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# Neighborhood, family, and childhood and adolescent epilepsy: A nationwide epidemiological study from Sweden

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#### ARTICLE INFO

### ABSTRACT

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Keywords: Childhood and adolescent epilepsy Cumulative incidence Multilevel modeling Neighborhood-level deprivation Sociodemographic factors *Purpose:* To examine whether neighborhood deprivation increases the odds of hospital registration for childhood and adolescent epilepsy, after accounting for family- and individual-level sociodemographic characteristics.

*Methods:* An open cohort of all children aged 2–17 years was followed between January 1, 2000 and December 31, 2010. Children's residential addresses were geocoded and classified according to neighborhood deprivation. Data were analyzed by multilevel logistic regression, with family- and individual-level characteristics at the first level and level of neighborhood deprivation at the second level.

*Results:* During the study period, among a total of 1,020,766 children, 9309 (0.9%) were registered with childhood and adolescent epilepsy. Age-adjusted cumulative hospital rates of childhood and adolescent epilepsy increased with increasing neighborhood-level deprivation across all family- and individual-level sociodemographic categories. The odds ratio (OR) for hospital registration for childhood and adolescent epilepsy for those living in high-deprivation neighborhoods versus those living in low-deprivation neighborhoods was 1.15. High level deprivation remained significantly associated with higher odds of childhood and adolescent epilepsy after adjustment for family- and individual-level sociodemographic characteristics (OR = 1.12, 95% CI = 1.04-1.21, p = 0.003).

*Conclusions:* Our results suggest that neighborhood characteristics modestly affect the odds of hospital registration for childhood and adolescent epilepsy independently of family- and individual-level sociodemographic characteristics.

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# 1. Introduction

Epilepsy is a common disabling condition, which affects approximately 3% of the world population during their lifetime. Epilepsy is a major health risk in childhood and adolescence,<sup>1</sup> although the specific mechanisms behind childhood and adolescent epilepsy are largely unknown, except for cerebrovascular disorders, head trauma, brain tumors, developmental disorders, generative disorders, and infections, which explain approximately 50% of the cases.<sup>2</sup> There is a growing body of evidence implicating individual risk factors such as family history of epilepsy<sup>3</sup> and low socioeconomic status as risk factors for epilepsy in children and adolescents.<sup>4,5</sup> These individual-level sociodemographic characteristics do not, however, fully explain the disparities in childhood

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and adolescent epilepsy risk that exist between different population groups. Efforts have therefore been made to study whether the socioeconomic environment is associated with the risk of childhood and adolescent epilepsy. $^{6-8}$ 

The present study had the following two aims: (1) to determine whether the relationship between neighborhood deprivation and odds of hospital registration for childhood and adolescent epilepsy remained significant after adjusting for individual-level sociodemographic factors; and (2) to examine possible cross-level interactions between individual-level sociodemographic factors and neighborhood-level deprivation in order to determine whether neighborhood-level deprivation has a differential effect on odds of childhood and adolescent epilepsy across subcategories of family- and individual-level variables (effect modification).

# 2. Methods

Data used in this study were retrieved from a nationwide database that contains information on the entire population of Sweden for a period of 40 years. The dataset we used contains

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nationwide information on parents and their offspring at the individual and neighborhood levels, including comprehensive demographic and socioeconomic data. The data sources come from several Swedish national registers. The registers used in the present study were the Total Population Register, the Multi-Generation Register, the Hospital Discharge Register, and the Outpatient Register. The Swedish nationwide population and health care registers have exceptionally high completeness and validity.<sup>9</sup> Individuals (children and their parents) were tracked using their personal identification numbers, which are assigned to each resident of Sweden. Their identification numbers were replaced with serial numbers to provide anonymity. The followup period ranged from January 1, 2000 until first hospitalization/ out-patient registration for epilepsy during the study period, death, emigration or the end of the study period on December 31, 2010.

### 2.1. Outcome variable: childhood and adolescent epilepsy

The outcome variable in this study was a first hospital or outpatient diagnosis of childhood and adolescent epilepsy (age at diagnosis 2–17 years) during the study period. Data on in-hospital or out-patient diagnoses of epilepsy were retrieved from the Hospital Discharge Register (2000–2010) and Outpatient Register (2001–2010). These registers include information on all hospital visits, including diagnoses. We searched the Hospital Discharge Register and Out-Patient Register for the International Classification of Diseases (ICD)-10 code G40, denoting for epilepsy as the main diagnosis during the study period. The serial numbers were used to ensure that each individual appeared only once in the dataset, for his or her first hospital diagnosis of epilepsy during the study period.

# 2.2. Neighborhood-level deprivation

The home addresses of all Swedish individuals have been geocoded to small geographic units with boundaries defined by homogeneous types of buildings. These neighborhood areas, called small area market statistics or SAMS, each contain an average of 1000 residents and were created by the Swedish Government-owned statistics bureau Statistics Sweden. SAMS were used as proxies for neighborhoods, as they were in previous research.<sup>10,11</sup> Neighborhood of residence is determined annually using the National Land Survey of Sweden Register.

A summary index was calculated to characterize neighborhoodlevel deprivation. The neighborhood index was based on information about female and male residents aged 20-64 because this age group represents those who are among the most socioeconomically active in the population (i.e., a population group that has a stronger impact on the socioeconomic structure in the neighborhood than children, younger women and men, and retirees do). The neighborhood index was based on four items: low education level (<10 years of formal education), low income (income from all sources, including that from interest and dividends, <50% of the median individual income), unemployment (excluding full-time students, those completing military service, and early retirees), and receipt of social welfare. The index was used to categorize neighborhood deprivation as low (more than one SD below the mean), moderate (within one SD of the mean), and high (more than one SD above the mean).<sup>12</sup>

#### 2.3. Individual-level sociodemographic variables

Sex of the child or adolescent: male or female.

Age ranged from 2 to 17 years and was divided into three categories: 2–4, 5–11, and 12–17 years. Because a poor antenatal

and intrapartum environment is known to be a risk factor for epilepsy in term newborns,<sup>13,14</sup> children's age was limited to ages over 1 year.

*Marital status* was grouped according to the maternal marital status, as (1) married/cohabitating or (2) never married, widowed or divorced.

*Family income* was calculated as annual family income divided by the number of people in the family. The family income parameter took into consideration the ages of the family members and used a weighted system whereby small children were given lower weights than adolescents and adults. The sum of all family members' incomes was multiplied by the individual's consumption weight divided by the family members' total consumption weight. The final variable was calculated as empirical quartiles from the distribution.

Maternal and paternal educational level was categorized as completion of compulsory school or less ( $\leq$ 9 years), practical high school or some theoretical high school (10–11 years), and completion of theoretical high school and/or college/university ( $\geq$ 12 years).

*Maternal and paternal country of birth* was categorized as Sweden, Western countries (Western Europe, USA, Canada, Oceania), and others.

*Urban/rural status*: mothers were classified as living in a large city, a middle-sized town, or a small town/rural area. This variable was included because urban/rural status may be associated with access to preventive antenatal care. Large cities were those with a population of  $\geq$ 200,000 (Stockholm, Gothenburg and Malmö). Middle-sized towns were towns with a population of  $\geq$ 90,000 but <200,000. Small towns were areas with population of  $\geq$ 27,000 and <90,000; rural areas were areas with populations smaller than those of small towns. This classification yielded three equal-sized groups.

*Mobility*: children were classified as having "not moved" or "moved" to another neighborhood with the same or a different level of deprivation within five years before the start of the followup.

Maternal age at child birth was classified as <20, 20–24, 25–29, 30–34, 35–39, 40–44, and  $\geq$ 45 years) and paternal age at child birth was classified as <20, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, and  $\geq$ 50 years.

Maternal and paternal comorbidity was defined as hospitalization (within 10 years before the start of the follow-up) for a main diagnosis of the following diseases: (1) chronic obstructive pulmonary disease (ICD-9 490–496 and ICD-10 J40–J49); (2) alcoholism and alcohol-related diseases (ICD-9 291 and 303 and ICD-10 F10 and K70).

Because epilepsy is known to cluster in families,<sup>3</sup> children were classified according to whether or not they had a *parental or sibling history of epilepsy*.

## 2.4. Statistical analysis

The rate of cumulative hospital registration rates for epilepsy was calculated for the total population and for each subgroup after assessment of neighborhood of residence for children. Multilevel logistic regression was performed with individuals at the first level and neighborhoods at the second level.<sup>15,16</sup> The fixed effects are presented as odds ratios (ORs) with 95% confidence intervals (CIs) (significance would be accepted at p < 0.05). The multilevel approach allowed us to calculate random effects; they were calculated as the variance between neighborhoods and the explained variance. Logistic regression was considered to be a good approximation of Cox's proportional hazard models because we had a large sample size, a relatively low incidence rate, risk ratios of moderate size, and a relatively short follow-up period.<sup>17</sup>

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