record. ‘Presence of predisposing factors’ and ‘presence of precipitating factors’ were defined as binary variables determined by the prevalence of any predisposing or precipitating factor respectively. Precipitating factors were not defined a priori but we relied on clinicians recording factors that they considered to be relevant
- 9) Investigations undertaken
- 10) Treatments and therapies utilised as extracted from the record; multiple treatments were counted separately
- 11) Length of admission where relevant
- 12) FND symptom outcome as recorded by the treating clinician from last clinical contact. FND symptom outcome was inferred by the researchers and grouped into ‘Poor symptom outcome’ (symptoms worsened, remained unchanged or evolved into new FND symptoms) and ‘Good symptom outcome’ (symptoms improved or fully resolved)
- 13) Duration of follow-up
- 14) Misdiagnosis at follow-up – where the presenting symptoms judged to be FND were, with the benefit of hindsight, considered to relate to an alternative diagnosis

Table 1: Symptoms in 97 children with FND; \*Children could have more than one FND or other somatic symptoms; \*\*Other FND symptoms include functional facial symptoms, swallowing symptoms, olfactory disturbance and deterioration in hand-writing; †Dissociative symptoms include depersonalisation and derealisation; ‡Other somatic symptoms include habitual cough, visual and auditory hallucinations, “feeling cold” and post-concussion syndrome

<b>Symptoms</b>			
<b>FND symptoms</b>	<b>Children, n (%) Total n=97*</b>	<b>Other somatic symptoms</b>	<b>Children, n (%) Total n=97*</b>
Functional motor symptoms	40 (41)	Headache (including chronic daily headache)	30 (31)
Limb weakness and paralysis	11 (11)	Pain (including complex regional pain)	26 (27)
Gait disorder	11 (11)	Gastrointestinal symptoms (including irritable bowel syndrome)	24 (25)
Jerks and tics	10 (10)	Dizziness (including persistent postural perceptual dizziness)	21 (22)
Tremor	6 (6)	Sleep difficulties	20 (21)
Speech disorder	2 (2)	Dissociative symptoms†	19 (20)
Functional sensory symptoms	40 (41)	Fatigue and lethargy	13 (13)
Visual loss and disturbance	19 (20)	Nausea	7 (7)
Somatosensory symptoms	14 (14)	Poor memory or concentration (including brain fog)	7 (7)
Auditory disorder	7 (7)	Urinary symptoms	6 (6)
Functional seizures including drop attacks	20 (21)	Poor behaviour	4 (4)
Other**	4 (4)	Poor appetite	4 (4)
		Other‡	3 (3)
		Paranoia	2 (2)

Table 2: Potential predisposing and precipitating factors in 97 children with FND; 76 and 36 children reported potential predisposing and precipitating factors respectively; children could have more than one factor present

Potential predisposing factors	Children, n (%)	Potential precipitating factors	Children, n (%)
Self-reported psychiatric symptoms before diagnosis of FND (including formal diagnoses and reports of low mood or anxiety)	34 (35)	Infection/inflammation	13 (13)
Formal diagnosis of psychiatric condition	8 (8)	Physical trauma/injury	11 (11)
Self-reports of anxiety, low mood or suicidal ideation	26 (27)	Migraine	6 (6)
Identified pressure from academic or sporting achievement (including perfectionism)	33 (34)	Acute physical illness	5 (5)
Recognised chronic physical illness	27 (28)	Panic attack	1 (1)
Social stressors (including bullying)	20 (21)	Emotional argument	1 (1)
(bullying)	11 (11)	Swimming in cold water	1 (1)
Loss/(parental) separation/bereavement	17 (18)		
Family history of psychiatric comorbidity	8 (8)		
Family history of FND	8 (8)		
Neurodevelopmental conditions	8 (8)		
Abuse or neglect (requiring Social Services involvement)	3 (3)		
Family conflict/violence	2 (2)		
Other (intellectual disability and gender dysphoria)	2 (2)		

Table 3: Comparison of related studies; Dx diagnosis; ED Emergency Department; F female; FHx family history; FU follow-up; IP inpatient; IR incidence rate; M months; NA not available; PY person-years; SES socioeconomic status; UK United Kingdom; USA United States of America; Y years; \*incidence proportion not reported; †median/mean age not reported

First author (year)	This study	Stephen (2021)	Hansen (2020)	Raper (2019)	Samuels (2019)	Ani (2013)	Kozłowska (2007)
Setting and study design	UK regional (Edinburgh) children's hospital active surveillance	USA nation-wide retrospective	Danish population retrospective (seizures only)	UK regional (Newcastle) Paediatric Neurology service retrospective	USA children's hospital retrospective	UK & Ireland active surveillance	Australian active surveillance
Number of children	97 (64 incident cases; 75 with FU)	3800 (ED) 1264 (IP)	386	124 (114 with FU)	42	204 (147 with FU)	194
Incidence (n/100,000)	18.3 (<10Y 7.1; 10-15Y 38.0)	NA	IR* (n/100,000 PY) Total 2.4, 2014 7.4	6.0	NA	1.3 (<10Y 0.3; 10-15Y 3.0)	2.3-4.2 (<10Y 0.8)
Age	Median 13Y	ED median 15Y IP median 14Y	Median 16Y	Mode 16Y <sup>†</sup>	<13Y 43%, <10Y 12%	Median 13Y	Mean 12Y <10Y 23%
Sex	70% F	ED 72% F, IP 73% F	83% F	56% F	59% F	75% F	71% F
Socioeconomic	Similar to population	Similar to non-FND	NA	NA	NA	NA	NA
Symptoms	Multiple (71%) Motor (41%), sensory (41%), seizures (21%) Headache (31%), pain (27%), fatigue (13%)	NA	Seizures only	Multiple (10%) Seizures (41%), sensory (18%)	Multiple (46%) Seizures (62%), motor (36%), sensory (14%) Somatic (e.g., headache, pain; 48%)	Multiple (69%) Motor (63%), abnormal movements (43%), seizures (40%) Pain (55%), fatigue (34%)	Multiple (55%) Motor (64%), sensory (24%), seizures (23%) Pain (56%), fatigue (34%)
Predisposing factors present	78%	NA	54%	NA	95%	81%	62%
Two most common predisposing factors (%)	Self-reported psychiatric symptoms (35%), pressure from achievement (34%)	NA	School bullying, interpersonal conflict (% NA)	NA	Change in household composition (24%), academic difficulties (24%)	Bullying requiring school action (24%), parental separation (19%)	Separation/loss (34%), family conflict/violence (20%)
Precipitating factors present	37%	NA	14%	15%	31%	NA	NA
Two most common precipitating factors (%)	Infection/inflammation (13%), injury (11%)	NA	NA	Minor injury, syncope	Medical procedure, illness	NA	NA
Admission	24% admitted	25% admitted	NA	NA	NA	79% admitted	70% admitted
FU duration Outcome	Median 15M	No FU	No FU	Median 8.3Y Ongoing FND (23%)	No FU	12M Improve (75-100%)	No FU

	Worse/unchanged/new FND symptom (51%), ongoing FND (78%)				Good function despite symptoms (55%)		
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Figure 1: PRISMA study flow diagram for case series

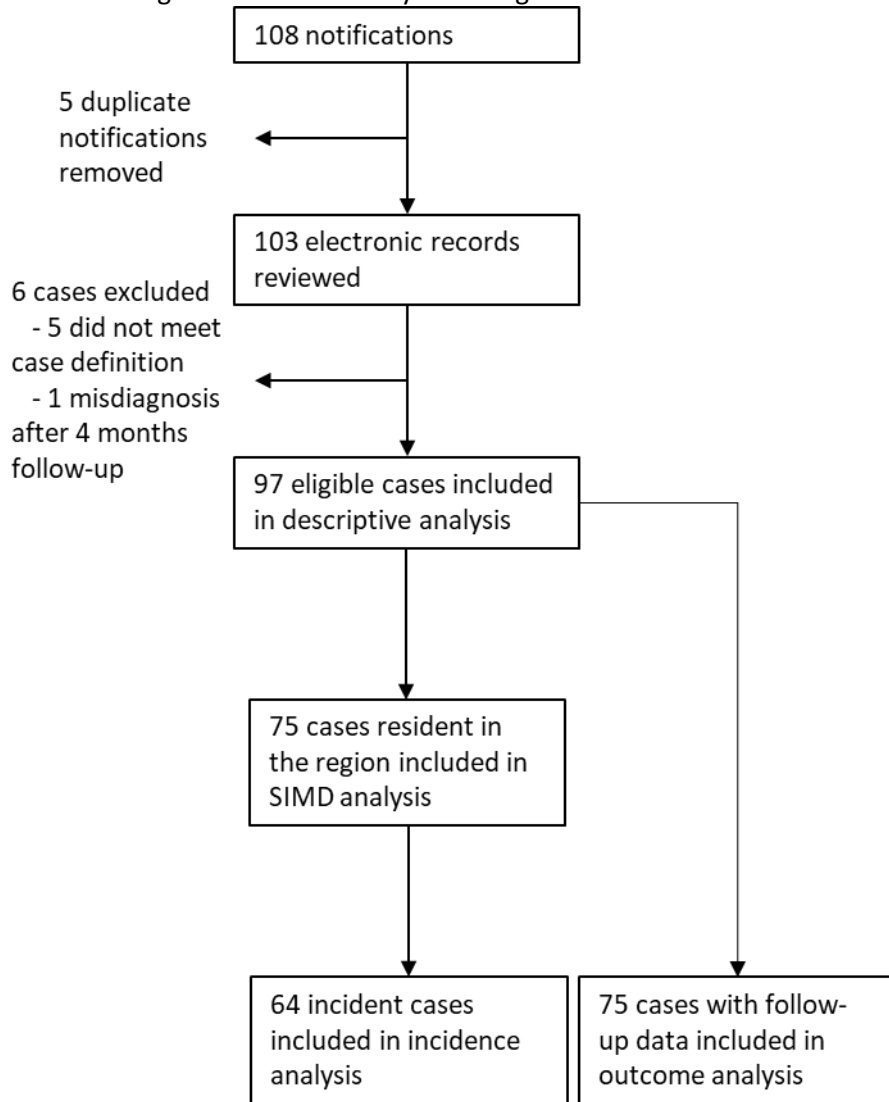


Figure 2: Sex distribution by age

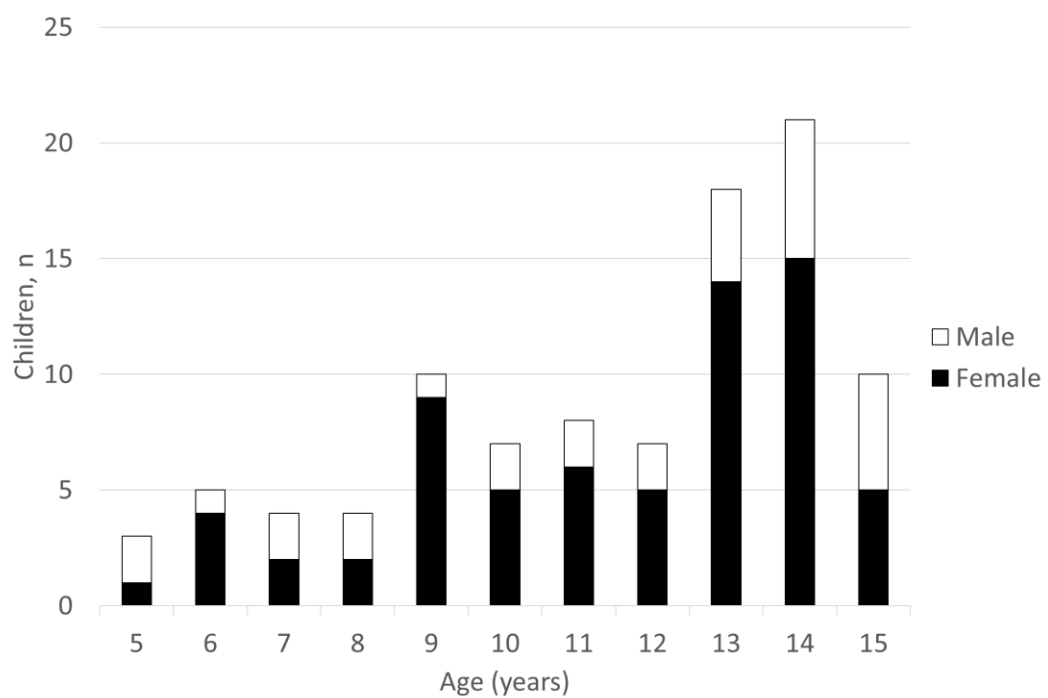


Figure 3: SIMD quintile distribution showing observed proportions in each deprivation category compared to expected numbers based on population<sup>[18]</sup>

