Risk of hospital-treated injury in children with cerebral palsy: a population-based cohort study

Laura Määttänen[1,2,3], Liisi Ripatti[4], Päivi Rautava[1,3], Mari Koivisto[3], Leena Haataja[5]

[1]Department of Public Health, University of Turku, Turku, Finland; [2]Department of Paediatric Neurology, University of Turku, Turku, Finland; [3]Turku Clinical Research Centre, Turku University Hospital, Turku, Finland; [4]Department of Paediatric Surgery, Turku University Hospital, Turku, Finland; [5]Children's Hospital, Paediatric Research Centre, Helsinki University Hospital, University of Helsinki, Helsinki, Finland

Correspondence to:

Liisi Ripatti, MD, PhD

Department of Pediatric Surgery, Turku University Hospital

Kiinamyllynkatu 4-8, 20520 Turku, Finland

Tel: +358 2 3130456

Email: liisi.ripatti@tyks.fi

Abstract

Aim

To study if cerebral palsy (CP) increases the risk of hospital-treated injuries in children up to 13 years of age.

Methods

A Finnish population-based cohort (*n*=328 903) of children born during 2001 to 2006 was followed up for hospital-treated injuries until the end of 2014 via linkage of nationwide registers. The rate of first injury was compared in children with and without CP. The effect of CP type, gender, severe comorbidities (intellectual disability, epilepsy, hearing, or visual impairment), and the type of injury was evaluated.

Results

Children with CP had an increased risk of injury compared to children without CP (unadjusted hazard ratio [HR] 1.2, 95% confidence interval [CI] 1.0–1.4, *p*=0.030). Females with CP (*n*=191) had a higher risk of injury compared to females without CP (29% versus 22%, HR 1.4, 95% CI 1.1–1.9, *p*=0.01). Any comorbidity increased the risk of injury (HR 1.5, 95% CI 1.1–2.2, *p*=0.015) among children with CP. Children with CP had a higher risk of traumatic brain injury (HR 1.7, 95% CI 1.2–2.4, *p*=0.002) than children without CP.

Conclusion

Females with CP had the highest risk of hospital-treated injury. Children with CP are particularly prone to traumatic brain injuries.

Key messages

What is already known on this subject

- Children with CP have been suggested to be susceptible to fractures and dental injury.

What this study adds

- An increased risk of hospital-treated injury was observed among females with CP.
- Any severe comorbidity increases the risk of hospital-treated injury in children with CP.
- Children with CP have an increased risk of traumatic brain injury.

Introduction

Cerebral palsy (CP) is the most common severe motor disability in children and has an incidence of 1.5 to 2.5 per 1000 live birhts.[1] CP is often accompanied with comorbidities such as epilepsy (25–33%), intellectual disability (50%), blindness (10%), or deafness (4%).[2] To date, research on CP and susceptibility to injury is scarce, includes only a small number of participants,[3-7] or has mainly focused on one injury outcome such as fracture[7,8] or dental injury[3-6]. Most previous studies also reported only single-centre injuries[3-6]. These results are difficult to generalize, as only the studies related to fractures are based on population-based data.[7,8]

Children with severe CP who do not have independent walking ability fit into the recently defined population of children with medical complexity.[9,10] These children have been reported to account for 30% of paediatric health care expenditures and are more likely to use emergency hospital services.[9] Meehan et al. have reported that injuries and poisonings were responsible for 18% of all emergency presentations of children with CP; the percentage is proportionally higher among children with severe CP.[11] However, the risk of hospital-treated injury compared to children without CP was not analysed.

Disability is a known risk factor for injuries among all children.[12-14] In general, medical complexity increases the risk of injuries[6,8.13], particularly fractures[7,8]. Related to CP, seizures have been reported to increase the risk of fall injuries.[3,5,6,13] In two small single-centre studies, individuals with hemiplegia[3] and diplegia[5] were more prone to falls and dental injury compared to quadriplegia or other subtypes of CP.

In general, males are reported to be more prone to injuries than females.[15] However, there are only few relatively old studies of the effect of gender and the risk of dental injury and fractures in children with CP, and the results are controversial.[4,6,8]

The aim of this study was to determine if CP increases the risk of hospital-treated injuries in children. In addition, we aimed to clarify the risk according to CP subtype, gender, comorbidity, and type of injury. We hypothesized that ambulatory males would have a higher risk for injuries because males are generally more prone to injuries than females. In addition, we assumed that any major comorbidity would increase the injury risk.

Methods

Study design

This population-based study is based on linkage of nationwide registers. The outcome measure was hospital-treated injury in CP children. Children were followed for injuries from birth until 31 December 2014 or until first hospital-treated injury or death. The main explanatory variables were the diagnosis of CP, CP subtype, and gender. Covariates included age and any severe comorbidity, namely diagnosis of intellectual disability (IQ<70), epilepsy, and visual or hearing impairments.

The study protocol was approved by the ethics committee of the National Institute for Health and Welfare.

Data sources

All residents in Finland have a personal social security number that is used in all national registers thus allowing linkage of data. Birth cohort and gender data were identified from the Finnish Medical Birth Register. This register includes maternal information for all births in Finland. Data is collected on pregnancy, birth, and every live-born child up to one week of age. The Register of Congenital Malformations was used to identify children with major congenital anomalies. This register holds data on major congenital anomalies defined according to the European Surveillance of Congenital Anomalies.[16] The Finnish Hospital Discharge Register was used to identify children diagnosed as having CP or other neurodevelopmental diagnoses and injuries. The Finnish Hospital Discharge Register includes hospital inpatient and outpatient data and data on dates and discharge diagnoses from emergency

department visits in special health care. Since 1 January 1996, the 10th revision of the International Classification of Diseases (ICD-10) has been used as the diagnostic classification system for reporting to The Finnish Hospital Discharge Register. Mortality data was obtained from the Cause of Death Register.

The Register of Congenital Malformations, The Finnish Hospital Discharge Register, and the Finnish Medical Birth Register are maintained by the National Institute for Health and Welfare. The Cause of Death register and The Finnish Central Population Register are maintained by the Finnish Population Register Centre. In Finland there is no separate national register of individuals with CP.

Definition of cerebral palsy

In Finland, the diagnosis of CP is confirmed by paediatric neurologists. The clinical diagnosis of CP is based on international standards.[17] ICD-10 codes G80.0–G80.9 were used to identify children with different CP subtypes; spastic quadriplegia (G80.0), spastic diplegia (G80.1), spastic hemiplegia (G80.2), and other including children with dyskinetic, ataxic, and unspecified subtypes (G80.3–G80.9). The latest ICD-10 diagnosis was chosen for reliability after the re-evaluation of CP diagnosis at the age of four years.

Definition of comorbidity

The diagnosis of any intellectual disability (ICD-10 code F70–F79), epilepsy (ICD-10 code G40), visual impairment (ICD-10 code H54, including blindness and low vision presenting visual acuity less than 6/60 in the better eye based on best-corrected visual acuity), and hearing impairment (ICD-10 code H90–H91, including conductive and

sensorineural loss and other hearing loss) were collected from the Finnish Hospital Discharge Register.

Definition of injury

Hospital-treated injuries were defined as the first outpatient or inpatient injury diagnosis in special health care during the follow-up period. Types of injuries were categorized as fractures, traumatic brain injuries (including ICD-10 codes S06.x and T90.5), burns, or other type of injury including superficial head injury, dislocation, strain of joints and ligaments, injury of nerves, blood vessels, and organs, foreign body entering through natural orifices, and certain other consequences of external causes.[18] Only the first of any primary injury and related codes on each child were included as we could not exclude repeated visits for the same injury.

Study population

Inclusion and exclusion criteria for the current study are shown in Figure 1. All live births from January 2001 to 31 December 2006 were identified (*n*=341 632). Deaths during the first three years of life (*n*=1232), including eight with presumed CP and children with a major congenital anomaly (*n*=11 497) were excluded. A total of 328 903 eligible participants remained. At the end of follow up, 582 children (0.18% of the study cohort) had received a diagnosis of CP. The diagnosis of CP was re-evaluated at the age of 4 years or older at the last hospital visit with CP diagnosis (*n*=532). Those with last CP diagnosis at under 4 years of age (*n*=50) were excluded for reliability reasons because the Surveillance of Cerebral Palsy in Europe (SCPE) recommends re-evaluating the diagnosis at the age of 4 years.[19] Children with diseases other than CP leading to a loss of motor function were excluded (*n*=87).

These included inflammatory diseases (G00–G09; *n*=20), systemic atrophies (G10–G14; *n*=8), extrapyramidal and movement disorders (G20–G26; *n*=9), other degenerative diseases of the nervous system (G30–G32; *n*=3), demyelinating diseases of the central nervous system (G35–G37; *n*=5), episodic and paroxysmal disorders (G42–G47; *n*=35), nerve, nerve root, and plexus disorders (G50–G59; *n*=7), polyneuropathies and other disorders of the peripheral nervous system (G60–G64; *n*=4), diseases of myoneural junction and muscle (G70–G73; *n*=4), and other disorders (G90–G99; *n*=60).

Children without CP diagnosis during follow up were chosen as controls. Overall, 445 children with CP and 328 321 children without CP were included.

Statistical analyses

The data were described using percentages and frequencies or with medians, IQR and minimum and maximum values. In addition, incidence rates were calculated. Categorical background variables were compared between children with CP and children without CP using Pearson's chi-squared test.

Cox proportional hazard models were used in assessing the risk for any injury and the risk for certain type of injury in children with CP compared with children without CP. In addition, analyses in assessing the risk for any injury were performed separately for both genders and for subtypes of CP. Subgroup analyses were conducted to evaluate the effect of gender and presence of any major neurodevelopmental comorbidities (intellectual disability, epilepsy, visual impairment, hearing impairment) on injury risk among children with CP. All Cox proportional hazard models included age as a

time dependent covariate. The outcome measure was the first hospital-treated injury in all the included children irrespective of CP status. Only the first of any hospital-treated injuries and related code(s) on each child were included to reduce the possible bias caused by repeated visits for the same injury. In case of multiple injury diagnosis at the same visit they were all reported in the frequency table. Results are presented with hazard ratios (HR), 95 % confidence interval and *p*-values.

The level of statistical significance was set at $p<0.05$. Statistical analyses were carried out using the SAS® system for Windows, version 9.4. (SAS Institute Inc., Cary, NC, USA).

Results

Background characteristics

A total of 445 (43% females) children with CP and 328 321 (49% females) children without CP were included. Gender distribution, CP subtype, and the rate of comorbidities are shown in Table I.

Injury and CP

By the end of the study, 127 (29%) out of the 445 of children with CP had at least one hospital-treated injury compared to 78 690 (24%) children without CP. Accordingly, the incidence of injuries was 30/1000 in children with CP and 25/1000 in children without CP. Among children with CP, the median age at time of injury was 5 years 8 months (IQR 6 years 3 months, range 4 months to 13 years 4 months); the corresponding median age for children without CP was 5 years 9 months (IQR 6 years 0 months, range 0 months to 13 years 6 months). Overall, the unadjusted HR was increased in children with CP when compared with children without CP (HR 1.2, 95% CI 1.02–1.4; p=0.030).

Effect of CP subtype

The highest proportion of children having had any hospital-treated injury were among children with quadriplegic CP (37 %, 11/30) followed by children with diplegia (31%, 38/124), ataxic, dystonic, or other type of CP (29 %, 27/94), and hemiplegia (26%, 51/197). The risk of injury was calculated separately for all subtypes of CP compared with children without CP. All comparisons showed statistically insignificant results.

Effect of gender

The rate of injury was 29% in females and 28% in males with CP. Accordingly, the incidence of injuries was 31/1000 in females and 29/1000 in males with CP. In the statistical analysis the difference according to gender was insignificant (HR 0.935, 95 % CI 0.659-1.328, p=0.708). The interaction between gender and CP subtype was also insignificant (p = 0.170). The corresponding incidence of injuries for children without CP were 22/1000 in females and 27/1000 in males.

Females with CP were more likely to sustain injury than females without CP (29% versus 22%, HR 1.4, 95% CI 1.1–1.9; p=0.01). Among males, the corresponding figures were not significant (28% versus 26%, HR 1.1, 95% CI 0.8–1.3; p=0.64). Spastic quadriplegia served as a reference as the absolute proportion of hospital-treated injuries was highest among patients with quadriplegia. Females with spastic hemiplegia and other CP types were significantly associated with a lower risk of injury compared with females with spastic quadriplegia (Table II). Among males, the risk according to any CP subtype was not significant (p=0.64).

Effect of comorbidity

Overall, 203 (46%) children with CP had at least one comorbidity and 69 out of 203 (34%) had a hospital-treated injury. A total of 115 (26%) children with CP had intellectual disability, 148 (33%) had epilepsy, 25 (6%) had severe hearing impairment, and 37 (8%) had severe visual impairment. The presence of any comorbidity increased the HR rate 54% (HR 1.5, 95% CI 1.1–2.2; p=0.015) for injuries compared to CP alone. Co-morbidity increased the risk of injury irrespective

of gender. The interaction between any co-morbidity and gender was statistically nonsignificant among children with CP (p=0.79).

Type of injury

The types of injury are shown in Table III. Children with CP had a 1.7-fold increased risk for traumatic brain injury (HR 1.7, 95% CI 1.2–2.4; p=0.002).

Discussion

This is the first study to analyse the risk of hospital-treated injury in children with CP on a population basis. We observed an increased risk of injury among children with CP compared with children without CP. By the end of follow up, 29% of the children with CP compared to 24% of controls had been hospital-treated for an injury. The highest proportion of children with any injury was observed among children with quadriplegic CP (37%). Furthermore, females with CP had a higher risk for hospital-treated injuries compared with females without CP. We also studied hospital-treated injuries with reference to severe comorbidities. Intellectual disability, epilepsy, and hearing or visual impairment increased the risk of injuries among children with CP irrespective of gender. Traumatic brain injury was more common among children with CP compared to children without CP.

Use of specific CP registers is recommended to prevent case selection bias.[20] There is no CP register available in Finland. Accordingly, we were not able to add information on severity of CP into statistical analysis. The Finnish Hospital Discharge Register was used as a source of patient data. The Finnish public health service is available for all citizens. Thus, we were able to collect population-based data and rely on the accurate diagnosis of CP. Furthermore, the data of the Finnish national registers are considered highly valid.[21,22] A limitation of our study is that we did not have a sufficient number of participants to study injury type in different CP subtypes.

In addition, only the first of any hospital-treated injury of each child was included to reduce the possible bias caused by repeated visits for the same injury. However, this

did not allow us to analyse the risk of repeated injury. Due to the study design the first recorded hospital-treated injury could have been at any age up to 13 years of age both in children with and without CP. However, the median age at time of injury was practically the same in children with and without CP. Since age has a significant effect on the risk of injury it was added as a time dependent variable in the statistical models.

In agreement with several other studies, the majority of children with CP in this study were male.[3,6,8,23] In general, males without CP are more often affected by recurrent injuries than females.[15] In this study, females with CP had more injuries than females without CP, however, there was no difference between males with and without CP.. Two previous studies found more dental injuries among females than males with CP[4,5] but Cardoso et al.[6] and Jalihal et al.[3] reported a similar injury risk among females and males with CP. In this study, there was no clinically or statistically significant gender related difference in incidence of injuries among children with CP.

In our study, females with hemiplegia seemed to have less injuries than females with quadriplegia. This is a novel observation and has not been discussed as such in the previous literature. On the basis of a literature review, Romeo et al. postulated that psychomotor development under the age of 4 years seems to be better in females than in males with hemiplegia.[23] Among children with hemiplegia younger than 4 years of age, females scored better than males for global development and showed better standing ability.[23]

Injury risk and cerebral palsy

Previous studies on the risk of injury in children with CP are rare and fragmented and have often concentrated of dental injuries and fractures. The relationship between CP and injuries is complex and requires measures across a broad range of variables.[24] As shown in our data and in previous reports of disability status, there is generally an increased injury risk among children with multiple disabilities.[13,25] The effect of intellectual disability on injury risk is commonly studied in combination with comorbidities. In a study of school-related injuries, children with multiple disabilities had a 70% increased risk of injury compared with those with developmental disabilities.[25] Epilepsy is a known risk factor of injury.[26] Consistent with previous studies,[27,28] a third of children with CP had epilepsy by the end of follow up in this study. In a previous study,[14] hearing impairment increased the risk of injuries among children. Visual impairment is also associated with risk of injuries.[12]

Children with CP may be at risk for fractures due to low bone mineral density and limited physical excersise.[7] Jalihal et al. proposed that the inability of individuals with CP to control abrupt body movements may be a predisposing factor that increases the risk of traumatic injuries to the teeth.[3] The limitations in motor coordination and balance may also contribute to the higher proportion of traumatic brain injuries in our population. In a hospital sample, head injuries also accounted for 42% of injuries among children with disabilities, most commonly in children with epilepsy and CP.[13]

In conclusion, we showed that females with CP had the highest risk of hospital-treated injury and children with CP are particularly prone to traumatic brain injuries. More

studies are needed on the causes of injury, injury severity and recurrence in children with CP to allow consideration of the need of preventive interventions.

References

1 Bax M, Goldstein M, Rosenbaum P, et al. Executive Committee for the Definition of Cerebral Palsy. Proposed definition and classification of cerebral palsy, April 2005. *Dev Med Child Neurol* 2005; **47**: 571–6.

2 Novak I, Hines M, Goldsmith S, Barclay R. Clinical prognostic messages from a systematic review on cerebral palsy. *Pediatrics* 2012; **130**: e1285–312.

3 Jalihal S, Nagarajappa R, Sharda A, Asawa K, Tak M. Assessment of dental trauma among cerebral palsy individuals in Udaipur city. *Dent Traumatol* 2012; **28**: 448–51.

4 Holan G, Peretz B, Efrat J, Shapira Y. Traumatic injuries to the teeth in young individuals with cerebral palsy. *Dent Traumatol* 2005; **21**: 65–9.

5 Santos MTBR, Souza CBC. Traumatic dental injuries in individuals with cerebral palsy. *Dent Traumatol* 2009; **25**: 290–94.

6 Cardoso AMR, Silva CRD, Gomes LN, Gomes Mda N, Padilha WWN, Cavalcanti AL. Dental trauma in Brazilian children and adolescents with cerebral palsy. *Dent Traumatol* 2015; **31**: 471–6.

7 Mughal MZ. Fractures in children with cerebral palsy. *Curr Osteoporos Rep* 2014; **12**: 313–8.

8 Uddenfeldt Wort U, Nordmark E, Wagner P, Duppe H, Westbom L. Fractures in children with cerebral palsy: a total population study. *Dev Med Child Neurol* 2013; **55**: 821–6.

9 Kuo DZ, Houtrow AJ, Council on Children with Disabilities. Recognition and Management of Medical Complexity. *Pediatrics* 2016; **138**: e20163021.

10 Murphy N. Emergency department visits for children with cerebral palsy: what triggers the call for help? *Dev Med Child Neurol* 2017; **59**: 1110.

11 Meehan E, Williams K, Reid SM, et al. Comparing emergency department presentations among children with cerebral palsy with general childhood presentations: a data linkage study. *Dev Med Child Neurol* 2017; **59**: 1188–95.

12 Roberts I, Norton R. Sensory deficit and the risk of pedestrian injury. *Inj Prev* 1995; **1**: 12–4.

13 Berggreen S. Accidents and surgical emergencies in a population of mentally retarded children. *Acta paediatr Scand* 1973; **62**: 289–96.

14 Mann JR, Zhou L, McKee M, McDermott S. Children with hearing loss and increased risk of injury. *Ann Fam Med* 2007; **5**: 528–33.

15 Madden C, Garrett JM, Cole TB, Runge JW, Porter CQ. The urban epidemiology of recurrent injury: beyond age, race, and gender stereotypes. *Acad Emerg Med* 1997; **4**: 772–5.

16 European Surveillance of Congenital Anomalies [Internet]. Cited 2018 Dec 3. Available from: http://www.eurocat-network.eu/content/EUROCAT-Guide-1.3.pdf

17 Smithers-Sheedy H, Badawi N, Blair E, et al. What constitutes cerebral palsy in the twenty-first century? *Dev Med Child Neurol* 2014; **56**: 323–8.

18 Fingerhut LA, Warner M. The ICD-10 injury mortality diagnosis matrix. *Inj Prev* 2006; **12**: 24–9.

19 Surveillance of Cerebral Palsy in Europe (SCPE) Reference and Training manual [Internet]. Cited 2018 Dec 3. Available from: http://www.scpenetwork.eu/

20 Goldsmith S, McIntyre S, Smithers-Sheedy H, et al. An international survey of cerebral palsy registers and surveillance systems. *Dev Med Child Neurol* 2016; **58** (Suppl 2): 11–7.

21 Greenlees R, Neville A, Addor MC, et al. Paper 6: EUROCAT member registries: organization and activities. *Birth Defects Res A Clin Mol Teratol* 2011; **91** (Suppl 1): S51–S100.

22 Sund R. Quality of the Finnish Hospital Discharge Register: a systematic review. *Scand J Public Health* 2012; **40**: 505–15.

23 Romeo DM, Cioni M, Battaglia LR, Palermo F, Mazzone D. Spectrum of gross motor and cognitive functions in children with cerebral palsy: gender differences. *Eur J Paediatr Neurol* 2011; **15**: 53–8.

24 Cairney J. Deficits in attention, motor control, and perception and increased risk of injury in children. *Dev Med Child Neurol* 2014; **56**: 1040–1.

25 Ramirez M, Peek-Asa C, Kraus JF. Disability and risk of school related injury. *Inj Prev* 2004; **10**: 21–6.

26 Wirrell EC. Epilepsy-related injuries. *Epilepsia* 2006; **47 (**Suppl 1): 79–86.

27 Sellier E, Uldall P, Calado E, et al. Epilepsy and cerebral palsy: characteristics and trends in children born in 1976–1998. *Eur J Paediatr Neurol* 2012; **16**: 48–55.

28 Andersen GL, Irgens LM, Haagaas I, Skranes JS, Meberg AE, Vik T. Cerebral palsy in Norway: prevalence, subtypes and severity. *Eur J Paediatr Neurol* 2008; **12**: 4–13.

Table I: Background characteristics of the study population (*n*=328,903).

	Cerebral Palsy, *n*=445 Total *n* (%)	Controls, N=328,321 Total *n* (%)	*p*-value
Gender			0.01
Female	191 (42.9)	160,883 (49.0)	
Male	254 (57.1)	167,438 (51.0)	
CP-specific stratum, (ICD-10), N=445			
Spastic quadriplegia (G80.0)	30 (6.7)		
Spastic diplegia (G80.1)	124 (27.9)		
Spastic hemiplegia (G80.2)	197 (44.3)		
Other CP (G80.3-9)	94 (21.1)		
Comorbidity	203 (45.6)		
Comorbidity without injury	134 (66.0)		
Comorbidity and injury	69 (34.0)		

Missing data 0%

Table II: Injury risk among children by type of cerebral palsy (CP) according to gender (adjusted for age).

	Total *n*	*n* with injury	%	HR (95% CI)	*p*-value
Female					0.11
Spastic quadriplegia	11	6	54.6	1[Reference]	
Spastic diplegia	51	18	35.3	0.56 (0.22−1.43)	0.23
Spastic hemiplegia	92	24	26.1	0.39 (0.16−0.97)	0.043
Other CP	37	8	21.6	0.32 (0.11−0.92)	0.034
Male					0.64
Spastic quadriplegia	19	5	26.3	1[Reference]	
Spastic diplegia	73	20	27.4	1.02(0.38−2.72)	0.97
Spastic hemiplegia	105	27	25.7	0.95 (0.37−2.49)	0.92
Other CP	57	19	33.3	1.38 (0.52−3.72)	0.52

Table III: Injury according to the type of first injury with respect to cerebral palsy (CP).

	CP *n*=445		No CP *n*=328,321		Hazard Ratio	*p*-value
Injuries	*n*	%	*n*	%	(95% CI)	
Any injury	127	28.5	78,690	24.0	1.21 (1.02-1.44)	0.03
Fracture	33	7.4	22,503	6.9	1.12 (0.80−1.57)	0.52
Traumatic brain injury	34	7.6	15,218	4.6	1.71 (1.22-2.40	0.002
Burn	5	1.1	3136	0.96	1.24 (0.52−2.98)	0.63
Other injury	55	12.4	38933	11.9	1.08 (0.83−1.41)	0.56

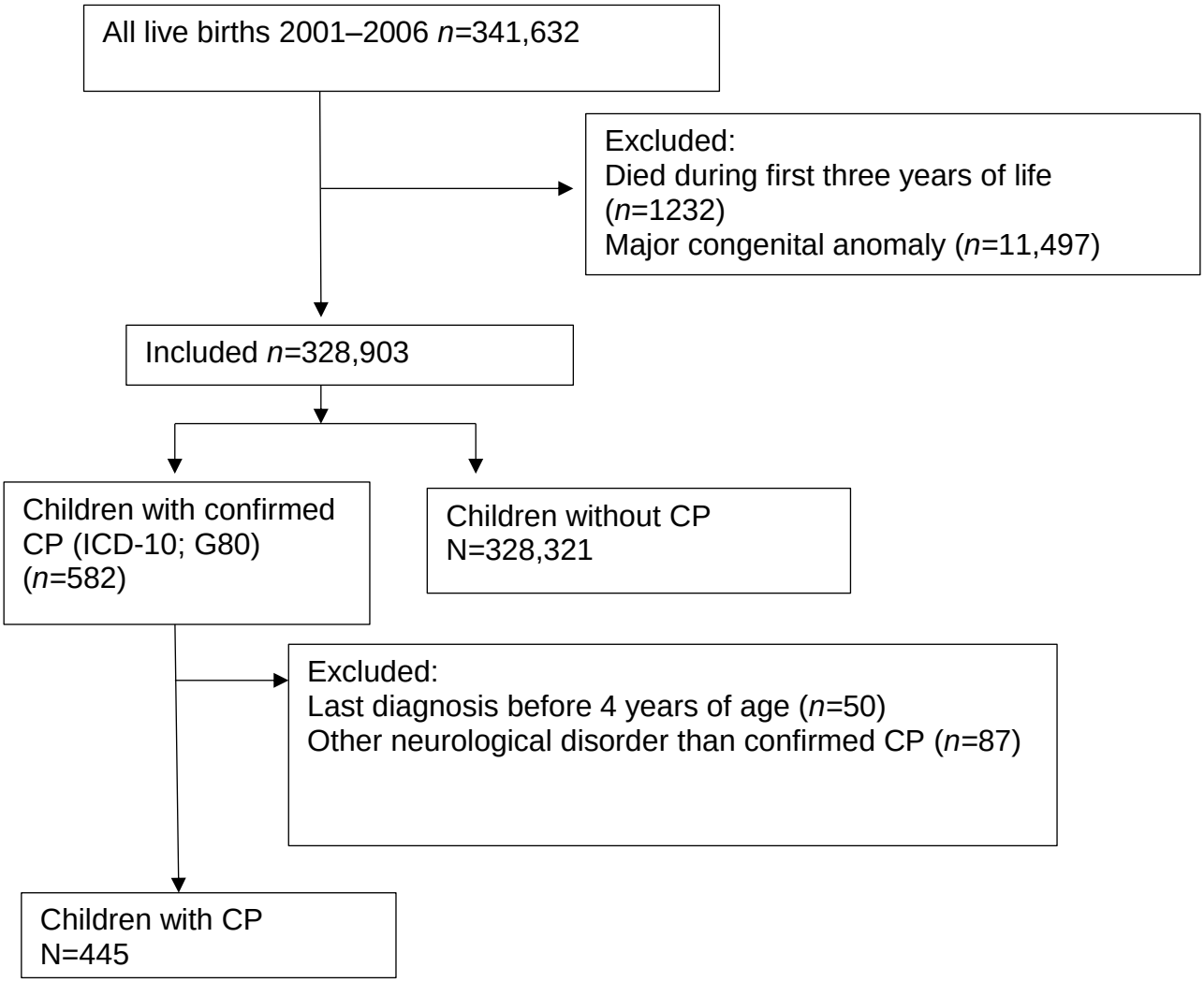

Figure 1. The flow chart of the study population