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RESEARCH ARTICLE

Association between social deprivation and incidence of first seizures and epilepsy: A prospective population-based cohort

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Abstract

Objective: Epidemiologic studies have investigated whether social deprivation is associated with a higher incidence of epilepsy, and results are conflicting, especially in children. The mechanisms underlying a potential association are unclear. This study examines whether there is an association between social deprivation and the incidence of first seizures (unprovoked and provoked) and new diagnosis of epilepsy by comparing incidence across an area-level measure of deprivation in a population-based cohort.

Methods: Multiple methods of case identification followed by individual case validation and classification were carried out in a defined geographical area (population 542 868) to identify all incident cases of first provoked and first unprovoked seizures and new diagnosis of epilepsy presenting during the calendar year 2017. An area-level relative deprivation index, based on 10 indicators from census data, was assigned to each patient according to registered address and categorized into quintiles from most to least deprived.

Results: The annual incidence of first unprovoked seizures ($n = 372$), first provoked seizures ($n = 189$), and new diagnosis of epilepsy ($n = 336$) was highest in the most deprived areas compared to the least deprived areas (incidence ratios of 1.79 [95% confidence interval (CI) = 1.26–2.52], 1.55 [95% CI = 1.04–2.32], and 1.83 [95% CI = 1.28–2.62], respectively). This finding was evident in both adults and children and in those with structural and unknown etiologies of epilepsy.

Significance: The incidence of first seizures and new diagnosis of epilepsy is associated with more social deprivation. The reason for this higher incidence is likely multifactorial.

KEYWORDS

epilepsy, incidence, seizures, social deprivation

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1 | INTRODUCTION

Some studies have shown a correlation between social deprivation and prevalence of epilepsy.[1–3] A higher prevalence of epilepsy among residents living in socially deprived areas may be due to "social drift," whereby factors associated with a diagnosis of epilepsy, for example, decreased employability, lead to a downward drift of the socioeconomic status of an individual.[4] An alternative explanation is "social causation," whereby factors associated with living in an area of social deprivation put an individual at increased risk of developing epilepsy.

A strong correlation between the incidence of epilepsy and social deprivation has been reported in Wales[4] and England.[5] Using census-based measures of social deprivation, these studies reported at least twice the annual incidence of epilepsy in the most deprived geographically defined areas compared to the least deprived areas. Furthermore, a community-based study in New York reported a higher incidence of unprovoked seizures in low-income compared to high-income households.[6] In contrast, a 1990 case-referent study from Sweden investigating the incidence of unprovoked seizures in adults found no difference in individual markers of sociodemographic status between cases and controls.[7]

Results from studies investigating the incidence of epilepsy in children in socially deprived areas have also been conflicting. Using an area-level measure of deprivation, a study in England found no difference in the incidence of epilepsy across four quartiles of social deprivation in children aged 29 days to 14 years.[8] In contrast, a Swedish study reported 1.15 times increased odds of registration for childhood and adolescent epilepsy in those living in high-deprivation neighborhoods compared to low-deprivation neighborhoods.[9] Finally, a case–control study from Iceland[10] found that low socioeconomic status, measured by low individual-level educational attainment or lack of home ownership, increased the risk of incident epilepsy in adults. However, no markers of socioeconomic status were associated with incident epilepsy in children.

To investigate further the magnitude and direction of the association with socioeconomic status, we sought to determine whether the incidence of provoked and unprovoked first seizures and of new diagnosis of epilepsy differed between areas of relatively high social deprivation compared to areas of relatively low social deprivation in our well-defined whole population cohort of children and adults.[11] Furthermore, we sought to investigate whether certain etiologic categories of epilepsy are associated with social deprivation.

Key Points

- Children and adults in the most socially deprived communities have an excess burden of seizure disorders
- Social causation, rather than social drift, may be the primary mechanism for increased prevalence in areas of relative social deprivation
- The etiology of this association is likely multifactorial

2 | MATERIALS AND METHODS

This study was carried out in the geographically defined area of Cork city and county, Ireland (estimated population 542 868 adults and children,[12] geographic area approximately 7500 km^2). The area contains one large urban development encompassing approximately one quarter of the total population (125 657 persons). The remaining population lives in smaller towns, villages, or rural dwellings. The Irish health care system consists of both public and private hospitals. Patients with seizures either self-present to the emergency department or are referred to the emergency department or neurology outpatient department by their general practitioner.

2.1 | Case ascertainment

A detailed description of the protocol applied to capture the case population has been previously published.[13] In brief, multiple overlapping prospective and retrospective sources of case ascertainment were applied to the geographically defined area to capture all potential first seizures and new diagnosis of epilepsy during the calendar year 2017. Briefly, prospective capture methods included daily review of emergency department triage and radiology ordering databases, and liaison with inpatient medical teams and clinical nurse specialists in departments with a high likelihood of encountering seizures and epilepsy (specifically, neurology, neurosurgery, oncology, geriatrics, and pediatrics). Retrospective methods included review of electroencephalographic (EEG) databases, review of case presentations at the single Rapid Access Seizure Clinic within the catchment area, liaison with hospital consultants in the aforementioned inpatient and outpatient specialties, and postal survey of primary care and residential and nursing home settings within the catchment area. Review of case records extended to March 31, 2018 to capture and complete the classification of patients who first presented in 2017. By restricting our count to

first presentation during 2017, we avoid over- or under-ascertainment in the 2017 calendar year, and the number classified will estimate the true incidence of each clinical subcategory.

2.2 | Inclusion criteria and case classification

Epileptic seizures were defined as a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.[15] Epilepsy was defined according to the International League Against Epilepsy (ILAE) operational definition[16]: (1) at least two unprovoked seizures occurring >24 h apart, (2) one unprovoked seizure and probability of further seizures of approximately 60% or greater over the next 10 years, or (3) diagnosis of an epilepsy syndrome. A person with a single unprovoked seizure was estimated to have an approximately 60% or greater risk of recurrence if one or more of the following risk factors were identified: persons with a structural or remote symptomatic etiology and/or epileptiform abnormality on EEG,[17–19] and adults with a significant structural brain imaging abnormality,[18,20,21] neurodegenerative dementia,[22] or extensive small vessel disease with juxtacortical lesions.[23] Patients with mild-to-moderate small vessel disease without juxtacortical involvement, other nonspecific findings, or normal investigations were classified as having single unprovoked seizures. Individuals who had a first seizure prior to 2017 (and were not diagnosed with epilepsy at that time) and then a second seizure in 2017 were included as "new diagnosis of epilepsy." Individuals who had a single seizure in 2017 and did not have a 60% or greater risk of recurrence, or who had a recurrence after 2017, were included as "first seizure" only.[11,13]

First seizures meeting the ILAE criteria for provoked seizures[24] were identified as a specific subcohort, and were separated from first unprovoked seizures and epilepsy during analysis. In accordance with the ILAE epidemiologic guidelines,[14] neonatal seizures and febrile seizures were excluded.

Review of documented medical history, EEG findings, and imaging was conducted by the study team (D.J.C. and E.M.M.) for patients with an address in the geographical area. In accordance with the ILAE epidemiologic guidelines,[14] the probability that an event was a seizure was defined as definite, probable, or possible, based on the evidence available; see previously published methodology[13] for detailed discussion. Only those meeting criteria for a definite or probable case were included in further analysis of seizures and epilepsy.

Patients with inadequate or unclear documentation were classified as indeterminate and were not included in further analysis.

2.3 | Epilepsy risk factors and etiology

Based on review of the medical notes, the presence or absence of risk factors associated with seizures was noted. Specifically, a history of febrile seizures, central nervous system infection (meningitis or encephalitis), developmental delay, cerebrovascular disease (hemorrhagic, ischemic, large vessel, or small vessel), head injury (history of loss of consciousness following head injury or requiring inpatient observation or neurosurgical intervention), illicit drug use, alcohol abuse (>14 units per week), or psychiatric disease or family history of epilepsy (first degree relative with seizures or epilepsy) was noted. As this was based on retrospective chart review, the presence of such risk factors was often undocumented, and in these cases was coded as "unknown."

For all definite and probable cases of epilepsy, the etiology was classified according to the 2017 ILAE classification[25] system as structural, genetic, immune, infectious, metabolic, or unknown.

2.4 | Measure of socioeconomic status

Electoral divisions are legally defined administrative areas in Ireland. There are 398 electoral divisions within the geographic area studied. The 2016 Pobal HP Deprivation Index[26] uses data from the 2016 Census of Population[12] to calculate a Relative Deprivation Index (RDI) for each electoral division. The RDI is calculated by a factor analytical approach combining 10 indicators: percentage change in population over the previous 5 years, percentage change in population <15 or >64 years of age, percentage of population with primary school education only, percentage of population with third-level education, percentage of single parent households, mean number of persons per room, percentage of households headed by professionals, percentage of households headed by semiskilled or unskilled manual workers, and male and female unemployment rates. For each census year, the RDI in Ireland has a mean Deprivation Index of zero and an SD of 10. A higher RDI represents relatively less deprivation.

Each electoral division within the defined geographic area was ranked according to its RDI from most deprived to least deprived and categorized as quintiles. Quintile 1 refers to the relatively most deprived one fifth of the whole

population and Quintile 5 to the relatively least deprived one fifth.

Each case included in the study was assigned an electoral division based on their registered address, and thereafter to the corresponding quintile of RDI. Subjects whose registered address was in a nursing home or residential care setting ($n = 18$, 2% of included cases), convent ($n = 5$, <1%), or prison ($n = 2$, <1%) or who were homeless ($n = 5$, <1%) were not assigned an electoral division and were not included in the sociodemographic analysis.

2.5 | Statistical analysis

Annual incidence of first unprovoked seizures, first provoked seizures, and new diagnosis of epilepsy in each quintile was calculated by dividing the number of people with a new diagnosis during the calendar year 2017 by the number of people living in the geographical area in that quintile and expressing it per 100 000 population. Ideally, people who already had a diagnosis of seizure or epilepsy prior to 2017 would be subtracted from the population of the geographic area when calculating incidence. However, the exact prevalence of seizures and epilepsy in the geographic area is unknown. Previous studies suggest that 10 per 1000 population of Ireland already have a diagnosis[27]; therefore, incidence and incidence ratios (IRs) are only slightly attenuated when prevalent cases are not removed from the denominator. IR and 95% confidence interval (CI) were used to compare incidence in the least deprived to the most deprived quintiles. IRs were deemed to be statistically significant for $p < .05$. Logistic regression of median RDI in each quintile was performed to assess trend across quintiles. Mantel–Haenszel method was used to adjust IRs for sex and age group (28 days to 14 years, 15–64 years, ≥65 years). Statistics were performed using SPSS version 26 for Mac.

To determine whether an association between incidence and socioeconomic status was present in children and/or adults, annual incidence and IRs were calculated for the population 28 days to 14 years and for those ≥15 years of age. We did not compare children to adults with provoked seizures, as there were only 10 childhood cases. To further investigate the influence of age, we compared IRs in those 15–64 years to those ≥65 years of age.

IRs of those with a new diagnosis of epilepsy with a structural, genetic, or unknown etiology were investigated between quintiles. Finally, we investigated whether there was a difference in the occurrence of specific risk factors for epilepsy between the five quintiles, where data were available.

2.6 | Standard protocol approvals

The study protocol was approved by the University College Cork Clinical Ethics Research Committee. Following ascertainment, the data were anonymized prior to analysis and storage.

2.7 | Role of the funding source

This study received no specific funding from any government, institution, or industry.

3 | RESULTS

We identified 1264 potential cases with first presentation in 2017 for inclusion. Crude annual incidence of all definite and probable cases of first unprovoked seizures ($n = 372$, 69 per 100 000), first provoked seizure ($n = 189$, 35 per 100 00), and new diagnosis of epilepsy ($n = 336$, 62 per 100 000) demonstrated a bimodal age-specific incidence. The male to female incidence ratio was 1.38 (95% CI = 1.13–1.70), 1.95 (95% CI = 1.44–2.63), and 1.34 (95% CI = 1.08–1.67), respectively.[11]

3.1 | Sociodemographic analysis

Table 1 shows the mean RDI for the geographic region overall (3.6) and for individuals with first unprovoked seizures (1.8), first provoked seizures (3.4), and new diagnosis of epilepsy (1.3).

Incidence was higher for each diagnostic category in the most deprived quintile compared to the least deprived quintile, ranging from 55% to 83% (see Table 2 and Figure 1). Adjustment for sex and age group attenuated results in the diagnostic categories of provoked seizures. Analysis of trend demonstrated that a one-unit increase in RDI is associated with an approximate 4% increase in first unprovoked seizures (95% CI = 2%–6%) and new diagnosis of epilepsy (95% CI = 2%–6%).

When age was dichotomized to separate children (aged 28 days to 14 years) from adults (aged ≥15 years), incidence remained highest in the most deprived compared to the least deprived quintile in adults and was almost twofold higher in children with first unprovoked seizures and new diagnosis of epilepsy (see Table 3).

When adults were divided into those aged 15–64 years and those aged ≥65 years, a higher incidence of first unprovoked and provoked seizures, and of new diagnosis of epilepsy, was present in the most deprived compared to the least deprived quintile for ages 15–64 years, but not in those aged ≥65 years (see Table S1).

TABLE 1 Study population characteristics and median Pobal 2016 HP RDI of cases of first unprovoked seizure, first provoked seizure, and new diagnosis of epilepsy occurring in Cork city and county during the calendar year 2017

Characteristic	Cork city and county		First unprovoked seizure	First provoked seizure	New diagnosis of epilepsy
Total persons	542 868		372	189	336
Mean age, (5th and 95th centiles)	37.6		45.9 (2.2, 86.8)	52.6 (9.5, 85.6)	46.4 (2.9, 86.8)
% male (*n*)	49.5 (268 675)		57.5 (214)	65.6 (124)	56.8 (191)
Median RDI (5th, 95th centiles)	3.6 (−11.2, 12.1)		1.8 (−13.3, 9.8)	3.4 (−15.9, 12.1)	1.3 (−15.6, 9.6)
Quintile 1 [most deprived]	*n*	108 753	90	61	85
	% male (*n*)	49.4 (53 726)	67.8 (61)	60.7 (39)	68.2 (58)
	Mean age, years (5th and 95th centiles)		43.7 (2.5, 86.8)	53.4 (20.2, 85.2)	43.9 (2.4, 87.4)
	Median RDI (5th, 95th centiles)	−5.6 (−18.1, −2.6)	−6.3 (−20.0, −2.5)	−8.0 (−19.8, −2.5)	−8.0 (−20.0, −2.6)
Quintile 2	*n*	108 396	91	23	87
	% male (*n*)	49.5 (53 682)	48.4 (44)	60.9 (14)	48.3 (42)
	Mean age, years (5th and 95th centiles)		50.5 (3.0, 85.9)	57 (18.7, 100.2)	50.5 (4.2, 85.2)
	Median RDI (5th, 95th centiles)	−.1 (−2.2, 1.7)	−.3 (−2.2, 1.6)	.7 (−2.0, 1.8)	−.3 (−2.2, 1.6)
Quintile 3	*n*	108 604	62	31	48
	% male (*n*)	49.8 (54 117)	61.3 (38)	80.6 (25)	56.3 (27)
	Mean age, years (5th and 95th centiles)		42.7 (.7, 89.0)	53.9 (1.3, 83.0)	44.9 (.8, 89.5)
	Median RDI (5th, 95th centiles)	3.7 (2.3, 4.9)	3.7 (2.8, 5.1)	3.6 (2.4, 5.0)	3.7 (2.1, 5.1)
Quintile 4	*n*	109 171	65	26	60
	% male (*n*)	49.3 (53 786)	53.8 (35)	69.2 (18)	53.5 (32)
	Mean age, years (5th and 95th centiles)		41.5 (1.1, 90.5)	53.5 (9.4, 80.7)	43 (1.7, 91.4)
	Median RDI (5th, 95th centiles)	6.7 (5.4, 7.4)	6.6 (5.5, 7.3)	6.6 (5.4, 7.3)	6.5 (5.4, 7.4)
Quintile 5 [least deprived]	*n*	107 944	50	39	46
	% male (*n*)	49.4 (53 364)	60 (30)	61.5 (24)	58.7 (27)
	Mean age, years (5th and 95th centiles)		46.5 (5.7, 87.3)	47.1 (3.6, 82.4)	46.9 (7.3, 85.5)
	Median RDI (5th, 95th centiles)	9.5 (7.8, 12.8)	9.2 (7.8, 12.1)	9.2 (7.7, 12.1)	9.2 (7.8, 12.3)

Note: The RDI of all electoral divisions in Cork city and county was ranked from most deprived to least deprived. The electoral divisions were divided into five quintiles based on an average population of approximately 108 000 per quintile. Quintile 1 represents the one fifth of the population living in the most deprived electoral divisions, and Quintile 5 represents the fifth of the population living in the least deprived electoral divisions. The number of cases and mean RDI in each group is shown. Only definite and probable cases were included in each diagnostic category. Persons living in nursing homes or convents, whose registered address was a prison, or who were homeless were not included in the sociodemographic analysis. For this reason, there were 14 persons with a first unprovoked seizure, nine persons with a provoked seizure, and 10 persons with a new diagnosis of epilepsy who were not included in the quintiles of their respective diagnostic group.

Abbreviation: RDI, Relative Deprivation Index.

When those with a new diagnosis of epilepsy were subdivided into those with a structural ($n = 175$), genetic ($n = 39$), or unknown etiology ($n = 101$), the incidence of epilepsy remained highest in the most deprived compared to the least deprived quintile (see Table 4). The number of cases with a genetic etiology was small, and results were not statistically significant in this group.

TABLE 2 Annual incidence of first unprovoked seizures, first provoked seizures, and new diagnosis of epilepsy per 100 000 population in the most deprived electoral divisions compared to the least deprived electoral divisions

		First unprovoked seizures		First provoked seizures		New diagnosis of epilepsy	
			Incidence (95% CI) IR (95% CI)		Incidence (95% CI) IR (95% CI)		Incidence (95% CI) IR (95% CI)
Quintile	Study population, *n*	*n*	Adj IR (95% CI)	*n*	Adj IR (95% CI)	*n*	Adj IR (95% CI)
1 [most deprived]	108 753	90	82.8 (66.9–101.2) IR = 1.79 (1.26–2.52), $p < .001$ Adj IR = 1.63 (1.51–2.30), $p = .006$	61	56.1 (43.3–71.6) IR = 1.55 (1.04–2.32), $p = .03$ Adj IR = 1.42 (.95–2.12), $p = .08$	85	78.2 (62.8–96.2) IR = 1.83 (1.28–2.62), $p < .001$ Adj IR = 1.66 (1.16–2.38), $p = .006$
2	108 396	91	83.9 (68.0–102.6) IR = 1.81 (1.28–2.56), $p < .001$ Adj IR = 1.63 (1.15–2.31), $p = .006$	23	21.2 (13.8–31.3) IR = .59 (.35–.98), $p = .04$ Adj IR = .53 (.31–.90), $p = .02$	87	80.3 (64.7–98.5) IR = 1.88 (1.32–2.69), $p < .001$ Adj IR = 1.69 (1.18–2.43), $p = .004$
3	108 604	62	57.1 (44.2–72.7) IR = 1.23 (.85–1.79), $p = .27$ Adj IR = 1.16 (.79–1.68), $p = .45$	31	28.5 (19.7–40.0) IR = .79 (.49–1.27), $p = .33$ Adj IR = .75 (.47–1.21), $p = .24$	48	44.2 (32.9–58.1) IR = 1.03 (.69–1.55), $p = .88$ Adj IR = .96 (.64–1.45), $p = .86$
4	109 171	65	59.5 (46.3–75.4) IR = 1.28 (.89–1.86), $p = .18$ Adj IR = 1.24 (.86–1.79), $p = .28$	26	23.8 (15.9–34.4) IR = .66 (.40–1.08), $p = .10$ Adj IR = .66 (.40–1.08), $p = .10$	60	55.0 (42.3–70.2) IR = 1.29 (.88–1.89), $p = .19$ Adj IR = 1.24 (.84–1.82), $p = .28$
5 [least deprived]	107 944	50	46.3 (34.8–60.6) Reference	39	36.1 (26.1–48.9) Reference	46	42.6 (31.6–56.3) Reference
p for trend		$p = .0001$		$p = .006$		$p < .0001$	

Note: Trend was calculated by logistic regression of median Relative Deprivation Index for cases and noncases in each quintile.

Abbreviations: Adj IR, Mantel–Haenszel adjusted IR for sex and age group; CI, confidence interval; IR, incidence ratio.

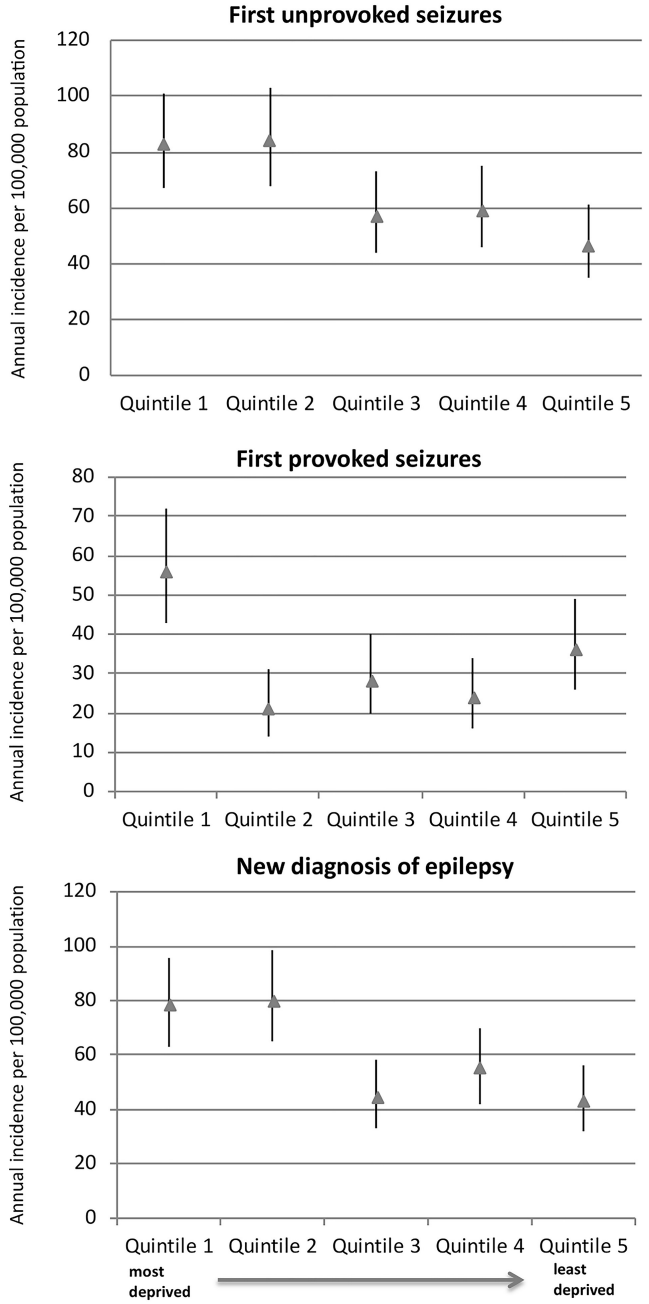


FIGURE 1 The annual incidence of first unprovoked seizures, first provoked seizures, and new diagnosis of epilepsy in the most deprived quintile (1) compared to the least deprived quintile (5) of the defined geographical area during the calendar year 2017

3.2 | Epilepsy risk factors

Whether there was a history of febrile seizure was documented in 223 (68%) of individuals with a new diagnosis of epilepsy. Among these, 19% ($n = 11$) of the cases who lived in the most deprived quintile had a positive history of febrile seizures compared to 3% ($n = 1$) in the least deprived (see Table 5).

Family history was documented in 235 (72%) cases of new diagnosis of epilepsy, and of these, 50 (21%) reported a positive family history. There was no clear association across quintiles of deprivation (13% in the least deprived compared to 19%–24% in the remainder). To examine whether the association between deprivation and new diagnosis of epilepsy differed by family history, we grouped cases into those with a positive family history ($n = 50$) and those without family history or with undocumented family history ($n = 276$). The IR comparing most to least deprived remained elevated in those without family history or with undocumented family history (IR = 1.68, 95% CI = 1.15–2.46).

For most risk factors, the proportion of missing responses did not correlate with deprivation quintiles, with the exception of a history of drug or alcohol abuse, in which the highest proportion of cases with an unknown or undocumented history was in the least deprived quintile ($n = 10$, 22%).

4 | DISCUSSION

We found that individuals living in the most deprived quintile of the defined geographical area studied are 55%–83% more likely to be diagnosed with a first unprovoked seizure, first provoked seizure, or new onset epilepsy than those living in the least deprived quintile. The higher incidence of new diagnosis of epilepsy and first unprovoked seizures in deprived areas is evident in both children and adults. Finally, we report a higher incidence of both structural and unknown etiologies of epilepsy in areas of relatively high sociodemographic deprivation.

Similar to our results, higher incidence of unprovoked seizures and epilepsy in areas of relative socioeconomic deprivation has been reported in adults in England,[5] Wales,[4] Iceland,[10] and northern Manhattan.[6] Although the measure used in each study to determine socioeconomic status differed, concordance of results supports the conclusions.

Establishing the mechanism of the association between seizures, epilepsy, and socioeconomic deprivation is important to identify potentially modifiable risk factors. One possible explanation is increased occurrence of risk factors for development of epilepsy, such as traumatic brain injury, in areas of relatively high deprivation.[28] However, we found a higher incidence of both structural and unknown etiologies of epilepsy in areas of deprivation. Environmental exposures are also worth considering. Air pollution has been found to be increased in areas of higher social deprivation.[29] A small number of studies have reported a positive association between air pollution exposure and hospital visits for seizures.[30–32] As a potentially modifiable risk factor that varies across areas of relatively high and low socioeconomic deprivation, the effect of air pollution on seizures and epilepsy deserves further study.

TABLE 3 Annual incidence of first unprovoked seizures and new diagnosis of epilepsy per 100 000 population in those aged 28 days to 14 years of age and in those 15 years of age and older in the most deprived electoral divisions compared to the least deprived electoral divisions

Quintile	Study population, *n*	First unprovoked seizure		New diagnosis of epilepsy	
		n	Incidence (95% CI)	*n*	Incidence (95% CI)
Persons 28 days–14 years old					
1 [most deprived]	20 341	20	98.3 (61.8–149.1)	21	103.2 (65.6–155.1)
			IR = 1.91 (.91–3.98), $p = .08$		IR = 2.20 (1.04–4.68), $p = .03$
2	22 862	19	83.1 (51.5–127.3)	14	61.2 (33.9–100.3)
			IR = 1.61 (.77–3.89), $p = .20$		IR = 1.31 (.58–2.94), $p = .52$
3	24 233	19	78.4 (48.6–120.15)	15	61.9 (36.0–99.8)
			IR = 1.52 (.72–3.20), $p = .26$		IR = 1.32 (.59–2.94), $p = .49$
4	24 761	20	80.8 (50.7–122.5)	18	72.7 (44.4–112.6)
			IR = 1.57 (.75–3.27), $p = .23$		IR = 1.55 (.72–3.36), $p = .26$
5 [least deprived]	21 334	11	51.6 (27.1–89.6)	10	46.9 (23.8–83.5)
			Reference		Reference
p for trend		$p = .13$	$p = .07$		
Persons ≥ 15 years old					
1 [most deprived]	88 412	70	79.2 (62.2–99.4)	64	72.4 (56.2–91.8)
			IR = 1.76 (1.19–2.60), $p = .004$	73	IR = 1.74 (1.16–2.62), $p = .007$
2	85 534	72	84.2 (66.4–105.4)		85.3 (67.4–106.7)
			IR = 1.87 (1.27–2.76), $p = .001$		IR = 2.05 (1.38–3.06), $p < .001$
3	84 371	43	51.0 (37.4–68.0)	33	39.1 (27.4–54.3)
			IR = 1.13 (.74–1.75), $p = .57$		IR = .94 (.59–1.51), $p = .80$
4	84 410	45	53.3 (39.4–70.7)	42	49.8 (36.3–66.6)
			IR = 1.18 (.77–1.82), $p = .44$		IR = 1.20 (.77–1.87), $p = .43$
5 [least deprived]	86 610	39	45 (32.5–60.9)	36	41.6 (29.6–56.9)
			Reference		Reference
p for trend		$p = .0003$	$p = .0002$		

Note: Trend was calculated by logistic regression of median Relative Deprivation Index for cases and noncases in each quintile.

Abbreviations: CI, confidence interval; IR, incidence ratio.

The number of cases in our study with a genetic etiology was small, and although incidence was highest in the most deprived areas, risk ratios in this subgroup were not statistically significant. In contrast, subgroup analysis of adult cases in Iceland found that low socioeconomic status, as indicated by educational attainment of the main wage earner and lack of home ownership, was significant only in the idiopathic/cryptogenic etiology subgroup and not in those with a remote symptomatic or progressive symptomatic etiology. Case numbers in the latter two groups were small.[10] We applied the updated ILAE classification systems for seizures[33] and epilepsy[25] type to our cohort. Application of these classification systems may have resulted in more accurate classification, revealing a true gradient.

In our study, 21% ($n = 50$) of cases of new diagnosis of epilepsy for whom it was recorded reported a positive family history. The proportion with a positive family history was lowest among those in the least deprived quintile (13%, $n = 4$), which may be consistent with the hypothesis of social drift. However, family history alone does not fully explain the difference in incidence, as the trend across quintiles was still evident after adjusting for family history. Our data on risk factors are incomplete, and we made an assumption that family history was negative in cases with an undocumented family history; therefore, it is difficult to draw firm conclusions from this aspect of our results. For most risk factors, the proportion of those without a documented history was similar across quintiles.

No evidence of social drift was found in Iceland by comparing the socioeconomic status of persons with epilepsy to controls whose parents had epilepsy.[10] In Wales, no evidence of social drift was found by following a cohort of patients with incident epilepsy for 10 years.[4] Taken together, studies to date therefore suggest that social causation, rather than social drift, is the dominant factor contributing to the higher prevalence of epilepsy[1–3]

TABLE 4 Annual incidence of new diagnosis of epilepsy of structural, genetic, or unknown etiology per 100 000 population in the most deprived electoral divisions compared to the least deprived electoral divisions

		Structural		Genetic		Unknown	
			Incidence (95% CI)		Incidence (95% CI)		Incidence (95% CI)
Quintile	Study population, *n*	*n*	IR (95% CI)	*n*	IR (95% CI)	*n*	IR (95% CI)
1 [most deprived]	108 753	47	43.2 (32.1–57.0) IR = 1.73 (1.08–2.78), $p = .02$	10	9.2 (4.7–16.4) IR = 1.98 (.68–5.81), $p = .20$	26	23.9 (16.0–34.5) IR = 2.15 (1.08–4.26), $p = .02$
2	108 396	44	40.6 (29.9–54) IR = 1.62 (1.00–2.62), $p = .04$	11	10.1 (5.3–17.6) IR = 2.19 (.76–6.30), $p = .14$	27	24.9 (16.8–35.7) IR = 2.24 (1.13–4.42), $p = .02$
3	108 604	26	23.9 (16–34.6) IR = .96 (.55–1.64), $p = .87$	6	5.5 (2.2–11.5) IR = 1.19 (.36–3.90), $p = .77$	16	14.7 (8.7–23.4) IR = 1.32 (.63–2.80), $p = .46$
4	109 171	31	28.4 (19.6–39.8) IR = 1.13 (.68–1.90), $p = .63$	7	6.4 (2.8–12.7) IR = 1.38 (.44–4.36), $p = .58$	20	18.3 (11.5–27.8) IR = 1.64 (.81–3.37), $p = .17$
5 [least deprived]	107 944	27	25.0 (16.8–35.9) Reference	5	4.6 (1.7–10.3) Reference	12	11.1 (6.0–19.2) Reference
p for trend		$p = .0038$		$p = .12$		$p = .02$	

Note: Due to very small numbers, those with an infectious etiology and or other etiology were not analyzed ($n = 4$ and $n = 7$ across all quintiles). Trend was calculated by logistic regression of median Relative Deprivation Index for cases and noncases in each quintile.

Abbreviations: CI, confidence interval; IR, incidence ratio.

in areas of social deprivation. However, investigation of multigenerational clustering of genes that lower seizure threshold would require prolonged follow-up, multigenerational family history, and detailed genetic analysis of participants and would be difficult to perform at a population level. Furthermore, genetic factors influencing development of seizures and epilepsy in many cases remain poorly understood. Therefore, it is difficult to entirely rule out social drift as a potential contributing factor.

Similar to studies in Sweden,[9] England,[5] and Wales,[4] we found the annual incidence of epilepsy in children was higher in the most deprived areas compared to the least deprived areas. The influence of a genetic etiology of epilepsy may be more relevant in younger persons than in adults, in whom focal epilepsy becomes more common. A genetic predisposition may be suggested by a history of febrile seizures, which was more common in the most deprived population quintiles compared to the least deprived quintiles. However, as our data were obtained from retrospective chart review, a proportion of cases in each quintile had unknown or undocumented risk factors.

The socioeconomic association was not seen in those aged ≥65 years. This may indicate that after a certain age, seizure risk is no longer influenced by socioeconomic factors. Alternatively, persons in less deprived areas may "delay" their risk to later in their lifetime, rather than "eliminate" it.

Analysis of trend demonstrated that a one-unit increase in RDI is associated with an approximate 4% increase in first unprovoked seizures, first provoked seizures, and new diagnosis of epilepsy. This trend was most evident when the 15–64-year-old subgroup was analyzed. Although the trend is not perfectly linear, taken together, our results suggest that the association between socioeconomic deprivation and seizures may be multifactorial.

To our knowledge, no previous study has reported the incidence of provoked seizures with regard to socioeconomic status. Increased incidence of provoked seizures in areas of higher deprivation could be related to higher prevalence of excessive alcohol intake and binge drinking.[34,35] Similarly, risk factors for other causes of provoked seizures, such as cerebrovascular accidents,[36] are more prevalent in areas of deprivation. Provoked seizures are associated with significant morbidity and mortality,[37] and addressing risk factors for their development should be part of health policy.

A major strength of our study is the use of the 2016 Pobal HP Deprivation Index,[26] which provides a multidomain, multivariable RDI as a continuous variable based on registered address that has been used to investigate the effect of socioeconomic status on survival in renal dialysis patients[38] and renal transplant patients.[39] Area-level measures similar to the RDI have been reported when investigating the association between epilepsy and socioeconomic

TABLE 5 Proportion of cases of definite or probable new diagnosis of epilepsy with a specific risk factor documented on retrospective chart review in each of the five quintiles, based on relative socioeconomic deprivation, of the defined geographic population

	Febrile seizures			CNS infection			Developmental delay			Family history of epilepsy		
Quintile	***n***	**%**	**%[a]**	***n***	**%**	**%[a]**	***n***	**%**	**%[a]**	***n***	**%**	**%[a]**
1 [most deprived]												
Yes	11	13	19	1	1	2	11	13	13	14	17	24
No	47	55	81	58	68	98	74	87	87	47	55	76
Unknown	27	32		26	31		0	0		24	28	
2												
Yes	5	6	8	1	1	2	8	9	9	15	17	23
No	55	63	92	61	70	98	76	88	91	49	56	77
Unknown	27	31		25	29		3	3		23	27	
3												
Yes	3	6	9	1	2	3	9	19	19	7	15	19
No	31	65	91	33	69	97	38	79	81	30	62	81
Unknown	14	29		14	29		1	2		11	23	
4												
Yes	1	2	2	0	0	0	6	10	10	10	17	24
No	41	68	98	45	75	100	53	88	90	32	53	76
Unknown	18	30		15	25		1	2		18	30	
5 [least deprived]												
Yes	1	2	3	1	2	3	5	11	11	4	9	13
No	28	61	97	29	62	97	40	87	91	27	59	87
Unknown	17	37		16	35		1	2		15	32	

	Drug or alcohol abuse			Head injury			Cerebrovascular disease			Psychiatric illness		
Quintile	***n***	**%**	**%[a]**	***n***	**%**	**%[a]**	***n***	**%**	**%[a]**	***n***	**%**	**%[a]**
1 [most deprived]												
Yes	5	6	7	4	5	7	30	35	35	5	6	6
No	72	85	93	54	63	93	55	65	65	80	94	94
Unknown	8	9		27	32		0	0		0	0	
2												
Yes	9	10	11	3	3	5	34	40	40	6	7	7
No	69	80	89	56	65	95	50	57	60	81	93	93
Unknown	9	10		28	32		3	3		0	0	
3												
Yes	6	12	15	3	6	5	13	27	27	3	6	6
No	35	73	85	56	63	95	35	73	73	45	94	94
Unknown	7	15		28	31		0	0		0	0	
4												
Yes	2	3	4	3	2	9	19	32	33	7	12	12
No	48	80	96	30	70	91	39	65	64	51	85	85
Unknown	10	17		15	28		2	3		2	3	
5 [least deprived]												
Yes	5	11	14	1	6	9	14	30	30	1	2	2
No	31	67	86	42	59	91	32	70	70	45	98	98
Unknown	10	22		17	35		0	0		0	0	

Note: "Unknown" indicates that the risk factor was unknown or undocumented.

Abbreviation: CNS, central nervous system.

[a]Percentage yes or no of those with a documented response.

deprivation in different geographical areas, specifically the Carstairs Index,[5] the Welsh Index for Multiple Deprivation,[4] and the Townsend Index.[1,8] The 2016 Pobal HP Deprivation Index uses more variables than other indices. Furthermore, it aims to assess lack of opportunity as a marker of social deprivation, which is particularly relevant in rural communities, thus allowing comparison of deprivation across the geographic area studied.

Area-level measures of deprivation have potential weaknesses. They do not measure individual-level deprivation and cannot account for the possibility of an individual living in an area of relative deprivation not being deprived themselves. It is reassuring that our results are concordant with prospective incidence studies that assessed socioeconomic deprivation on an individual level.[6,10] Participant-level data from individual cases would have allowed examination of individual-level socioeconomic deprivation and adjustment for confounding. However, such detail would be difficult to attain for such a large population cohort, and prospectively interviewing each participant was beyond the scope of this study. Similarly, as previously outlined, variability in the documentation of risk factors for seizures and epilepsy is a limitation of our study. Although this study recruited from a large population, case numbers were small in some subgroups, for example, in those with a genetic etiology of epilepsy, limiting interpretation of results, and larger studies are needed to investigate this further.

Children and adults in the most socially deprived communities have an excess burden of seizure disorders with lifelong consequences including loss of educational and earning potential.[40] Our study suggests that the increased incidence may be multifactorial. Detailed prospective studies that deeply phenotype participants and their environments are needed to identify risk factors, particularly those that could be modified at the individual, community, or policy level. The effects of seizures and epilepsy have lifelong implications and deserve further study and modification where possible.

AUTHOR CONTRIBUTIONS

Eimer M. Maloney: Conceptualization, data curation, formal analysis, investigation, methodology, writing–original draft. Paul Corcoran: Methodology, writing–review and editing. Daniel J. Costello: Conceptualization, project administration, supervision, writing–review and editing. Éilis J. O'Reilly: Conceptualization, project administration, supervision, formal analysis, validation, writing–review and editing.

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CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

Anonymized data can be shared by request from any qualified investigator.

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SUPPORTING INFORMATION

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