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FULL-LENGTH ORIGINAL RESEARCH

Incidence and prevalence of psychogenic nonepileptic seizures in a Norwegian county: A 10-year population-based study

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Abstract

Objective: This study was undertaken to measure the incidence and prevalence of active psychogenic nonepileptic seizures (PNES) in a Norwegian county.

Methods: Using the Norwegian patient registry, we identified patients in Møre and Romsdal County in Norway diagnosed with F44.5 (conversion disorder with seizures or convulsions) or R56.8 (convulsions, not elsewhere classified) in the period January 2010 to January 2020. A review of the patients' medical records and an assessment of diagnostic validity were performed. PNES were diagnosed according to the recommendations by the International League Against Epilepsy Nonepileptic Seizures Task Force. Point prevalence of PNES on January 1, 2020 and incidence rates for the period 2010–2019 were determined.

Results: Based on PNES within the past 5 years, we found a PNES prevalence of 23.8/100 000 (95% confidence interval [CI] = 17.9–29.6), including all levels of diagnostic certainty. For the highest level of diagnostic certainty (video-electroencephalographically confirmed), the prevalence was 10.6/100 000 (95% CI = 6.7–14.5). The highest prevalence was found in the age group 15–19 years, at 59.5/100 000 (95% CI = 22.6–96.3). The mean annual incidence rate between 2010 and 2019 was 3.1/100 000/year (95% CI = 2.4–3.7).

Significance: We report for the first time a population-based estimate of the prevalence of PNES. Our findings suggest that the prevalence of PNES is within the range of estimates from non-population-based data. We found a strikingly high prevalence of PNES in the 15–19-year age group.

KEYWORDS

adolescents, diagnostic coding, epidemiology, psychogenic nonepileptic seizures

1 | INTRODUCTION

Psychogenic nonepileptic seizures (PNES) are among the most common functional neurological disorders,[1] seen frequently in various clinical contexts. In epilepsy clinics, up to one third of patients are diagnosed with PNES.[2] PNES are categorized as a dissociative (conversion) disorder in International Classification of Diseases, 10th revision (ICD-10) or conversion (functional neurological symptom) disorder in Diagnostic and Statistical Manual of Mental Disorders, 5th edition.[3,4]

PNES may affect many aspects of life for patients and their families. Many patients are first misdiagnosed with epilepsy, exposing them to potentially harmful and unnecessary treatment.[5] Health care costs are high, mainly due to frequent emergency room visits, hospital admissions, including intensive care units, and repeated, extended investigations.[6] Diagnosing PNES can be difficult, and health care practitioners often report uncertainty regarding the diagnosis.[7] The combination of ictal recordings on video-electroencephalography (EEG) and a history indicative of PNES is considered the diagnostic gold standard.[8]

Epidemiological data on PNES are scarce.[9] Incidence rates of between 1.4 and 4.9/100 000/year have been reported from different adult populations.[10–12] A recent nationwide study in a Danish pediatric population showed an incidence of 2.4/100 000/year.[13]

PNES prevalence is difficult to determine and has not been directly measured. A long delay from onset to diagnosis and patients with PNES disengaging from medical follow-up are considerable obstacles for epidemiological studies.[9] Based on numbers of patients with PNES attending epilepsy centers, the prevalence has been estimated at 2–50/100 000.[9,14]

Epidemiological studies that provide good estimates of the occurrence of PNES are crucial for health care planning. We therefore investigated the incidence and prevalence of PNES during the past decade in a Norwegian county.

Key Points

- Epidemiologic data on PNES are scarce
- In this 10-year population-based study that included all age groups and a systematic case validation using definitions recommended by the ILAE Nonepileptic Seizures Task Force, we investigated incidence rates and prevalence of PNES
- Prevalence of PNES was 23.8/100 000 including all levels of diagnostic certainty
- This is the first population-based estimate of prevalence of PNES; the obtained prevalence was within estimates from the literature based on non-population-based data

2 | MATERIALS AND METHODS

2.1 | Data source

Participants were identified through the Norwegian Patient Registry (NPR). This is a mandatory administrative registry containing discharge diagnosis data from hospitals and outpatient clinics owned or reimbursed by the Norwegian government, which account for more than 99% of health services in Norway.[15] Diagnoses are coded by physicians according to ICD-10.[3]

Based on our clinical experience indicating a lack of consensus for a diagnostic code for PNES and the finding that many clinicians use the nonspecific code R56.8 "convulsions, not elsewhere classified" rather than F44.5 "conversion disorder with seizures or convulsions," we decided to include all patients registered with a primary diagnosis of ICD-10 code F44.5 or R56.8 in the period from January 1, 2010 to January 1, 2020 at the hospitals in the county of Møre and Romsdal, Norway. Other diagnostic codes that might apply for PNES (e.g., Z03.3 "observation for suspected nervous system disorder") are not commonly used and were therefore not included.

The Regional Committee for Medical Research Ethics, Norway, Regional Ethical Committee Central (ethical agreement 2018/24712) approved this study. This study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) reporting guideline.

2.2 | Design

This is a population-based, cross-sectional study of the incidence and prevalence of PNES in the county of Møre and Romsdal, Norway between January 1, 2010 and January 1, 2020.

2.3 | Study population

Norway has a well-developed public health care system that provides comprehensive health services to everyone. In primary health care, every inhabitant has an assigned general practitioner. Specialist health care is provided by hospital services run and owned by the state.

Møre and Romsdal is a county in the western part of Norway covering an area of 14 356 km². At the end of the study, on January 1, 2020, Møre and Romsdal had a population of 265 238 (135 213 men, 130 025 women), which is a 5.6% increase on the population at the beginning of the

study, and constitutes approximately 4.9% of the Norwegian population. Immigrants born outside of Norway, primarily from Central Europe, constituted 11.7% of the population of the county. The prevailing immigrant nationalities were from Poland, Lithuania, and Germany. Non-European immigrants mainly from Syria, Eritrea, and Thailand accounted for 4.4% of the total population. Regarding age, 2.6% of the population in Møre and Romsdal was younger than 20 years, 56.7% was between 20 and 64 years, and 19.7% was 65 years or older. According to Statistics Norway, demographic data in Møre and Romsdal, such as socioeconomic status, degree of urbanization, age distribution, and access to health care, are similar to those in Norway as a whole.[16]

Inpatient and outpatient neurological services are centered in two hospitals, each with an EEG department. Pediatric services are located in three hospitals. No private neurologists or pediatricians practice in the county.

Norwegian guidelines specify that all patients suspected of having seizures or epilepsy are referred to a neurologist or pediatrician for clinical evaluation and EEG.[17] These patients are therefore seen at one of the hospitals in the county and registered in the NPR. Norway has one tertiary center for epilepsy care, the National Center for Epilepsy at Oslo University Hospital, which is a referral resource for difficult cases.

2.4 | Medical record data

For each case identified by diagnostic code (F44.5/R56.8) in the NPR, the medical history, seizure assessment, EEG, magnetic resonance imaging, blood samples, treatment, and other relevant information were reviewed. A minimum dataset, including demographic and clinical information, was recorded in a database.

Cases were validated and classified by the first author (A.V.). A random subsample of 124 participants (10% of the study sample) was rated independently by the last author (M.I.L.). Both are senior consultants in neurology and epileptologists at the National Center for Epilepsy. In instances of nonconsensus, the medical records were reviewed again, cases were discussed, and consensus was reached.

PNES was defined as the occurrence of events clinically resembling epileptic seizures, but not caused by ictal epileptiform activity, and having psychological basis and causes.[9] Cases were validated using the approach to diagnosing PNES proposed by the International League Against Epilepsy (ILAE) in 2013.[8] Based on history, witnessed events, and EEG findings, the ILAE defined four diagnostic levels of certainty for PNES, namely: (1) possible, (2) probable, (3) clinically established, and (4) documented (Table 1).

Time of onset was defined as the year of onset of symptoms suggestive of PNES. We defined comorbid epilepsy as confirmed when there was a history of at least two unprovoked seizures consistent with epileptic seizures and at least one EEG showed epileptiform activity. Comorbid epilepsy was considered as probable when one of the above criteria (epileptiform activity, clinical information) were indicative for epilepsy. Psychiatric comorbidity was registered as mentioned in the medical record (e.g., depressive symptoms, anxiety, posttraumatic stress disorder [PTSD]).

People living in Møre and Romsdal County on January 1, 2020, fulfilling the ILAE criteria mentioned above, and having had at least one documented PNES during the past 5 years were defined as prevalent cases. Figures based on PNES within the past 2 years are also presented. The prevalence rate was calculated as the total number of cases per 100 000 inhabitants using ascertained cases as the numerator and the 2020 census on January 1, 2020 (265 238) as the denominator.

Cases were considered incident if the PNES diagnosis had been made between January 1, 2010 and December 31, 2019. Annual incidence rates were estimated using the population on January 1 of each year as the denominator and the number of subjects diagnosed with PNES during that year as a numerator.

TABLE 1 Diagnostic levels of certainty for the diagnosis of psychogenic nonepileptic seizures

Diagnostic level	History	Witnessed event	EEG
Possible	Consistent with PNES	By witness of self-report	No epileptiform activity in interictal EEG
Probable	Consistent with PNES	By clinician in person or reviewed video recording	No epileptiform activity in interictal EEG
Clinically established	Consistent with PNES	By clinician experienced in seizure disorders (in person or on video)	No epileptiform activity in routine or ambulatory ictal EEG during a typical event
Documented	Consistent with PNES	By clinician experienced in seizure disorders (in person or on video) while on video-EEG	No epileptiform activity immediately before, during, or after a typical event captured on ictal video-EEG

Note: Adapted from LaFrance et al.[8]

Abbreviations: EEG, electroencephalography; PNES, psychogenic nonepileptic seizures.

2.5 | Statistical analysis

Continuous variables were summarized by the median and range, categorical variables by frequencies and percentages. For comparing differences between age groups (children/adolescents ≤19 years old vs. adults ≥20 years old) the chi-squared test was used for categorical variables and the Mann–Whitney test for continuous variables. Fisher exact test was calculated in the event of less than five expected cases per cell.

3 | RESULTS

In total, 1241 potential PNES cases were identified (Figure 1). Twenty-five patients had an ICD-10 diagnosis of F44.5 and 1216 patients of R56.8 in the NPR. After case validation, 101 patients were rated PNES cases, 21 registered with F44.5 and 80 with R56.8. Among the non-PNES cases, 216 had epilepsy and 924 had other paroxysmal events such as acute symptomatic seizures, febrile seizures, and unspecific paroxysmal symptoms. The interrater reliability test showed an almost perfect agreement[18] between the two raters; Cohen kappa was .88. The positive predictive value of the more specific ICD diagnosis F44.5 was 83.3%, and it was 6.6% for the unspecific diagnosis of R56.8. Sensitivity for the diagnostic codes of F44.5 and R56.8 were 20.8% and 79.2%, respectively.

3.1 | Prevalence

Including all patients with PNES during the previous 5 years, we found 63 cases prevalent on January 1, 2020, resulting in a point prevalence for PNES of 23.8/100 000 (95% confidence interval [CI] = 17.9–29.6). Of these, 44% (n = 28) had documented PNES or clinically established PNES, 30% (n = 19) had probable PNES, and 22% (n = 14) had possible PNES. Including only cases with the highest level of diagnostic certainty (documented PNES), the prevalence was 10.6/100 000 (95% CI = 6.7–14.5). The highest prevalence was found in the age group 15–19 years, with 59.5/100 000 persons (95% CI = 22.6–96.3). The sex ratio was 3.2:1, with a female prevalence of 36.9/100 000 (95% CI = 26.5–47.4) and a male prevalence of 11.1/100 000 (95% CI = 5.5–16.7).

When considering patients with PNES during the previous 2 years, 30 cases with PNES within 2 years were recognized as prevalent on January 1, 2020, resulting in a point prevalence for PNES of 11.3/100 000 (95% CI = 7.3–15.4). Of these, 37% (n = 11) had documented PNES, 7% (n = 2) had clinically established PNES, 37% (n = 11) had probable PNES, and 20% (n = 6) had possible PNES. Including only the highest level of certainty of diagnosis with documented cases of PNES, the prevalence was 4.1/100 000 (95% CI = 1.7–6.6). The highest prevalence was found in the age group 15–19 years, with 23.8/100 000 (95% CI = 0–256.8). The sex ratio was 3.3:1, with a female prevalence of 17.7/100 000 (95% CI = 10.5–24.9) and a male prevalence of 5.2/100 000 (95% CI = 1.3–9.0).

3.2 | Incidence rates

During the study period, 79 cases of PNES were diagnosed. The mean annual incidence rate between 2010 and 2019 was 3.1/100 000/year (95% CI = 2.4–3.7). There was no clear trend in the annual incident rates over the study period. The incidence rate was highest in 2010, with 4.4/100 000/year, and lowest in 2011, with 1.2/100 000/year. The mean annual incidence rate was 4.7/100 000/year (95% CI = 1.0–8.6) for females and 1.4/100 000/year (95% CI = 0–4.3) for males. This gives a female:male ratio of 3.3:1. For age-specific incidence, the rate peaked at 15–19 years, at 9.81/100 000/year (95% CI = 0–24.7). Among the 79 incident PNES cases, 41% (n = 32) had documented PNES, 3% (n = 2) had clinically established PNES, 30% (n = 24) had probable PNES, and 27% (n = 21) had possible PNES.

Prevalence rates and mean annual incidence rates by age groups are shown in Table 2.

3.3 | Clinical characteristics

The median age at diagnosis of PNES was 27 years, and the modal age was 15 years. Most (77%) of the patients were female. Clinical characteristics for the study population are shown in Table 3.

Although the mean diagnostic delay was 3.2 years, for 49% of the cases (n = 41) the diagnosis was made in the same year as the onset of seizures.

Considering patients with documented PNES, 31% (n = 11) were diagnosed with the classification F44.5.

Children and adolescents were more often diagnosed with F44.5 “dissociative seizures” than adults (54% vs. 19%, p = .01), and the diagnostic delay was significantly shorter for children and adolescents (1.3 vs. 4.2 years, p = .03) than for adults aged 20 years or older.

4 | DISCUSSION

We are not aware of any previous measurement of the prevalence of PNES, and previous estimates did not specify a definition of "prevalent."[9,14] Our study was designed to provide a population-based estimate using hospital coding. This implies that part of our definition of having PNES required

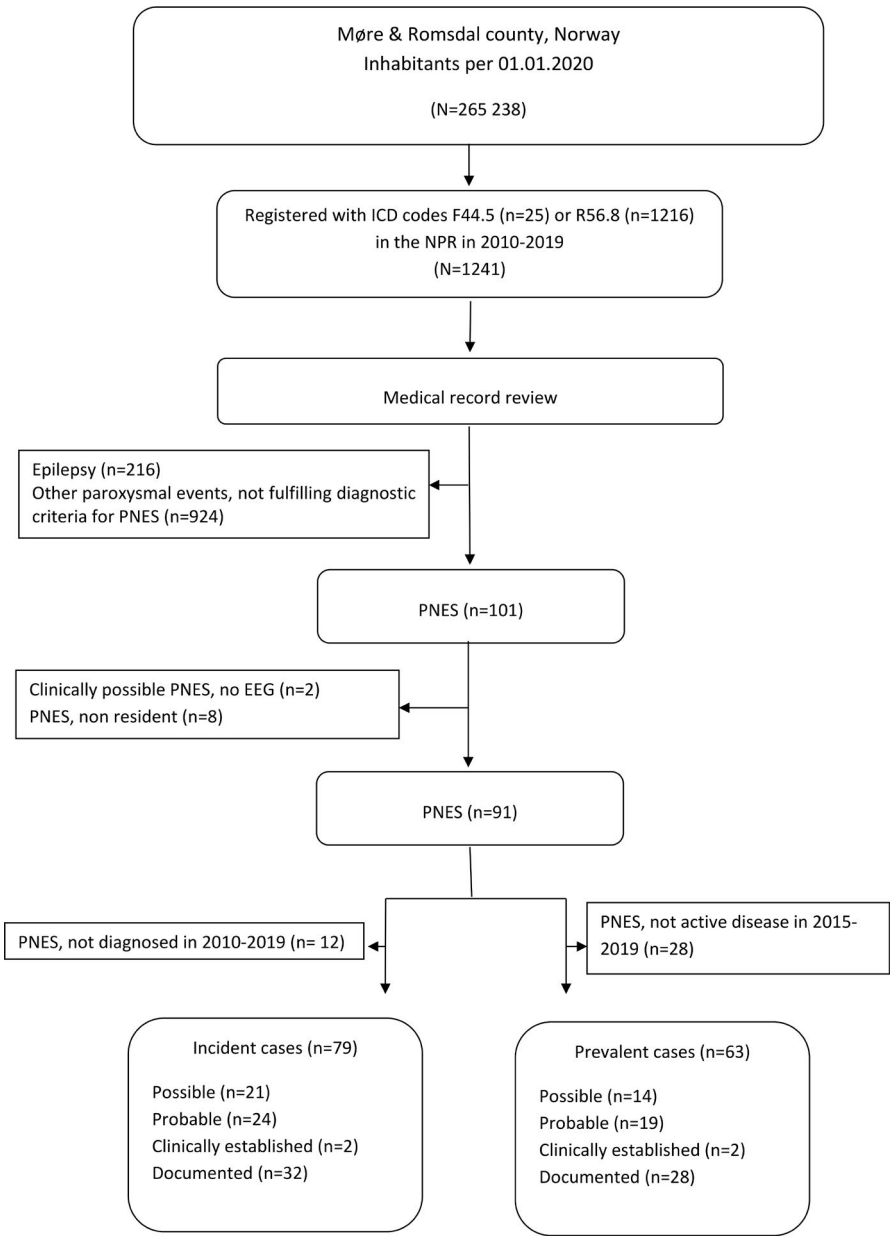

FIGURE 1 Flowchart study participants. EEG, electroencephalogram; ICD, International Classification of Diseases; NPR, Norwegian Patient Registry; PNES, psychogenic nonepileptic seizures

TABLE 2 Mean annual incidence and prevalence of PNES by age groups

	Mean annual incidence		Prevalence, PNES within past 2 years		Prevalence, PNES within past 5 years	
Age groups	*n* (range)	Per 100 000 person-years	*n*	Per 100 000	*n*	Per 100 000
5–14 years	1.0 (0–2)	3.1	1	3.1	1	3.1
15–19 years	1.7 (0–5)	9.8	4	23.8	10	59.5
20+ years	5.3 (2–8)	2.7	25	12.3	52	25.6
All	7.9 (3–11)	3.1	30	11.3	63	23.8

Abbreviation: PNES, psychogenic nonepileptic seizures.

the patient presenting to health care with indicative symptoms. Previous investigations suggest that many patients with PNES cease to access medical care at some point after diagnosis.[19] We chose to report prevalence based on 2-year and 5-year timeframes, in keeping with ILAE recommendations for epilepsy.[20] Our overall 5-year prevalence figure, at

TABLE 3 Clinical and demographic data for the PNES cohort (incident and prevalent cases) in Møre and Romsdal County, Norway

Clinical values	PNES cohort, incident and prevalent cases ($N = 84$)
Female sex, *n* (%)	65 (77)
Age at diagnosis, years, median (range)	27 (11–78)
ICD-10 code, *n* (%)	
F44.5	20 (24)
R56.8	64 (76)
Diagnosis at type of hospital/department, *n* (%)	
Pediatric department	12 (14)
Neurologic department	49 (58)
National epilepsy center	23 (27)
Diagnostic delay, years, mean (range)	3.2 (0–24)
Diagnostic certainty, *n* (%)	
Possible	22 (26)
Probable	25 (30)
Clinically established	2 (2)
Documented	35 (42)
Comorbid epilepsy, *n* (%)[a]	
Confirmed	6 (7)
Probable	5 (6)
Psychiatric comorbidity, *n* (%)[b]	52 (62)

Abbreviations: ICD, International Classification of Diseases; PNES, psychogenic nonepileptic seizures.

[a]Comorbid epilepsy is defined as confirmed when there was a history of at least two unprovoked seizures consistent with epileptic seizures and at least one electroencephalogram showed epileptiform activity. Comorbid epilepsy was considered to be probable when one of the above were indicative for epilepsy.

[b]Psychiatric comorbidity as mentioned in the medical record (e.g., depressive symptoms, anxiety, posttraumatic stress disorder).

23.8/100 000, was around midrange of previous estimates,[9,14] and the 2-year figure (11.3/100 000) was substantially lower. As up to two thirds of patients may experience PNES many years after diagnosis, but do not present to health care with them,[21] our 5-year prevalence figure might be more accurate, but is still most likely an underestimate of the actual PNES prevalence.

Even when a diagnosis of epilepsy is made by a clinician with appropriate expertise, there will inevitably be some cases in which a diagnosis of PNES is missed. Unfortunately, we were unable in the context of the present study to review cases coded as epilepsy. However, other epidemiological studies of PNES have had similar circumstances and did not address diagnostic standards for epilepsy in their base populations.[11,12] The present study has the advantage that our base population has a defined referral pathway for patients with possible epilepsy and has good access to neurological services. The diagnoses of epilepsy were made by clinicians who themselves had unrestricted access to a full range of EEG and imaging investigations. We might have missed further patients with PNES primarily diagnosed by psychiatrists, for example patients with PTSD and dissociative episodes, who were not referred to a neurologist. The question of consistency of use of ICD codes is likely to be an issue in many countries, and was beyond the scope of the present study. Due to a lack of consensus regarding use of diagnostic codes for PNES, some cases might be registered under other diagnostic codes, such as Z03.3 "observation for suspected nervous system disorder" or R55 "syncope and collapse," which were not included in our study. Some incident patients with mild or few seizures might have remained in primary care. The number of such cases is difficult to estimate.

Our study found a mean annual incidence rate between 2010 and 2019 of 3.1/100 000/year, with no consistent pattern of change in the annual incidence rates over the study period. A nationwide Icelandic study that included subjects aged 15 years and older reported a much lower incidence rate of 1.4 per 100 000/year.[11] However, this estimate was based on only 14 incident cases, of whom seven had comorbid epilepsy. A US study including adults[12] and a Scottish study that included cases aged 13 years and older[10] reported PNES incidence rates of 3.0 and 4.9/100 000/year, respectively, which is in approximate agreement with our incidence figure. However, these studies included only video-EEG-confirmed cases, and the Scottish study excluded cases with comorbid epilepsy.[10] Our comparable incidence data

(video-EEG-confirmed cases) was only 1.26/100 000/year. Inclusion of only video-EEG-confirmed cases is likely to underestimate incidence, and therefore, there seems to be a true difference between the Scottish and US populations and ours, although differing diagnostic practices might also contribute.

A Danish study, including children and adolescents 5–17 years of age, reported a lower incidence rate than we found, at 2.4/100 000/year.[13] The inclusion criteria in the Danish study were similar to ours, using a staged approach with different levels of diagnostic certainty. However, the EEG criteria were modified, and EEG information was missing or not performed in 13% of the cases. In the Danish study, the highest incidence rate was found among 16-year-old patients, with a 3.3-fold higher incidence rate at 7.9/100 000/year, which is consistent with our findings.[13]

We found a particularly high prevalence (59.5/100 000/year) and incidence (9.8/100 000/year) in the 15–19 years age group in our study. Our findings should increase the awareness of PNES in adolescents and young adults.

In our cohort, the mean delay was 3.2 years from the first PNES to a confirmed diagnosis. This is consistent with previous findings; the mean diagnostic delay was 1.7 years in the Scottish study and 6.8 years in the US study.[10,12] In a review study, the mean diagnostic delay varied between .6 and 11.18 years,[22] but none of the reviewed reports included children younger than 13 years. We found that the diagnostic delay among children and adolescents was significantly shorter than among adults (1.3 years vs. 4.2 years).

Among our patients, 13% (11 of 84) had either confirmed or probable comorbid epilepsy. Previous studies on the incidence of PNES have found 14.2%–50% with comorbid epilepsy.[11–13] A meta-analysis reported the frequency of epilepsy in patients with PNES to be 22%.[23] The authors discussed that the high frequency of dual diagnoses could reflect that patient recruitment is from specialized epilepsy centers in most studies. The relatively low proportion of comorbid epilepsy among PNES cases in our study is probably due to the population-based inclusion approach, but might to some degree also reflect missing cases with epilepsy and undiagnosed PNES.

The prevalence of psychiatric comorbidity in PNES has been reported to range between 53% and 100%.[24] In our study, 62% of included patients had a psychiatric condition noted in their medical record. This is likely to be an underestimate, as pediatricians and neurologists might not always explore psychiatric issues thoroughly in a busy clinical routine. We did not have access to psychiatric records.

In our cohort, only 24% of the patients had "dissociative seizures" (F44.5) registered as a diagnosis, and more than 75% had a nonspecific diagnosis. Even among those with a video-EEG-confirmed diagnosis, the proportion of those registered with a diagnosis of "dissociative seizures" was only slightly higher, as low as 32%. Surveys among health care professionals have indicated that only a minority use the ICD-10 code F44.5 when diagnosing PNES.[25,26] Our findings are consistent with the known lack of consensus on coding and terminology for PNES. This may hamper clear communication with patients and presents an obstacle for epidemiologic studies. Because there is no substantial change in the upcoming 11th revision of the ICD-11 regarding dissociative neurological symptom disorders,[27] the challenge of finding a more widely accepted term remains.

The main strength of our study was the population-based design, including all age groups, and the systematic case validation using recommended definitions. This approach enabled us to estimate incidence and prevalence values based on ILAE-defined levels of certainty.

However, as discussed above, our method would not identify all PNES cases, and our findings are therefore likely an underestimate. Although inclusion of patients with lower levels of diagnostic certainty provides a more nuanced and complete picture of incidence and prevalence, some inaccurate diagnoses may have been included.

5 | CONCLUSIONS

Our population-based estimate of the prevalence of PNES was within the range of estimates based on non-population-based data available in the literature. We found a strikingly high incidence and prevalence of PNES in adolescents, suggesting the need for further study of this challenging patient group. The current term for PNES in ICD-10, "dissociative seizures," seems to be poorly accepted among clinicians. There is an urgent need for international consensus on a more widely acceptable term. In addition, further work is needed to provide a better understanding of the epidemiology of PNES and to evaluate possible regional differences.

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CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

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