Injury Among Children and Young Adults With Epilepsy

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KEY WORDS
epilepsy, injury, fractures, burns, poisoning

ABBREVIATIONS
ADHD—attention-deficit/hyperactivity disorder
AED—antiepileptic drug
CI—confidence interval
CPRD—Clinical Practice Research Datalink
GP—general practitioner
HR—hazard ratio
SHA—Strategic Health Authority

Dr Prasad conceived the idea for the study, conducted the data management, and drafted the initial manuscript; Professor Kendrick conceived the idea for the study and provided clinical input and interpretation throughout the project; Drs Sayal and Thomas made contributions to the design of the study and provided clinical input and interpretation throughout the project; Dr West conceived the idea for the study, guided the data management, and provided clinical input and interpretation throughout the project; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2013-2554

doi:10.1542/peds.2013-2554

Accepted for publication Jan 24, 2014

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: Dr Prasad received research grant support administered via the University of Nottingham from the National Institute for Health Research In-Practice Fellowship scheme and later the Doctoral Research Fellowship scheme; the other authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by National Institute for Health Research grant DRF-2011-04-116.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

WHAT'S KNOWN ON THIS SUBJECT: Injuries in children and young adults commonly cause morbidity and mortality. Epilepsy is common among children. Injury risk may be greater among those with epilepsy, but there are few large, population-based studies, making it difficult to estimate risk.

WHAT THIS STUDY ADDS: Children and young adults with epilepsy are at a greater risk of medicinal poisonings, thermal injuries, and fractures than those without epilepsy. Young adults with epilepsy are at particularly high risk of medicinal poisonings.

abstract

OBJECTIVE: To investigate whether children and young adults with epilepsy are at a greater risk of fracture, thermal injury, or poisoning than those without.

METHODS: A cohort study was conducted by using the Clinical Practice Research Datalink (1987–2009), a longitudinal database containing primary care records. A total of 11 934 people with epilepsy and 46 598 without, aged between 1 and 24 years at diagnosis, were followed for a median (interquartile range) of 2.6 (0.8–5.9) years. The risk of fractures (including long bone fractures), thermal injuries, and poisonings (including medicinal and nonmedicinal poisonings) was estimated.

RESULTS: Adjusting for age, gender, Strategic Health Authority region, deprivation, and calendar year at study entry (and, for medicinal poisonings, behavior disorder), people with epilepsy had an 18% increase in risk of fracture (hazard ratio [HR] = 1.18; 95% confidence interval [CI], 1.09–1.27), a 23% increase in risk of long bone fracture (HR = 1.23; 95% CI, 1.10–1.38), a 49% increase in risk of thermal injury (HR = 1.49; 95% CI, 1.27–1.75), and more than twice the risk of poisoning (HR = 2.47; 95% CI, 2.15–2.84), which was limited to poisoning from medicinal products (medicinal HR = 2.54; 95% CI, 2.16–2.99; nonmedicinal HR = 0.96; 95% CI, 0.61–1.52).

CONCLUSIONS: Children and young adults with epilepsy are at a greater risk of fracture, thermal injury, and poisoning than those without. The greatest risk is from medicinal poisonings. Doctors and other health care professionals should provide injury and poison prevention advice at diagnosis and epilepsy reviews. *Pediatrics* 2014;133:827–835

Epilepsy is a chronic neurologic condition causing unprovoked recurrent seizures due to excessive cerebral neurologic activity.[1,2] It is common, affecting ~2 million adults and 468 000 children in the United States.[2] Worldwide, injuries are a leading cause of morbidity and mortality in children.[3] Unintentional injuries are an important public health problem in the United States,[4] with an incidence of 2000 medically attended injuries per 10 000 person-years[5] and a total lifetime cost in <25-year-olds of $130 billion in 2000.[5] The epidemiology of injury varies by age,[6–9] and boys are more likely than girls to sustain injuries, especially as teenagers.[9–11] Fractures are common, with incidence estimates ranging from 133 to 201 per 10 000 person-years in children[12–14] to 254 per 10 000 person-years in all ages[5] for medically attended fractures. Thermal injuries are common in children and young adults,[15,16] with an incidence in the United States of 34 medically attended injuries per 10 000 person-years in <25-year-olds and a total lifetime cost of $440 million in 2000.[5] Unintentional poisonings are a significant cause of deaths worldwide[17] in children and young adults and were the third leading cause of injury hospitalizations in the United States in 2000,[5] with an incidence of 60 medically attended injuries per 10 000 person-years in <25-year-olds and a total lifetime cost of $583 million.[5]

Previous studies, mainly in adults, suggest epilepsy is associated with a higher risk of injuries,[18,19] thought to be caused by the seizures themselves, and adverse effects of antiepileptic drugs (AEDs).[20,21] Earlier studies on epilepsy and injuries may have overestimated injury risk by using populations with more severe epilepsy, such as institutionalized adults[22] or those in epilepsy clinics.[18] Questionnaire-based studies ascertaining injury retrospectively are subject to recall bias, with caregivers or relatives more likely to recall an injury if the participant has epilepsy.[19] Few studies have measured the rate of injuries prospectively in the general population.[23–25] A prospective European study in >5-year-olds found no greater injury risk associated with epilepsy,[25] whereas a US study concluded that the risk of serious injuries in epilepsy is minor,[23] and a UK study using the Clinical Practice Research Datalink (CPRD) reported the risk of fracture in people with epilepsy to be twice that of those without epilepsy.[26] None of these studies focused on children and young adults with epilepsy; therefore, there is a lack of data for informing people with epilepsy about injury risk. We therefore investigated whether children and young adults with epilepsy are at greater risk of fracture, thermal injury, or poisoning than people without epilepsy and estimated the risk of injury ≤5 years after diagnosis with epilepsy.

METHODS

Study Population

We conducted a cohort study using medical records of children and young adults from the CPRD, a primary care database containing medical records of ~12 million people (66 million person-years of follow-up) from 625 general practitioner (GP) practices, representing 8% of the UK population.[27] The CPRD is subjected to rigorous data quality checks (eg, ensuring that a minimum of 95% of patient encounter events are recorded, validation checks, and audits[28]), and a recent systematic review[29] demonstrated the high validity of a range of diagnoses in the CPRD, with a median of 89% of cases confirmed by GP record request, algorithm, and manual review.[29] The CPRD contains information on consultations with the GP, hospital attendances, and admissions coded by using Read codes[30] and information on prescriptions. Read codes use a system similar to the Systematized Nomenclature of Medicine or International Classification of Disease systems used in UK primary care.[30] Lists of Read and drug codes for epilepsy were drawn up by 2 researchers. CPRD extracted records of people who had a code for epilepsy or AED recorded while registered in the database before the age of 25 years from January 1, 1987 to December 31, 2009. People with epilepsy were frequency-matched by practice and 5-year age band to ≤5 people who did not have epilepsy. The lists of Read code descriptions and drug codes used are available from the authors on request.

We took the date of the first Read code or AED prescription to be the date of diagnosis with epilepsy. We randomly assigned a date of "pseudodiagnosis" for those without epilepsy that could be on any date starting from 3 months after they registered with the practice up to the date they left the practice using a computer algorithm. Age was described in terms of age at pseudodiagnosis.

Definition of Epilepsy

Epilepsy was defined as having ≥2 Read codes for epilepsy or ≥2 AED prescriptions. To ensure that the group of people with epilepsy included those with an incident diagnosis, made after they joined the current GP practice, we explored the time between the date of registration with the GP and diagnosis of epilepsy for each age group, based on work that showed that in people of all ages, the time taken for incidence rates of chronic conditions to reach a plateau after registration can vary from 4 to 12 months, depending on ages and the condition.[31] Our work suggested that incident diagnoses were those made >3 months from registration with the GP for children ≤14 years old and >6 months after registration for people

>15 years old. People with prevalent epilepsy or with only 1 epilepsy Read code or AED prescription were excluded from the analyses.

Definition of Outcome and Follow-up

The outcome was the first injury to occur after pseudodiagnosis of epilepsy. Each injury type (fractures, thermal injuries, and poisonings) was chosen a priori and identified by using a list of Read codes (descriptions available on request). We included both mechanisms of injury (eg, accidents caused by fire and flames) and anatomic sites of injury (eg, burn of lower limbs) to maximize ascertainment of injuries. We followed people from the date of diagnosis of epilepsy (or the pseudodiagnosis date for those without epilepsy) to the earliest of the date of the first injury code, of leaving the CPRD (eg, transfer to a new practice), or December 31, 2009. People who had a record of the injury before the date of pseudodiagnosis were excluded from the analysis of that injury type because people with a previous injury have a higher risk of a subsequent injury.[32,33] We also explored the relationship between epilepsy and long bone fractures (as indicators of severe injury[34,35]) and between epilepsy and medicinal and nonmedicinal poisonings separately (because those with epilepsy may have greater access to medicines than those without).

Confounders

Estimates were adjusted for age, gender, Strategic Health Authority (SHA) region of the practice, socioeconomic status, and calendar year at study entry. We used the Index of Multiple Deprivation of the GP practice as a proxy measure of the person's socioeconomic status. Index of Multiple Deprivation scores were categorized into national (England, Scotland, Wales, and Northern Ireland) quintiles. By using Read codes, we identified several comorbid conditions that may confound the relationship between epilepsy and injury. These included attention-deficit/hyperactivity disorder (ADHD), behavior disorder (including oppositional defiant disorder, antisocial behavior, and behavior disorder), learning disability, and cerebral palsy.

Statistical Analysis

We described categorical variables by using frequencies and proportions. The age bands chosen were 1, 2, 3, 4, 5 to 9, 10 to 14, 15 to 18, and 19 to 24 years for analyses on fractures, but in the analyses on thermal injuries and poisonings, children <5 years old were grouped together because of small numbers of events. We estimated crude rates for the first type of each injury after diagnosis for people with and without epilepsy, with 95% confidence intervals (CIs). We estimated hazard ratios (HRs) for people with epilepsy compared with those without, using a Cox regression model. We adjusted HRs for confounders (age, gender, SHA region, practice-level deprivation, and calendar year at study entry). We then adjusted for each comorbid condition (ADHD, behavior disorder, learning disability, cerebral palsy) in turn. When adjustment for a comorbid condition led to a change of >10% in the adjusted HR, the confounder was retained in the model, and the remaining comorbid conditions were assessed for inclusion in the model as described.

We explored interactions by age and gender by adding interaction terms to the models, with $P < .05$ taken as statistically significant. Models were checked by inspection of plots of the logarithm of cumulative hazard against time, Schoenfeld residuals against time, and a statistical test for nonproportional hazards for people with epilepsy compared with those without in the final model. The number of people in 1000 who had an injury within 5 years of diagnosis was estimated for each injury type. We undertook sensitivity analyses assessing the robustness of our findings in terms of our definition of epilepsy. First, we used a stricter definition of epilepsy (people with ≥2 AED prescriptions and ≥2 diagnosis codes); second, we excluded those with a first AED of either pregabalin or gabapentin because these drugs can be prescribed for other diagnoses; and third, we excluded those with AED prescriptions but no Read code for diagnosis of epilepsy. We also recalculated the risk of injuries in those aged 1 to 21 years to assess whether the estimates of risk differed when young adults >21 years old were excluded from the population. Last, because almost all those with long bone fractures would have attended secondary care, we assessed completeness of ascertainment of long bone fracture risk in the practice records using approximately half the sample who had linked hospital records from the Hospital Episodes Statistics database. Hospital Episodes Statistics data include diagnosis codes, using the International Classification of Diseases version 10,[36] and procedure codes, using the Office of Population Censuses and Surveys version 4,[37] from inpatient admissions to hospitals in England. All long bone fracture codes recorded during study follow-up in the hospital records were identified. People who had a long bone fracture recorded in the hospital but not by the GP were then reclassified as having a long bone fracture in a separate analysis of the risk of long bone fractures. Statistical analysis was performed by using Stata version 12MP (Stata Corp, College Station, TX).

Ethics

Approval was obtained from the CPRD's own independent scientific advisory

committee. CPRD data are anonymized, and additional ethics approval was not required.

RESULTS

Table 1 shows participant characteristics. In the analysis of fractures, there were 10 447 eligible people with epilepsy and 42 181 without. In total, there were 231 478 person-years of follow-up. The characteristics of those included in the analyses for thermal injuries and poisonings were similar to those included in the analyses for fractures.

Table 2 shows risk of injury in people with epilepsy compared with those without. The highest rate of injuries was for any fractures, 16.8 (95% CI, 15.8–17.9) per 1000 person-years in epilepsy versus 14.4 (95% CI, 13.8–15.0) per 1000 person-years in those without; followed by any poisoning, 6.2 (95% CI, 5.6–6.8) versus 2.5 (95% CI, 2.3–2.8) per 1000 person-years; and thermal injuries, 3.8 (95% CI, 3.3–4.3) versus 2.5 (95% CI, 2.3–2.8) per 1000 person-years. After we adjusted for age, gender, SHA region, practice-level deprivation, and calendar year at study entry, people with epilepsy had more than twice the risk of poisoning than those without (adjusted HR = 2.47; 95% CI, 2.15–2.84), a 1.5-fold increase in the risk of thermal injury (adjusted HR = 1.49; 95% CI, 1.27–1.75), and an 18% increase in risk of fracture (adjusted HR = 1.18; 95% CI, 1.09–1.27). Restricting analyses to long bone fractures had little effect on HR estimates (adjusted HR = 1.23; 95% CI, 1.10–1.38). The HR for medicinal poisonings was reduced after we adjusted for behavior disorder (HR = 2.54; 95% CI, 2.16–2.99), but adjustments for this and for other comorbidities made little difference to the other HR estimates. Analysis by poisoning agent revealed that the greater risk of poisoning in people with epilepsy reflected medicinal poisonings (HR = 2.54; 95% CI, 2.16–2.99) rather than poisonings by nonmedicinal products (HR = 0.96; 95% CI, 0.61–1.52).

We explored whether the greater risk of injury in people with epilepsy varied by age and gender. There was some evidence of an interaction with gender for medicinal poisonings (test for interaction $P = .04$), with a greater HR for males than for females (adjusted HR = 3.11; 95% CI, 2.41–4.01) versus 2.23 (95% CI, 1.81–2.74), adjusting for age, SHA region, practice-level deprivation, calendar year at study entry, and behavior disorder. There was no evidence of an interaction with gender for other injury types. There was strong evidence that the relative risk of poisoning varied by age (test for interaction $P < .001$), with the greatest increased risk in 19- to 24-year-olds (adjusted HR = 3.94; 95% CI, 2.94–5.27) and least in the 10- to 14-year-olds (adjusted HR = 1.52; 95% CI, 1.15–2.01), adjusting for age, gender, SHA region, practice-level deprivation, and calendar year at study entry. After analyses were restricted to medicinal poisonings (Fig 1), these age-specific patterns of increased risk persisted (test for interaction $P = .01$; adjusted HR for 19- to 24-year-olds = 3.59; 95% CI, 2.65–4.86; adjusted HR in 10- to 14-year-olds = 1.71; 95% CI, 1.23–2.37), adjusting for gender, SHA region, practice-level deprivation, calendar year at study entry, and behavior disorder. The drug involved in the poisoning incident was recorded in only 5% of medicinal poisonings in people with epilepsy and 5% of those without epilepsy. A total of 2% of all medicinal poisonings in people with epilepsy were caused by an AED.

Absolute risks of injury in the 5-year period after pseudodiagnosis in people with and without epilepsy are shown in Table 3. Per thousand people, those with epilepsy experienced an extra 23 poisonings (21 of which were medicinal poisonings), an extra 12 fractures (2 of which were long bone fractures), and an extra 7 thermal injuries.

Our findings were robust to restricting analyses to people with ≥2 drug prescriptions and ≥2 diagnosis codes for epilepsy, to excluding those prescribed pregabalin or gabapentin as their first AED, and to excluding 3554 people with AED prescriptions but no Read code for a diagnosis of epilepsy. Results for people aged 1 to 21 years were similar to those for people aged 1 to 24 years: fractures 1.15 (95% CI, 1.06–1.25), thermal injuries 1.39 (95% CI, 1.18–1.65), poisonings 2.26 (95% CI, 1.95–2.62), long bone fractures 1.20 (95% CI, 1.06–1.35), medicinal poisonings 2.39 (95% CI, 2.01–2.84), and nonmedicinal poisonings 0.89 (95% CI, 0.56–1.42). A total of 25 723 people had hospital records linked to their GP records. The risk of long bone fractures for this subgroup was similar to the whole population (adjusted HR = 1.25; 95% CI, 1.07–1.46).

DISCUSSION

Children and young adults with epilepsy are at greater risk of fractures, thermal injuries, and poisonings than those without epilepsy. In people with epilepsy, fractures are 18% more likely, thermal injuries 50% more likely, and poisonings more than twice as likely as in people without epilepsy, with the greater risk being limited to medicinal poisonings. Among young adults with epilepsy, aged 19 to 24 years, the risk of medicinal poisoning was 4 times that of the general population of the same age. The absolute risk of injury in the 5-year period after diagnosis was an additional 12 fractures (2 long bone), 7 thermal injuries, and 23 poisonings (21 medicinal poisonings). Those with epilepsy aged between 19 to 24 years were at

TABLE 1 Characteristics of People With Epilepsy and Those Without for Analyses of Fractures, Thermal Injuries, and Poisonings

Study Cohort[a]		Fractures		Thermal Injuries		Poisonings	
Characteristic		No Epilepsy, *n* = 42 181	Epilepsy, *n* = 10 447	No Epilepsy, *n* = 46 598	Epilepsy, *n* = 11 934	No Epilepsy, *n* = 46 576	Epilepsy, *n* = 11 720
Age group at pseudodiagnosis of epilepsy (y), *n* (%)	1	1751 (4.2)	535 (5.1)	1751 (3.8)	535 (4.5)	1754 (3.8)	540 (4.6)
	2	1623 (3.9)	459 (4.4)	1623 (3.5)	457 (3.8)	1643 (3.5)	460 (3.9)
	3	1589 (3.8)	485 (4.6)	1605 (3.4)	489 (4.1)	1610 (3.5)	494 (4.2)
	4	1764 (4.2)	448 (4.3)	1759 (3.8)	489 (4.1)	1787 (3.8)	448 (3.8)
	5–9	8598 (20.4)	2115 (20.3)	8950 (19.2)	2223 (18.6)	9021 (19.4)	2247 (19.2)
	10–14	8983 (21.3)	2009 (19.2)	10 059 (21.6)	2284 (19.1)	10 109 (21.7)	2311 (19.7)
	15–18	6826 (16.2)	1792 (17.2)	7909 (17.0)	2183 (18.3)	7889 (16.9)	2135 (18.2)
	19–24	11 047 (26.2)	2604 (24.9)	12 942 (27.8)	3317 (27.8)	12 763 (27.4)	3085 (26.3)
Gender, *n* (%)	Males	19 953 (47.3)	5291 (50.7)	22 598 (48.5)	6185 (51.8)	22 705 (48.8)	6152 (52.5)
SHA region, *n* (%)	East Midlands	2422 (5.7)	542 (5.2)	2422 (5.7)	542 (5.2)	5957 (12.8)	1523 (13.0)
	East of England	4457 (10.6)	1111 (10.6)	4457 (10.6)	1111 (10.6)	4548 (9.8)	1105 (9.4)
	London	4288 (10.2)	1013 (9.7)	4530 (9.7)	1119 (9.4)	3483 (7.5)	976 (8.3)
	North East	1118 (2.7)	288 (2.8)	1118 (2.7)	288 (2.8)	3878 (8.3)	1005 (8.6)
	North West	5386 (12.8)	1341 (12.8)	5963 (12.8)	1549 (13.0)	4190 (9.0)	933 (8.0)
	Northern Ireland	1219 (2.9)	369 (3.5)	1219 (2.9)	369 (3.5)	4569 (9.8)	1184 (10.1)
	Scotland	3036 (7.2)	828 (7.9)	3484 (7.5)	1003 (8.4)	3959 (8.5)	994 (8.5)
	South Central	3586 (8.5)	877 (8.4)	3586 (8.5)	877 (8.4)	4893 (10.5)	1198 (10.2)
	South East Coast	3542 (8.4)	891 (7.9)	3875 (8.3)	1033 (8.7)	3439 (7.4)	927 (7.9)
	South West	3792 (9.0)	854 (8.2)	4196 (9.0)	944 (7.9)	2371 (5.1)	557 (4.8)
	Wales	3076 (7.3)	791 (7.6)	3457 (7.4)	938 (7.9)	2686 (5.8)	587 (5.0)
	West Midlands	4138 (9.8)	1047 (10.0)	4563 (9.8)	1198 (10.0)	1380 (3.0)	417 (3.6)
	Yorkshire and Humber	2121 (5.0)	495 (4.7)	2371 (5.1)	556 (4.7)	1223 (2.6)	314 (2.7)
Deprivation, *n* (%)[b]	Least deprived	6674 (15.8)	1692 (16.2)	7437 (16.0)	1945 (16.3)	7414 (15.9)	1911 (16.3)
	2nd least deprived	7443 (17.7)	1713 (16.4)	8273 (17.8)	1966 (16.5)	8307 (17.8)	1938 (16.5)
	Medium deprivation	8160 (19.4)	2018 (19.3)	8993 (19.3)	2290 (19.2)	9000 (19.3)	2257 (19.3)
	2nd most deprived	9307 (22.1)	2327 (22.3)	10 266 (22.0)	2632 (22.1)	10 246 (22.0)	2587 (22.1)
	Most deprived	10 593 (25.1)	2695 (25.8)	11 624 (25.0)	3099 (26.0)	11 604 (24.9)	3025 (25.8)
Calendar year at study entry	1987–1989	230 (0.6)	44 (0.4)	237 (0.5)	47 (0.4)	237 (0.5)	47 (0.4)
	1990–1994	4804 (11.4)	1122 (10.7)	5048 (10.8)	1217 (10.2)	5042 (10.8)	1211 (10.3)
	1995–1999	7228 (17.1)	1925 (18.4)	7786 (16.7)	2112 (17.7)	7806 (16.8)	2097 (17.9)
	2000–2004	12 271 (29.1)	3382 (32.4)	13 455 (28.9)	3850 (32.3)	13 487 (29.0)	3786 (32.3)
	2005 onward	17 648 (41.8)	3974 (38.0)	20 072 (43.1)	4708 (38.5)	20 004 (43.0)	4579 (39.1)
Behavior disorder		1550 (3.7)	1303 (12.5)	1817 (3.9)	1507 (12.6)	1770 (3.8)	1443 (12.3)
Learning disability		318 (0.8)	961 (9.2)	372 (0.8)	1038 (8.7)	368 (0.8)	1029 (8.8)
ADHD		374 (0.9)	363 (3.5)	426 (0.9)	426 (3.6)	428 (0.9)	421 (3.6)
Cerebral palsy		13 (<0.1)	29 (0.3)	14 (<0.1)	31 (0.3)	14 (<0.1)	30 (0.3)

[a] Each study population included those without a history of the injury of interest.

[b] Deprivation is at practice level.

a greater risk of poisonings than those without epilepsy.

To our knowledge, this is the first study to explore associations between epilepsy and fractures, thermal injuries, and poisonings in children and young adults in the primary care population. Because the primary care record contains information on diagnoses made in both secondary and primary care, this provides a more complete picture of the risk of fractures, thermal injuries, and poisonings than previous studies. Misdiagnosis of epilepsy is unlikely because childhood epilepsy is diagnosed by specialists in secondary care, with ongoing prescriptions provided in primary care.[38,39] Misclassification of epilepsy could have occurred, but our sensitivity analyses using stricter criteria to define epilepsy made little difference to the estimated risks of injuries, suggesting that any misclassification is likely to have minimal impact on our findings. Misclassification of the injuries could have occurred if an injury was not coded by the GP or an injury that had not occurred was incorrectly coded as occurring. However, we found similar HRs for all fractures and for long bone fractures, which we expected to have high levels of ascertainment.[40] For a subgroup including long bone fractures recorded in hospital records, we found a similar estimated risk. We included both mechanisms of injury (eg, accidents caused by fire and flames) and anatomic sites of injury (eg, burn of lower limbs) to maximize ascertainment of injuries. There is a potential risk of ascertainment bias, whereby people with epilepsy who may have higher GP consultation rates have more opportunities to report injuries than people

TABLE 2 Risk of Fractures, Thermal Injuries, and Poisonings in Children and Young Adults With Epilepsy Compared With Those Without

Injury Category	Epilepsy or No Epilepsy	Events, *n*	Person-years at Risk	Rate per 1000 (95% CI)	HR (95% CI)	Adjusted HR[a] (95% CI)
Any fractures	No epilepsy	2066	143 336	14.4 (13.8–15.0)	1	1
	Epilepsy	948	56 310	16.8 (15.8–17.9)	1.15 (1.07–1.24)	1.18 (1.09–1.27)
Thermal injuries	No epilepsy	415	164 247	2.5 (2.3–2.8)	1	1
	Epilepsy	253	67 231	3.8 (3.3–4.3)	1.51 (1.29–1.77)	1.49 (1.27–1.75)
Any poisonings	No epilepsy	417	165 376	2.5 (2.3–2.8)	1	1
	Epilepsy	408	66 021	6.2 (5.6–6.8)	2.57 (2.24–2.95)	2.47 (2.15–2.84)
			Injury subgroups			
Long bone fractures	No epilepsy	931	155 637	6.0 (5.6–6.4)	1	1
	Epilepsy	438	63 454	6.9 (6.3–7.6)	1.17 (1.04–1.31)	1.23 (1.10–1.38)
Medicinal poisonings	No epilepsy	293	164 946	1.8 (1.6–2.0)	1	1
	Epilepsy	341	65 786	5.2 (4.7–5.8)	3.06 (2.62–3.59)	2.54[b] (2.16–2.99)
Nonmedicinal poisonings	No epilepsy	72	164 121	0.4 (1.9–0.6)	1	1
	Epilepsy	26	64 760	0.4 (1.9–0.6)	0.92 (0.59–1.45)	0.96 (0.61–1.52)

[a] All HRs were adjusted for age, gender, SHA region, deprivation, and calendar year at study entry.
[b] HR additionally adjusted for behavior disorder.

without epilepsy. Our findings of similar HRs for all fractures and for long bone fractures suggest this was not occurring to a large degree. We have no reason to suspect that misclassification for poisonings or thermal injuries would be greater than that for fractures, and any possible misclassification would tend the HR toward unity, meaning our estimates were conservative estimates of injury risk. Although we adjusted for key confounders, it is possible that some residual confounding remains. We were unable to explore the contribution of AEDs to the greater risk of poisoning because the drug involved was not recorded in most cases of poisoning.

Although comparisons of rates of all injury types in our study with those of previous work are limited, because of the lack of population-based studies in comparable age groups, the rates of fractures in people without epilepsy are broadly comparable to those from previous studies[12–14,41] but lower than those in 1 CPRD study in all ages that estimated an age- and gender-adjusted incidence rate ratio for fractures among patients with epilepsy compared with those without of 1.89 (95% CI, 1.81–1.98).[26] The greater fracture risk in that study may be at least partly explained by the severity of epilepsy because the study population included those with active epilepsy, with drugs or diagnosis codes recorded for >1 year. There are no previous studies comparing the risk of thermal injuries or poisonings between people with epilepsy and those without in the general population, so comparison of our findings with previous studies is not possible.

Potential explanations for the greater risk of injuries associated with epilepsy include injuries occurring as a result of seizures (eg, fractures[42,43] and thermal injuries[44–47]). Epilepsy itself may be associated with pathology of the central nervous system that increases injury risk and, in the case of poisonings, greater access to medicines (for unintentional poisoning or for self-harm with any medication[48]) or inadvertent overdosage of AEDs. We found that 19- to 24-year-olds with epilepsy had the highest risk of poisonings, with potential explanations including self-harm or greater risk-taking behavior. Previous work suggests that people with epilepsy may have a greater risk of suicide than those without epilepsy.[49] It is therefore possible that some of the observed greater risk of poisoning was intentional as opposed to unintentional poisoning. Although we were unable to explore associations between poisoning with specific drugs and epilepsy, it is possible that easy access to AEDs may be important in this context. Although this study does not allow us to explore the reasons why injury risks are greater in people with epilepsy, it allows quantification of risk and highlights that the absolute risk of poisoning is substantially greater than that for fractures or burns.

CONCLUSIONS

All health care professionals can use these findings to inform parents, children, and young adults diagnosed with epilepsy of their absolute risk of injuries as part of counseling for unintentional injury prevention[50] and to inform existing guidelines on treatment.[51] For fractures and thermal injuries, the increase in absolute risk associated with epilepsy is small. Given the greater risk of poisoning, particularly among young adults, efforts should be made to prevent this injury. For example, information could be provided on the risk of medicinal poisoning and advice about safely storing all medicines (not just AEDs), not transferring medicines to other containers, supervising children taking medicine, and understanding the dangers of overdosing.[52–54] This information could be provided when physicians prescribe

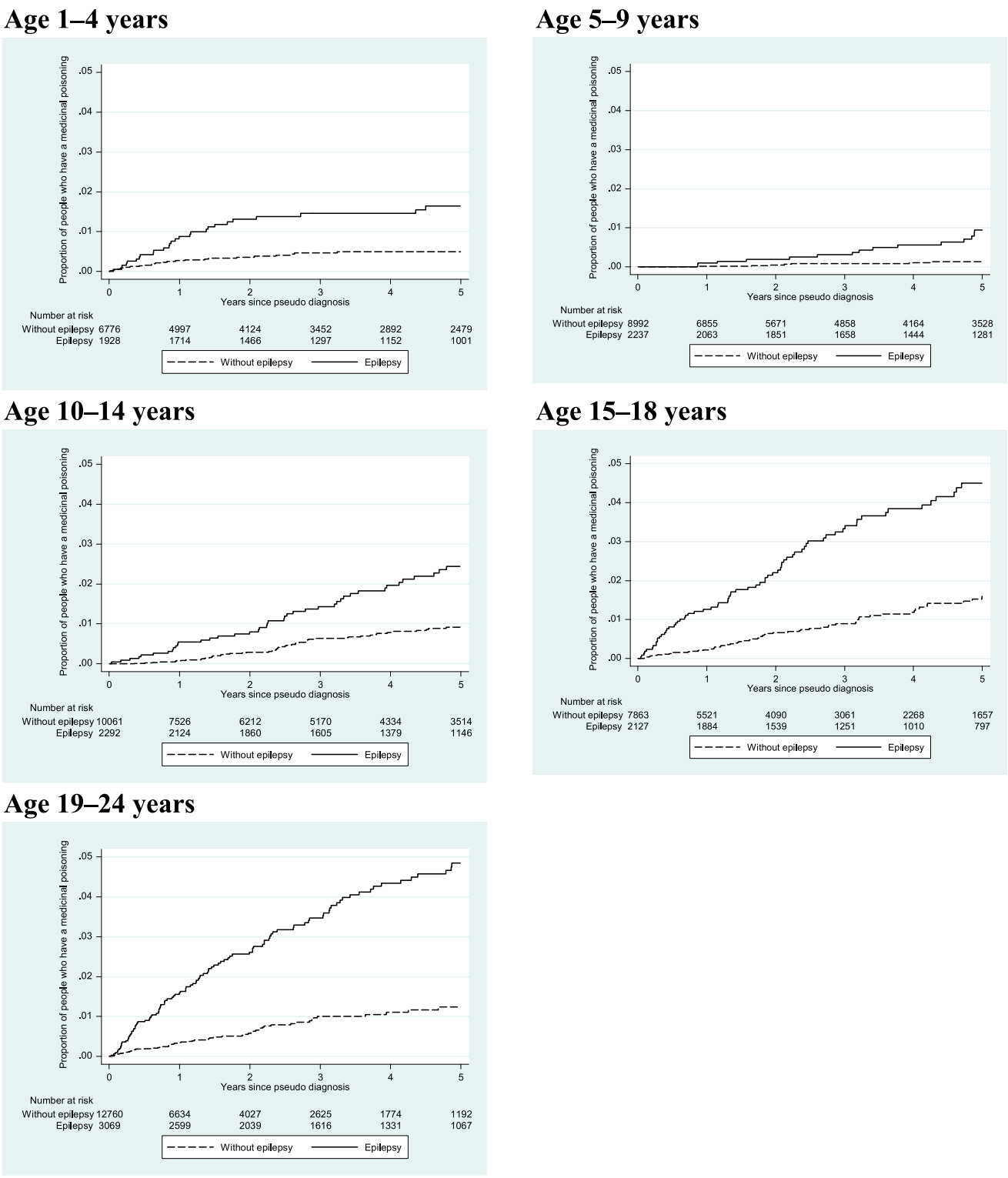

FIGURE 1

Risk of medicinal poisonings in people with epilepsy compared with those without by age at pseudodiagnosis. Numbers of people in study by year since pseudodiagnosis are shown for people with epilepsy and those without.

medication and during epilepsy reviews, and pharmacists can also provide such information when dispensing AEDs to children and young adults. More research is needed to distinguish intentional from unintentional poisonings, especially in older children and young adults, so that the greater risk of poisoning, by intent, can be described in

TABLE 3 Absolute Risks of Injury in the 5-Year Period After Pseudodiagnosis in People With Epilepsy and Without Epilepsy

Time Since Diagnosis	No Epilepsy			Epilepsy			Excess Injuries per 1000 (95% CI)
	Total at Risk, *n*	Events, *n*	Injuries per 1000 (95% CI)	Total at Risk, *n*	Events, *n*	Injuries per 1000 (95% CI)	
Any fractures, ≤5 y	10 605	976	69.5 (65.7 to 73.4)	4520	427	81.1 (74.6 to 88.1)	11.6 (8.9 to 14.7)
Thermal injuries, ≤5 y	12 303	189	12.3 (10.9 to 13.9)	5416	115	19.2 (16.5 to 22.4)	6.9 (5.6 to 8.5)
Any poisonings, ≤5 y	12 411	194	11.9 (10.6 to 13.5)	5310	186	34.7 (30.9 to 38.9)	22.8 (20.3 to 25.4)
			Injury subgroups				
Long bone fracture, ≤5 y	11 592	479	31.5 (1.3 to 34.1)	5099	200	33.9 (2.1 to 38.3)	2.4 (0.8 to 4.2)
Medicinal poisonings, ≤5 y	12 377	136	8.2 (7.1 to 9.5)	5293	157	29.3 (25.8 to 33.2)	21.1 (18.7 to 23.7)
Nonmedicinal poisonings, ≤5 y	12 312	34	2.1 (1.6 to 2.9)	5220	10	2.0 (1.2 to 3.2)	−0.1 (−0.4 to 0.3)

children and young adults with epilepsy. Additional research exploring the contribution of AEDs to poisonings in children with epilepsy would also be helpful in providing more specific prevention advice to parents, children, and young adults.

ACKNOWLEDGMENTS

We thank Dr Elizabeth Orton for helping compile the original code lists, Dr Ed Tyrell for categorizing the code list for poisonings into medicinal and nonmedicinal groups, and Dr Ruth Baker for categorizing the code list for fractures into long bone and non–long bone groups. This article presents independent research funded by the National Institute for Health Research. The views expressed are those of the authors and not necessarily those of the National Health Service, the National Institute for Health Research, or the Department of Health.

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Pediatrics 2014;133;827
DOI: 10.1542/peds.2013-2554 originally published online April 14, 2014;

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