Cerebral Palsy Among Children Born Moderately and Late Preterm

WHAT'S KNOWN ON THIS SUBJECT: The incidence of cerebral palsy is dependent on the gestational age in very preterm infants and risk factors have been identified for term infants. The risk has also proved to be greater among late preterm births compared with term.

WHAT THIS STUDY ADDS: The incidence of cerebral palsy was 24-fold in moderately preterm and 6-fold in late preterm infants compared with full-term infants. The most prominent risk factors included asphyxia and intracranial hemorrhage. The incidence diminished over time and with increasing gestational age.

abstract

OBJECTIVE: To compare the incidence of and risk factors for cerebral palsy (CP) in moderately preterm (MP) (32^{+0}–33^{+6} weeks) and late preterm (LP) (34^{+0}–36^{+6} weeks) infants with those in very preterm (VP) ($<32^{+0}$ weeks) and term infants ($\geq$37 weeks).

METHODS: The national register study included all live-born infants in Finland from 1991 to 2008. Infants who died before the age of 1 year, had any major congenital anomaly, or had missing data were excluded. A total of 1 018 302 infants were included in the analysis and they were analyzed in 4 subgroups (VP, MP, LP, and term) and 3 time periods (1991–1995, 1996–2001, and 2002–2008).

RESULTS: By the age of 7 years, 2242 children with CP were diagnosed (0.2%). CP incidence was 8.7% in the VP, 2.4% in the MP, 0.6% in the LP, and 0.1% in the term group. The risk of CP was highest in the study period 1991–1995 in all groups. Factors predictive of an increased CP risk in the MP and LP groups included resuscitation at birth (odds ratio 1.60; 95% CI 1.01–2.53 and 1.78; 1.09–2.90), antibiotic treatment during the first hospitalization (1.63; 1.08–2.45 and 1.67; 1.13–2.44), 1-minute Apgar score <7 (1.70; 1.15–2.52 and 1.80; 1.21–2.67) and intracranial hemorrhage (7.18; 3.60–14.3 and 12.8; 5.58–29.2).

CONCLUSIONS: The incidence of CP is higher in LP and MP infants compared with term infants. There is a nonlinear decrease in incidence over time and with increasing gestational age. *Pediatrics* 2014;134:e1584–e1593

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KEY WORDS

cerebral palsy, preterm, moderately preterm, late preterm, infant

ABBREVIATIONS

CI—confidence interval
CP—cerebral palsy
GA—gestational age
HDR—Hospital Discharge Register
ICD—*International Classification of Diseases*
LP—late preterm
MBR—Medical Birth Register
MP—moderately preterm
MRI—magnetic resonance imaging
NIHW—National Institutes of Health and Welfare
OR—odds ratio
PROM—premature rupture of membranes
RDS—respiratory distress syndrome
SGA—small for gestational age
VP—very preterm

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The preterm birth rate has increased markedly during the past decades, mainly due to the increase in late preterm (LP) births in a number of countries, especially in the United States.[1,2] LP infants are defined as infants born between gestation weeks 34^{+0} and 36^{+6}; they account for more than 70% of all prematurely born infants in the United States.[2,3] This group has commonly been referred to as "near term" infants, but the description has been felt inappropriate in that it underestimates the risks of these preterm infants.[3] Moderately preterm (MP) (32^{+0}–33^{+6} gestation weeks) and LP infants comprise >80% of all preterm births together.[4,5] The rate of preterm delivery in Finland has not increased significantly, in contrast to trends in other countries.[6]

The brain of the MP and LP infant is more vulnerable to injury than the brain of full-term infants. The weight of the brain at 34 weeks of gestation is only 65% of the term brain and the total brain volume increases linearly with increasing gestational age (GA).[7] Morbidity and mortality levels among MP and LP infants are higher compared with term.[8–10] In the United States and the United Kingdom, LP infants have been found to have poorer neurodevelopmental outcomes than term infants,[4,11–18] but some studies did not find more neurodevelopmental problems among healthy LP children.[19] Outcome data may vary due to diverse conditions in different countries and populations. Thus, more data and large prospective studies are needed. No statistics on the long-term outcome of MP and LP infants have been reported from the Nordic countries.

Cerebral palsy (CP) is defined as a disorder of motor behavior attributable to disturbances in the developing fetal or infant brain.[20] According to the standard guideline, the diagnosis of CP is based on medical history, imaging (ultrasound, high-resolution magnetic resonance imaging [MRI]) data, and clinical multidisciplinary evaluations in the pediatric neurology units. The CP incidence has been shown to be dependent on GA in very preterm (VP) infants.[21] Also in LP infants, the risk has been almost threefold compared with the term group.[22] Risk factors of CP have been identified for term infants,[23] but less for MP and LP infants.

Our aim was to compare the CP incidence among LP and MP infants to that among VP and term infants and to identify risk factors for CP in the Finnish population. The hospitalizations, reimbursements for medicine expenses, and disability allowances due to CP were established to study the burden of CP. Also the effect of time period on the incidence of CP was studied.

METHODS

This national register study population consisted of all, a total of 1 039 263 infants born in Finland from 1991 to 2008. The baseline characteristic data were collected from the Medical Birth Register (MBR), maintained by the National Institutes of Health and Welfare (NIHW). This register contains information on the mother's health and interventions during pregnancy and delivery and on the infant's health and procedures undergone during the first 7 days of life. It collects data on all live births and stillbirths from the GA of 22^{+0} weeks onward and/or birth weight of at least 500 g.

Data on deaths were obtained from the Cause-of-Death Register maintained by Statistics Finland and data on major structural anomalies and chromosomal defects[24] from the Register of Congenital Malformation, maintained by the NIHW. Infants who died before the age of 1 year (n = 2613), children with at least 1 major congenital anomaly (n =13 007), and cases lacking data on GA were excluded (n = 5520).

The remaining 1 018 302 infants (98.0% of all) comprised the cohort for analysis. Infants were followed up to 7 years of age or to 2009. The study population was divided into subgroups, the gestation-week categories being VP ($\leq 32^{+0}$ weeks, n = 6347), MP (32^{+0}–33^{+6} weeks, n = 6799), LP (34^{+0}–36^{+6} weeks, n = 39 932), and term ($\geq$37 weeks, n = 965 224). The GA was based on early pregnancy ultrasound and correction of GA was made if the ultrasound-based estimation had a discrepancy of 5 to 7 days or more compared with menstrual anamnesis.

Pregnancy- and delivery-related diagnoses of mothers were collected from the Hospital Discharge Register (HDR). This is also maintained by the NIHW and contains information on admission and discharge dates, diagnoses, and surgical procedures. Since 1998, the data also cover hospital outpatient visits. Diagnoses were coded according to the *International Classification of Diseases, Ninth Revision* (ICD-9) in 1987 to 1995 and according to the *10th Revision* (ICD-10) from 1996. Three different time periods were compared: 1991 to 1995, 1996 to 2001, and 2002 to 2008. These periods were chosen because the classification system of disease was changed in 1996 from ICD-9 to ICD-10 and the MBR changed the data collection forms 1.10.1990 and 1.1.1996.

Preeclampsia was defined as high blood pressure, edemas, and proteinuria by ICD-10 codes O10 to O16 (ICD-9 codes 6420–6429). Premature rupture of membranes (PROM) was sought via ICD-10 codes O42.0 to O42.9 (ICD-9 codes 6581–6583) in the mothers' diagnoses. Pregnancy-related risk factors were the number of fetuses and their order, timing of birth, in vitro fertilization, and cervical cerclage. Resuscitation at birth included intubation, mechanical ventilation, and/or chest compressions. Phototherapy has been given according to guidelines depending on gestation weeks and some minor variance may exist in guidelines between hospitals. Respiratory distress syndrome (RDS) was diagnosed on the basis of typical changes in chest radiograph, excessive

need of oxygen supply, and surfactant therapy. It was traced in the register with ICD-10 code P22.0 (ICD-9 code 769). Small for GA (SGA) infants were defined as those with a birth weight <2 SDs below the mean weight for GA and large for GA infants as those with a birth weight >2 SDs over the mean weight for GA according to the Finnish gender-specific fetal growth curves.[25] Umbilical artery pH cutoff <7.05 was used to define fetal acidemia.[26,27]

Only variables with good validity in the registers were chosen for the analysis.[28,29] Intracranial hemorrhage diagnosis was based on the head ultrasound or MRI findings and classified according to the Papile classification system.[30] MP and LP infants do not undergo routine head ultrasounds but infants with asphyxia and/or neurologic symptoms, and/or with need of intensive care are routinely examined with head ultrasound. One-minute Apgar scores were included in the multivariate analysis, but 5-minute scores were excluded because it was found from the register only from 2004 onward. Information on maternal hypertension was available only in combination with preeclampsia. Mother's diabetes included gestational diabetes, and type 1 and 2 diabetes. Neither data on chorioamnionitis nor antenatal viral infection was possible to define reliably according to registers. Infants were defined to be asphyxiated when they had a 1-minute Apgar score <7 and needed intubation during delivery room resuscitation.

All inpatient and outpatient visits due to a CP diagnosis in public hospitals were registered according to the HDR. The diagnosis of CP in Finland is based on medical history, ultrasound and MRI data, and multidisciplinary evaluations in the pediatric neurology units of 20 secondary-level central hospitals and 5 tertiary-level university hospitals. CP is usually evident within first 2 years of life and almost always by the age of 3 to 4 years, and the diagnosis is included in the HDR as soon as it has been established. Information on special reimbursements and benefits for disability were collected from the register of the Social Insurance Institution of Finland. All data linkages were done by using unique personal identity codes anonymized by the authorities.

A case with CP was recorded if the individual was detected in the HDR and/or in the Reimbursement Register of the Social Insurance Institution with ICD-10 codes G80 to G83 in 1996 to 2008 and ICD-9 codes 342 to 344 in 1991 to 1995. Subtypes of CP were defined by topographic involvement (hemiplegia, diplegia, quadriplegia, and other types) and sought from registers with corresponding ICD codes (hemiplegia ICD-10 G80.2/ICD-9 343.1 and 343.4; diplegia G80.1/343.0; quadriplegia G80.0/343.2 and other types including the rest of CP diagnoses according to the baseline ICD code definitions).

Statistical Analysis

Characteristics of infants alive at age of 1 year and those of their mothers were described by means with SDs in the case of normal distributed continuous variables, by medians with interquartile range in skew distributed variables, and otherwise if variables were categorical by number of values with percentages. GA groups were compared for each other by Mann-Whitney test, χ^2 test, or Fisher's exact test (Tables 1, 2, and 3). Risk factors for CP were sought by logistic regression analysis by using multivariate enter models for each GA group separately (Table 4). In enter model, all variables were entered simultaneously into the model separately for each gestational week class. Association of gestation weeks for CP was studied by adjusting a multivariate model by gestation week classes, term class as reference. Results were shown by odds ratios (ORs) with 95% confidence intervals (95% CIs) in modeling risk factors for CP. A large number of variables were included in the analysis, because in a large population, also less well-known predictors for CP can be detected. Statistical analyses were performed on IBM SPSS Statistics version 20.0.0 (IBM SPSS Statistics, IBM Corporation, Chicago, IL). $P < .05$ was considered statistically significant.

RESULTS

LP infants accounted for 75% and MP infants for 13% of all prematurely born infants in Finland during this study period. Characteristics of newborns and mothers are shown in Table 1. Proportion of all preterm births was 5.02% from 1991 to 1995, 5.43% from 1996 to 2001, and 5.18% from 2002 to 2008. The proportion of MP and LP infants remained constant; MP infants accounted for 0.63% to 0.69% and LP infants from 3.82% to 4.08% of all births.

After combining the register data, 2242 CP cases were identified. The incidence of CP was 0.22%, and it decreased nonlinearly with increasing GA, and with time. The decrease by time was greatest in the VP group, and during the latest time period (ie, after 2001) (Table 2, Fig 1). The analysis of CP subtypes showed that the proportion of diplegia cases was greatest in the VP group and of hemiplegia cases in the term group (Table 3).

Birth during the earliest period, 1991 to 1995, 1-minute Apgar score <7, and intracranial hemorrhage predicted CP in all GA categories in the logistic regression model (Table 4). Resuscitation at birth was associated with an increased risk in MP and LP groups and in the term group. SGA and antibiotic treatment during the first hospitalization seemed to predict an increased risk of CP in the LP and the term groups. PROM was associated with an increased and antenatal steroid treatment with a decreased risk of CP in the MP group. Antenatal steroid administration was registered from 2004 onward. In the analysis for 2004 to 2008, the OR for CP

TABLE 1 Characteristics of Infants Alive at Age of 1 Year and Their Mothers, Followed to Age of 7 Years, 1991–2008 (n = 1 018 302; Infants Who Died When Younger Than 1 Year and Infants With Major Congenital Malformations Excluded)

	VP <32 wk, n = 6347		MP 32^{+0}–33^{+6} wk, n = 6799		LP 34^{+0}–36^{+6} wk, n = 39 932		Term ≥37 wk, n = 965 224		p^1 MP versus VP	p^2 LP versus VP	p^3 MP versus T	p^4 LP versus T
Study period, y, n (%)									P = .725	P = .080	P = .002	P < .001
1991–1995	1780	(0.58)	1937	(0.63)	11 779	(3.82)	293 233	(95.0)				
1996–2001	2159	(0.66)	2270	(0.69)	13 362	(4.08)	309 893	(94.6)				
2002–2008	2408	(0.63)	2592	(0.68)	14 791	(3.87)	362 098	(94.8)				
Mother												
Age, mean (SD)	30.2	(5.8)	29.8	(5.7)	29.7	(5.5)	29.2	(5.3)	P < .001	P < .001	P < .001	P < .001
Smoking, n (%)	1192	(18.8)	1186	(17.4)	6605	(16.5)	144 097	(14.9)	P < .001	P < .001	P < .001	P < .001
Primipara, n (%)	3329	(52.4)	3792	(55.8)	20 041	(50.2)	392 588	(40.7)	P < .001	P = .001	P < .001	P < .001
Earlier deliveries, Md (IQR)	0	(0–1)	0	(0–1)	0	(0–1)	1	(0–2)	P < .001	P = .092	P < .001	P < .001
Diabetes, n (%)	92	(1.4)	148	(2.2)	969	(2.4)	8468	(0.9)	P = .002	P < .001	P < .001	P < .001
Pregnancy												
No. of fetuses, n (%)									P < .001	P < .001	P < .001	P < .001
1	4525	(71.3)	4593	(67.6)	31 065	(77.8)	948 715	(98.3)				
2	1621	(25.5)	1955	(28.8)	8549	(21.4)	16 490	(1.7)				
≥3	201	(3.2)	251	(3.7)	318	(0.8)	19	(0.0)				
Assisted reproductive technology, n (%)	609	(9.6)	768	(11.3)	2764	(6.9)	16 264	(1.7)	P = .001	P < .001	P < .001	P < .001
Cervical cerclage, n (%)	69	(1.1)	40	(0.6)	102	(0.3)	515	(0.1)	P = .002	P < .001	P < .001	P < .001
Delivery												
Place of birth, n (%)									P < .001	P < .001	P < .001	P < .001
University hospital (level III)	4957	(78.1)	3995	(58.8)	17 156	(43.0)	299 477	(31.0)				
Central hospital (level II)	1343	(21.2)	2727	(40.1)	17 553	(44.0)	444 961	(46.1)				
Other[a]	42	(0.7)	77	(1.1)	5220	(13.1)	220 659	(22.9)				
Mode of delivery, n (%)									P < .001	P < .001	P < .001	P < .001
Vaginal	2537	(40.0)	3212	(47.2)	26 687	(66.8)	820 961	(85.1)				
Cesarean	3798	(59.8)	3584	(52.7)	13 212	(33.1)	143 493	(14.9)				
Newborn												
Boys, n (%)	3441	(54.2)	3730	(54.9)	21 660	(54.2)	490 223	(50.8)	P = .457	P = .967	P < .001	P < .001
Birth weight, g, Md (IQR)	1290	(995–1570)	1970	(1730–2200)	2670	(2360–2985)	3590	(3276–3910)	P < .001	P < .001	P < .001	P < .001
≤1500 g	4406	(69.4)	735	(10.8)	253	(0.6)	23	(<0.1)				
>1500 g	1925	(30.3)	6056	(89.1)	39 658	(99.3)	964 956	(100)				
Gestational weight, n (%)									P < .001	P < .001	P < .001	P < .001
SGA	1021	(16.1)	883	(13.0)	3245	(8.1)	16 664	(1.7)				
AGA	4974	(78.4)	5639	(82.9)	34 685	(86.9)	919 989	(95.3)				
LGA	284	(4.5)	277	(4.1)	2002	(5.0)	28 571	(3.0)				
Apgar 1 min, Md (IQR)	7	(5–8)	8	(7–9)	9	(8–9)	9	(9–9)	P < .001	P < .001	P < .001	P < .001
Apgar 1 min 0–3, n (%)	1014	(16.0)	326	(4.8)	891	(2.2)	7495	(0.8)	P < .001	P < .001	P < .001	P < .001
Apgar 1 min 0–6, n (%)	2958	(46.6)	1350	(19.9)	3560	(8.9)	35 072	(3.6)	P < .001	P < .001	P < .001	P < .001
Admission to neonatal unit, n (%)	5703	(89.9)	5975	(87.9)	19 158	(48.0)	58 370	(6.0)	P < .001	P < .001	P < .001	P < .001
Ventilator, n (%)	3665	(57.7)	1416	(20.8)	1667	(4.2)	2797	(0.3)	P < .001	P < .001	P < .001	P < .001
Resuscitation at birth, n (%)	1909	(30.1)	626	(9.2)	795	(2.0)	3076	(0.3)	P < .001	P < .001	P < .001	P < .001
Phototherapy, n (%)	4203	(66.2)	3822	(56.2)	14 153	(35.4)	36 673	(3.8)	P < .001	P < .001	P < .001	P < .001
Antibiotic therapy, n (%)	4511	(71.1)	2961	(43.6)	5038	(12.6)	23 852	(2.5)	P < .001	P < .001	P < .001	P < .001
Died by 7 y of age, n (%)	31	(0.5)	7	(0.1)	40	(0.1)	648	(0.1)	P < .001	P < .001	P = .235	P = .013
Age of death, y, Md (IQR)	0.03	(0.00–1.96)	1.01	(0.24–3.01)	3.17	(1.81–4.70)	3.07	(1.81–4.87)	P = .192	P < .001	P = .003	P = .634

Statistical differences were tested by Pearson χ^2 test or Fisher's exact or by Mann-Whitney test: p^1 = MP versus VP; p^2 = LP versus VP; p^3 =MP versus term; p^4 =LP versus term. AGA, appropriate for gestational age; IQR, interquartile range; LGA, large for gestational age; Md, median; T, term.

[a] Regional hospital, private hospital, health center, home birth.

TABLE 2 Diagnoses of CP and Data on Reimbursements Due to CP

	VP <32 wk, *n* = 6347		MP 32^{+0}–33^{+6} wk, *n* = 6799		LP 34^{+0}–36^{+6} wk, *n* = 39 932		Term ≥37 wk, *n* = 965 224	
CP (HDR), *n* (%), total	538	(8.5)	157	(2.3)	216	(0.5)	1244	(0.1)
Years, *n* (% of study period)								
1991–1995	244	(13.7)	75	(3.9)	85	(0.7)	446	(0.2)
1996–2001	205	(9.5)	45	(2.0)	82	(0.6)	442	(0.1)
2002–2008	89	(3.7)	37	(1.4)	49	(0.3)	356	(0.1)
Hospital, *n* (% of level)								
University hospital	399	(8.0)	104	(2.6)	105	(0.6)	358	(0.1)
Central hospital	139	(10.3)	50	(1.8)	91	(0.5)	617	(0.1)
Other	0	(0)	3	(3.9)	18	(0.3)	269	(0.1)
No. of admissions, Md (IQR), total	12	(6–22)	11	(4–19)	7.5	(2–17)	6	(2–14)
Days in hospital, Md (IQR), total	62	(16-cont)	37	(9-cont)	23	(8-cont)	14	(4–116)
The age at diagnosis, y, Md (IQR), total	1.5	(1.0–2.3)	1.4	(0.9–2.4)	1.6	(0.8–3.0)	1.5	(0.8–3.3)
Reimbursements for medicine expenses due to CP, *n* (%)	16	(0.3)	2	(<0.1)	5	(<0.1)	27	(<0.1)
The age (years) of child at first reimbursement, Md (IQR)	3.5	(1.6–5.5)	1.0	(0.1–1.9)	1.6	(1.1–3.2)	1.9	(1.1–3.5)
Disability allowance due to CP by the age of 7 y, *n* (%)	266	(4.2)	96	(1.4)	121	(0.3)	602	(0.1)
The age (years) of child at start of the allowance, Md (IQR)	1.9	(0.8–3.6)	1.4	(0.6–3.3)	1.5	(0.7–3.2)	1.5	(0.7–3.3)
The duration of the allowance (years), Md (IQR)	2.0	(1.0–3.3)	2.0	(1.2–3.9)	1.7	(1.0–3.3)	1.7	(1.0–3.0)
The number of granted allowance periods, Md (IQR)	1	(1–2)	1	(1–2)	1	(1–2)	1	(1–2)

Diagnosis of CP from the HDR; reimbursements due to CP from the social insurance institution. Data include newborns alive at age of 1 year, followed to age of 7 years without major congenital anomalies, 1991–2008 (*n* = 1 018 302).

Statistical differences were tested by Pearson χ^2 test or Fisher's exact or by Mann-Whitney test: MP versus VP: all $P < .001$; LP versus VP: all $P < .001$; MP versus term: all $P < .001$; LP versus term: all $P < .001$; cont, continuing; IQR, interquartile range; Md, median.

in the MP group with antenatal steroid was 0.24 (95% CI 0.08–0.76). RDS predicted a decreased risk of CP in the LP group. Independent ORs for CP in premature gestational week groups compared with the full-term group were in the VP group 9.37 (95% CI 7.34–11.96), in the MP group OR 5.12 (95% CI 4.13–6.34), and in the LP group OR 2.35 (95% CI 1.99–2.77).

DISCUSSION

In this population the incidence and risk for CP were higher among MP and LP infants compared with those born at term. The burden of CP to the families of the MP and LP children, in terms of medicine expenses, is comparable with term-born babies. Also the need of disability allowance seems to be significantly less common in the MP and LP groups than in the VP cases. Birth at an earlier period, being SGA, and having asphyxia and intracranial hemorrhage emerged as significant predictors for CP, whereas antenatal corticosteroid therapy seemed to reduce the risk. Our results can be used in the counseling of parents and in planning guidelines for follow-up practices of MP and LP newborns.

The most prominent weakness of register studies is that recording practices may differ significantly among individuals, sites, and regions. The classification system of diseases was changed in 1996. Although diagnoses were converted to be identical, this change might have affected the diagnostic categories. Children born during the last years of the latest study period 2002 to 2008 had shorter follow-up time, which also may have influenced the decrease in CP risk compared with the earlier periods. However, the CP diagnosis was usually made by the age of 1.5 years. Data of 5-minute Apgar score were not available from the register during this study period and we used the 1-minute score, which is a relatively vague marker

TABLE 3 Diagnoses of CP (*n* = 2242) and Distribution of CP Subtypes in Gestational Week Categories

	VP <32 wk, *n* = 6347		MP 32^{+0}–33^{+6} wk, *n* = 6799		LP 34^{+0}–36^{+6} wk, *n* = 39 932		Term ≥37 wk, *n* = 965 224	
CP total, *n* (% of children in GA group)	550	(8.7)	160	(2.4)	225	(0.6)	1307	(0.1)
CP subtype, *n* (% of CP cases in GA group)								
Hemiplegia	80	(14.5)	37	(23.1)	57	(25.3)	425	(32.5)
Diplegia	213	(38.7)	48	(30.0)	52	(23.1)	165	(12.6)
Quadriplegia	37	(6.7)	11	(6.9)	16	(7.1)	84	(6.4)
Other types	220	(40.0)	64	(40.0)	100	(44.4)	633	(48.4)

Diagnoses of CP from combined data of HDR and social insurance institution. Newborns alive at age of 1 year, followed to age of 7 years without major congenital anomalies, 1991–2008 (*n* = 1 018 302).

Statistical differences were tested by Fisher's exact test: MP versus VP: all $P < .001$; LP versus VP: all $P < .001$; MP versus term: all $P < .001$; LP versus term: all $P < .001$.

TABLE 4 Risk Factor Analysis for CP (n = 2242) in 1991–2008 by the Age of 7 Years Using Time From Birth to First Hospital Visit as Following Time Separately for 4 Gestation Week Categories (n = 1 018 302)

	VP <32 wk, n =550/N = 6347			MP 32^{+0}–33^{+6} wk, n =160/N = 6799			LP 34^{+0}–36^{+6} wk, n =225/N = 39 932			Term ≥37 wk, n =1307/N = 965 224)		
	n	OR	(95% CI)	n	OR	(95% CI)	n	OR	(95% CI)	n	OR	(95% CI)
Study period												
1991–1995	1780	4.03[a]	(3.12–5.94)[a]	1937	2.55[a]	(1.55–4.20)[a]	11 779	2.41[a]	(1.62–3.60)[a]	293 233	1.77[a]	(1.53–2.05)[a]
1996–2001	2159	2.63[a]	(1.94–3.57)[a]	2270	1.28	(0.78–2.09)	13 362	1.97[a]	(1.36–2.87)[a]	309 893	1.57[a]	(1.36–1.80)[a]
2002–2008	2408	1.00		2592	1.00		14 790	1.00		362 095	1.00	
Mother												
Age												
<40	6124	1.00		6579	1.00		38 897	1.00		947 588	1.00	
≥40	223	1.14	(0.69–1.89)	220	0.85	(0.33–2.17)	1034	1.40	(0.70–2.78)	17 633	1.10	(0.75–1.61)
Smoking												
No	4814	1.00		5393	1.00		32 293	1.00		799 160	1.00	
Yes	1192	1.06	(0.84–1.33)	1186	1.20	(0.81–1.79)	6605	1.28	(0.92–1.80)	144 097	1.25[a]	(1.08–1.44)[a]
Primipara												
No	3018	1.00		3007	1.00		19 890	1.00		572 633	1.00	
Yes	3329	1.00	(0.82–1.22)	3792	0.60[a]	(0.42–0.85)[a]	20 041	1.01	(0.76–1.36)	392 588	0.94	(0.84–1.06)
Earlier cesarean delivery												
No	5779	1.00		6228	1.00		36 445	1.00		890 139	1.00	
Yes	568	1.26	(0.92–1.74)	571	0.94	(0.52–1.69)	3486	0.97	(0.58–1.60)	75 082	0.99	(0.81–1.22)
Diabetes												
No	6255	1.00		6651	1.00		38 962	1.00		956 753	1.00	
Yes	92	0.71	(0.30–1.68)	148	1.46	(0.55–3.89)	969	0.70	(0.27–1.80)	8468	1.11	(0.70–1.77)
Pregnancy												
No. fetuses												
1	4525	1.00		4593	1.00		31 064	1.00		948 712	1.00	
2	1621	0.94	(0.70–1.26)	1955	0.83	(0.48–1.44)	8549	0.77	(0.47–1.27)	16 490	0.98	(0.58–1.66)
3 or more	201	1.24	(0.63–2.45)	251	0.88	(0.28–2.81)	318	0.51	(0.07–3.92)	19	[b]	
Order of fetuses												
A	5418	1.00		5670	1.00		35 468	1.00		956 983	1.00	
B	857	0.98	(0.68–1.41)	1046	1.11	(0.57–2.13)	4359	0.99	(0.54–1.80)	8233	1.25	(0.66–2.39)
C	70	0.59	(0.19–1.82)	82	2.02	(0.45–8.97)	104	1.79	(0.11–29.7)	5	[b]	
D	2	[b]		1	[b]		0	[b]		0	[b]	
Assisted reproductive technology												
No	5738	1.00		6031	1.00		37 167	1.00		948 957	1.00	
Yes	609	1.08	(0.76–1.53)	768	0.93	(0.48–1.78)	2764	1.50	(0.89–2.51)	16 264	0.98	(0.65–1.48)
Cervical cerclage												
No	6278	1.00		6759	1.00		39 829	1.00		964 706	1.00	
Yes	69	0.93	(0.43–2.00)	40	2.70	(0.76–9.63)	102	[b]		515	2.22	(0.54–9.11)
Chorion villus biopsy												
No	6266	1.00		6727	1.00		39 540	1.00		956 213	1.00	
Yes	81	0.98	(0.46–2.10)	72	0.59	(0.08–4.41)	391	1.43	(0.51–4.04)	9008	1.15	(0.68–1.94)
PROM (042.0–9/658.1–3)[c]												
No	6213	1.00		6661	1.00		39 469	1.00		962 977	1.00	
Yes	134	1.39	(0.58–3.34)	138	3.05[a]	(1.02–9.12)[a]	462	1.11	(0.26–4.75)	2244	0.84	(0.21–3.41)
Preeclampsia (010.0–0.16/642.0–9)[c]												
No	6069	1.00		6516	1.00		38 617	1.00		953 440	1.00	
Yes	278	0.30[a]	(0.09–0.97)[a]	283	1.33	(0.48–3.66)	1314	0.30	(0.07–1.26)	11 781	0.68	(0.37–1.24)
Delivery												
Time of birth												
Mon–Fri 08.00–15.59	2516	1.00		2643	1.00		14 051	1.00		300 069	1.00	
Mon–Fri 16.00–07.59	2335	0.94	(0.76–1.17)	2600	0.79	(0.54–1.17)	16 771	1.08	(0.80–1.47)	434 806	1.00	(0.88–1.14)
Weekend	1496	0.98	(0.77–1.24)	1556	1.10	(0.73–1.67)	9109	0.85	(0.58–1.25)	230 346	0.95	(0.81–1.12)
Antenatal steroid[d]												
No	5509	1.00		6163	1.00		39 017	1.00		963 782	1.00	
Yes	838	0.80	(0.49–1.30)	636	0.27[a]	(0.09–0.80)[a]	914	1.01	(0.35–2.91)	1439	2.31	(0.85–6.26)

TABLE 4 Continued

	VP <32 wk, *n* =550/*N* = 6347			MP 32^{+0}–33^{+6} wk, *n* =160/*N* = 6799			LP 34^{+0}–36^{+6} wk, *n* =225/*N* = 39 932			Term ≥37 wk, *n* =1307/*N* = 965 224)		
	n	OR	(95% CI)	*n*	OR	(95% CI)	*n*	OR	(95% CI)	*n*	OR	(95% CI)
Place of birth												
University hospital	4957	1.00		3995	1.00		17 156	1.00		299 477	1.00	
Central hospital	1343	1.15	(0.91–1.45)	2727	0.80	(0.55–1.16)	17 552	0.94	(0.70–1.28)	444 958	1.22[a]	(1.06–1.39)[a]
Other[e]	42	[b]		77	1.71	(0.50–5.85)	5220	0.88	(0.51–1.52)	220 659	1.15	(0.98–1.37)
Mode of delivery												
Vaginal	2537	1.00		3212	1.00		26 687	1.00		820 961	1.00	
Cesarean	3798	0.87	(0.71–1.16)	3584	0.87	(0.59–1.27)	13 212	1.23	(0.90–1.67)	143 493	1.55[a]	(1.34–1.78)[a]
Newborn												
Gender												
Boy	3441	1.34[a]	(1.11–1.61)[a]	3730	1.11	(0.80–1.55)	21 659	0.98	(0.75–1.28)	490 221	1.23[a]	(1.10–1.37)[a]
Girl	2906	1.00		3069	1.00		18 272	1.00		475 000	1.00	
Gestational weight												
SGA	1021	0.75	(0.57–0.99)	883	1.10	(0.57–2.13)	3244	1.85[a]	(1.25–2.75)[a]	16 661	2.35[a]	(1.84–3.01)[a]
LGA	284	1.35	(0.89–2.06)	277	1.02	(0.45–2.31)	2002	1.11	(0.58–2.11)	28 571	0.93	(0.68–1.27)
AGA	4974	1.00		5639	1.00		34 685	1.00		919 989	1.00	
Birth weight <1500g												
No	1925	1.00		6056	1.00		39 658	1.00		964 956	1.00	
Yes	4406	1.84[a]	(1.44–2.36)[a]	735	2.12	(1.08–4.15)	253	1.47	(0.62–3.46)	21	5.14	(0.63–41.8)
Apgar 1 min												
4–10	5222	1.00		6397	1.00		38 907	1.00		956 467	1.00	
0–3	1014	1.35[a]	(1.05–1.73)[a]	326	0.87	(0.44–1.70)	891	1.79[a]	(1.07–3.01)[a]	7495	1.71[a]	(1.27–2.30)[a]
Apgar 1 min												
7–10	3278	1.00		5373	1.00		36 238	1.00		928 890	1.00	
0–6	2958	1.26	(1.01–1.56)[a]	1350	1.70[a]	(1.15–2.52)[a]	3560	1.80[a]	(1.21–2.67)[a]	35 072	1.84[a]	(1.47–2.29)[a]
Umbilical artery pH												
≥7.05	4097	1.00		4258	1.00		22 583	1.00		465 861	1.00	
<7.05	90	1.13	(0.58–2.24)	85	1.00	(0.33–3.07)	313	1.84	(0.94–3.63)	6343	1.87[a]	(1.37–2.56)[a]
Unknown	2160	1.17	(0.96–1.44)	2456	0.80	(0.55–1.18)	17 035	0.90	(0.66–1.22)	493 017	1.10	(0.97–1.25)
Admission to neonatal unit												
No	644	1.00		824	1.00		20 773	1.00		906 851	1.00	
Yes	5703	0.68	(0.50–0.94)	5975	0.87	(0.50–1.50)	19 158	1.58[a]	(1.10–2.25)[a]	58 370	1.89	(1.55–2.30)[a]
Ventilator												
No	2682	1.00		5383	1.00		38 265	1.00		962 424	1.00	
Yes	3665	1.53[a]	(1.17–2.01)[a]	1416	1.22	(0.77–1.93)	1666	3.25[a]	(2.06–5.12)[a]	2797	3.27[a]	(2.39–4.48)[a]
Resuscitation at birth												
No	4438	1.00		6173	1.00		39 136	1.00		962 145	1.00	
Yes	1909	1.20	(0.98–1.46)	626	1.60[a]	(1.01–2.53)[a]	795	1.78[a]	(1.09–2.90)[a]	3076	2.08[a]	(1.53–2.85)[a]
Phototherapy												
No	2144	1.00		2977	1.00		25 778	1.00		928 548	1.00	
Yes	4203	0.76[a]	(0.60–0.96)[a]	3822	0.99	(0.68–1.43)	14 153	0.89	(0.65–1.22)	36 673	1.34[a]	(1.03–1.74)[a]
Antibiotic therapy												
No	1836	1.00		3838	1.00		34 893	1.00		941 369	1.00	
Yes	4511	1.14	(0.87–1.50)	2961	1.63[a]	(1.08–2.45)[a]	5038	1.67[a]	(1.13–2.44)[a]	23 852	1.69[a]	(1.32–2.17)[a]
Respiratory distress syndrome (P22.0/769)[c]												
No	3811	1.00		5794	1.00		38 883	1.00		964 874	1.00	
Yes	2536	1.01	(0.82–1.24)	1005	1.05	(0.66–1.66)	1098	0.34[a]	(0.17–0.68)[a]	347	0.85	(0.30–2.38)
Sepsis (P36.0–8/77181)[c]												
No	5924	1.00		6561	1.00		39 231	1.00		959 163	1.00	
Yes	423	0.94	(0.62–1.43)	238	1.35	(0.60–3.05)	700	1.50	(0.73–3.10)	6058	0.76	(0.48–1.20)
Intracranial hemorrhage (P52.0–9/7721)[c]												
No	6111	1.00		6693	1.00		39 852	1.00		965 082	1.00	
Yes	236	3.05[a]	(2.08–4.47)[a]	106	7.18[a]	(3.60–14.3)[a]	79	12.8[a]	(5.58–29.2)[a]	139	4.89[a]	(2.13–11.2)[a]
Convulsions (P90/7790)[c]												
No	6325	1.00		6795	1.00		39 897	1.00		964 757	1.00	

TABLE 4 Continued

	VP <32 wk, *n* =550/*N* = 6347			MP 32^{+0}–33^{+6} wk, *n* =160/*N* = 6799			LP 34^{+0}–36^{+6} wk, *n* =225/*N* = 39 932			Term ≥37 wk, *n* =1307/*N* = 965 224)		
	n	OR	(95% CI)	*n*	OR	(95% CI)	*n*	OR	(95% CI)	*n*	OR	(95% CI)
Yes	22	4.28[a]	(1.52–12.0)[a]	4	9.86	(0.92–106)	34	2.18	(0.28–17.0)	464	7.42[a]	(4.75–11.6)[a]
Hyperbilirubinemia (P59.0–9/774)[c]												
No	4904	1.00		5005	1.00		31 851	1.00		942 250	1.00	
Yes	1443	0.87	(0.65–1.15)	1794	0.58	(0.34–0.98)	8080	0.82	(0.52–1.28)	22 971	1.07	(0.74–1.53)

Logistic regression multivariate models were used, with results given as the ORs and 95% CIs. AGA, appropriate for gestational age; LGA, large for gestational age.

[a] Statistically significant ($P < .050$) ORs with 95% CIs. Categories of missing values are not shown.

[b] Cannot be computed due to the small sample size.

[c] Associated ICD-10 and ICD-9 codes (ICD-10/ICD-9).

[d] Register data available from year 2004.

[e] Regional hospital, private hospital, health center, home birth.

for outcome. Recording practices for hypoxic-ischemic encephalopathy and multiorgan failure had substantial variance and, thus, could not be included in analysis.

Strengths of this study are reliable and comprehensive population-based register data and the substantial number of infants. The national health registers in Finland are well-established and validated. The MBR is a high-quality register covering more than 99.9% of all births.[29,31] The data quality, completeness, and accuracy of the HDR have been varied from satisfactory to very good in a systematic review.[28] Infants were followed to the age of 7 years, by which time the diagnosis of CP is generally made. CP diagnoses can be regarded as reliable, because they are made in public hospitals in specialized units of child neurology. The prevalence of congenital anomalies has been 2.2 times greater in infants born at 32 to 36 weeks of gestation compared with term infants,[32] which is a significant confounder when seeking perinatal risk factors. Here, as elsewhere,[33] all infants with major congenital anomalies were excluded.

The CP incidence was in accordance with the literature.[34] It was higher in the preterm groups compared with the term group and began to decrease clearly after 28 weeks of gestation. Small rates of CP at 24 and 25 weeks of gestation are probably due to small numbers of cases. In our study, the risk of CP was 5.12 (OR) in the MP compared with the term group. In the United States, the risk of CP has been threefold in LP subjects compared with children born at term,[22] whereas the risk in our population was 2.35 (OR) compared with term-born children. In the current study, the risk of CP decreased over time in all subgroups. The drop was greatest in the VP group,

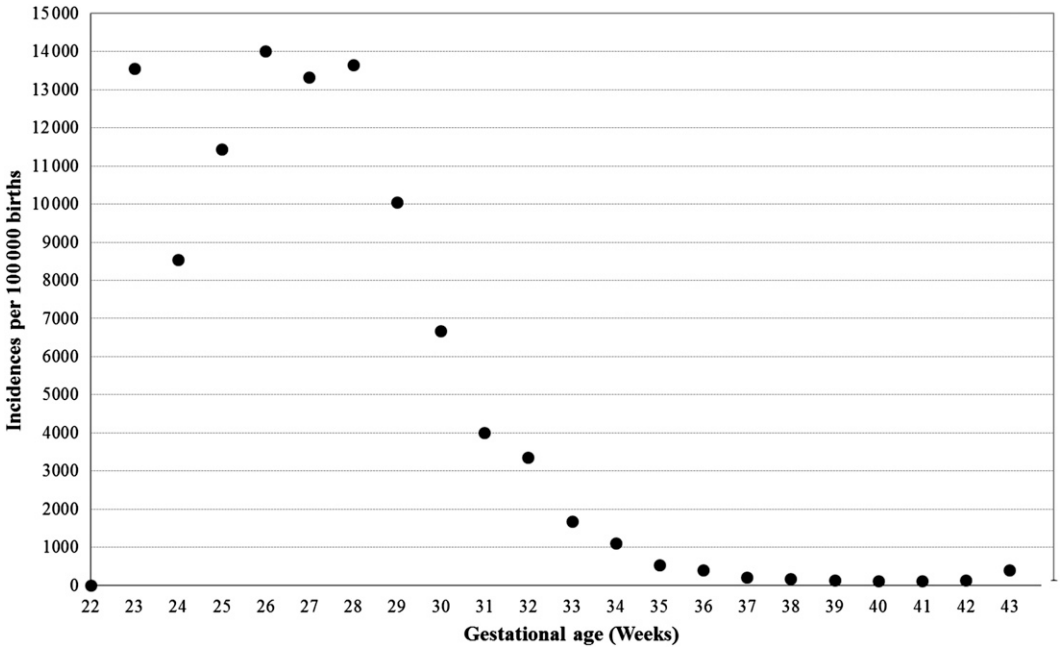

FIGURE 1
Incidences of cerebral palsy (*n* = 2242) per 100 000 births by age of 7 years by gestational age, birth years 1991–2008 (*n* = 1 018 302).

probably due to advances in perinatal and neonatal care. The prevalence of CP among MP infants also decreased in the European register study between 1980 and 1998.[35] In contrast, according to a recent systematic review and meta-analysis, the overall CP prevalence has remained constant in recent years.[36]

SGA predicted the CP risk in the Finnish LP and term infants. In contrast, in a Swedish cohort of 334 cases with CP and 668 controls matched for gestation, gender, and delivery unit, SGA associated with CP in term, but not LP infants.[37] In their study, growth status was determined by using customized birth weight percentiles, based on the growth potential calculated for each infant, whereas we used population-based birth weight standards. The different study designs probably explain the conflicting results.

Resuscitation at birth and low Apgar score were significant risk factors for CP in this study, showing asphyxia at birth to be a major cause of hypoxic ischemic brain injury, and of later motor disability. Efforts to prevent and treat asphyxia seem to be an effective means of preventing CP also in the MP and LP infants. Intracranial hemorrhage increased the risk of CP significantly in all subgroups. It is obvious, and also previously demonstrated, that brain injury visible in brain imaging correlates with the development of CP.[38]

An antibiotic treatment appeared to predict a CP risk in groups from moderately preterm to term infants. Premature labor might be predisposed by infection and it is thus common practice to start antibiotic therapy for a premature newborn. Also, most infants who need intensive care are treated with antibiotics in cases of suspected sepsis. Thus, antibiotic treatment is rather a marker of the sickness of the infant than a causative factor for CP. Conversely, true sepsis was not a significant risk factor, possibly because of the small number of cases with a proven sepsis diagnosis. PROM was a predictor for CP in the MP group. PROM can be regarded as a relevant marker of chorioamnionitis in register studies.[39,40] Instead, true incidence of chorioamnionitis, a well-known risk factor for CP,[41,42] cannot be established in a register study by using the ICD-9 or ICD-10 diagnoses, because histologic or clinical confirmation is rarely available.

LP infants evince a higher neonatal morbidity compared with term-born infants, this including higher rates of RDS.[43] In the current study, RDS was associated with a decreased risk of CP in the LP group and ventilator treatment with an increased risk in the VP, LP, and term groups. Infants who needed mechanical ventilation for reasons other than RDS may have had other morbidities, such as asphyxia or infection, which might be more harmful to the developing brain than RDS only. Antenatal steroid treatment predicted a decreased risk of CP in MP infants. According to earlier national guidelines, mothers expected to deliver before 34^{+0} weeks of gestation were treated with glucocorticoids. The updated guideline recommends antenatal glucocorticoid treatment to be administered later (ie, before 35^{+0} weeks' gestation).[44] This change seems to be beneficial also in reducing the risk of CP in this group.

CONCLUSIONS

The incidence of CP increases nonlinearly with decreasing GA. LP and MP infants are at a significantly greater risk compared with term infants. The risk has decreased in all GA groups over time. Asphyxia and intracranial hemorrhage emerge as the most prominent risk factors in all gestation week categories. Efforts to prevent and treat asphyxia are of prime importance in reducing the risk of CP. Antenatal steroid treatment appears to reduce the risk among MP infants. Guidelines for management and risk assessment need to be established for LP and MP infants.

REFERENCES

1. Shapiro-Mendoza CK, Lackritz EM. Epidemiology of late and moderate preterm birth. *Semin Fetal Neonatal Med*. 2012;17(3):120–125
2. Davidoff MJ, Dias T, Damus K, et al. Changes in the gestational age distribution among US singleton births: impact on rates of late preterm birth, 1992 to 2002. *Semin Perinatol*. 2006;30(1):8–15
3. Raju TN, Higgins RD, Stark AR, Leveno KJ. Optimizing care and outcome for late-preterm (near-term) infants: a summary of the workshop sponsored by the National Institute of Child Health and Human Development. *Pediatrics*. 2006;118(3):1207–1214
4. Vohr B. Long-term outcomes of moderately preterm, late preterm, and early term infants. *Clin Perinatol*. 2013;40(4):739–751
5. Kochanek KD, Kirmeyer SE, Martin JA, Strobino DM, Guyer B. Annual summary of vital statistics: 2009. *Pediatrics*. 2012;129(2):338–348
6. Jakobsson M, Gissler M, Paavonen J, Tapper AM. The incidence of preterm deliveries decreases in Finland. *BJOG*. 2008;115(1):38–43
7. Hüppi PS, Warfield S, Kikinis R, et al. Quantitative magnetic resonance imaging of brain development in premature and mature newborns. *Ann Neurol*. 1998;43(2):224–235
8. Cheng YW, Kaimal AJ, Bruckner TA, Halloran DR, Caughey AB. Perinatal morbidity associated with late preterm deliveries compared with deliveries between 37 and 40 weeks of gestation [published correction appears in *BJOG*. 2011;118(13):1687]. *BJOG*. 2011;118(12):1446–1454
9. Kitsommart R, Janes M, Mahajan V, et al. Outcomes of late-preterm infants: a retrospective, single-center, Canadian study. *Clin Pediatr (Phila)*. 2009;48(8):844–850
10. Teune MJ, Bakhuizen S, Gyamfi Bannerman C, et al. A systematic review of severe morbidity in infants born late preterm. *Am J Obstet Gynecol*. 2011;205(4):374.e1–374.e9.

11. Kugelman A, Colin AA. Late preterm infants: near term but still in a critical developmental time period. *Pediatrics*. 2013;132(4):741–751
12. Chyi LJ, Lee HC, Hintz SR, Gould JB, Sutcliffe TL. School outcomes of late preterm infants: special needs and challenges for infants born at 32 to 36 weeks gestation. *J Pediatr*. 2008;153(1):25–31
13. Gray RF, Indurkhya A, McCormick MC. Prevalence, stability, and predictors of clinically significant behavior problems in low birth weight children at 3, 5, and 8 years of age. *Pediatrics*. 2004;114(3):736–743
14. Huddy CL, Johnson A, Hope PL. Educational and behavioural problems in babies of 32–35 weeks gestation. *Arch Dis Child Fetal Neonatal Ed*. 2001;85(1):F23–F28
15. Woythaler MA, McCormick MC, Smith VC. Late preterm infants have worse 24-month neurodevelopmental outcomes than term infants. *Pediatrics*. 2011;127(3). Available at: www.pediatrics.org/cgi/content/full/127/3/e622
16. Morse SB, Zheng H, Tang Y, Roth J. Early school-age outcomes of late preterm infants. *Pediatrics*. 2009;123(4). Available at: www.pediatrics.org/cgi/content/full/123/4/e622
17. Quigley MA, Poulsen G, Boyle E, et al. Early term and late preterm birth are associated with poorer school performance at age 5 years: a cohort study. *Arch Dis Child Fetal Neonatal Ed*. 2012;97(3):F167–F173
18. Talge NM, Holzman C, Wang J, Lucia V, Gardiner J, Breslau N. Late-preterm birth and its association with cognitive and socioemotional outcomes at 6 years of age. *Pediatrics*. 2010;126(6):1124–1131
19. Gurka MJ, LoCasale-Crouch J, Blackman JA. Long-term cognition, achievement, socioemotional, and behavioral development of healthy late-preterm infants. *Arch Pediatr Adolesc Med*. 2010;164(6):525–532
20. 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(8):571–576
21. Himpens E, Van den Broeck C, Oostra A, Calders P, Vanhaesebrouck P. Prevalence, type, distribution, and severity of cerebral palsy in relation to gestational age: a meta-analytic review. *Dev Med Child Neurol*. 2008;50(5):334–340
22. Petrini JR, Dias T, McCormick MC, Massolo ML, Green NS, Escobar GJ. Increased risk of adverse neurological development for late preterm infants. *J Pediatr*. 2009;154(2):169–176
23. McIntyre S, Taitz D, Keogh J, Goldsmith S, Badawi N, Blair E. A systematic review of risk factors for cerebral palsy in children born at term in developed countries. *Dev Med Child Neurol*. 2013;55(6):499–508
24. EUROCAT guide 1.3 and reference documents. Instructions for the registration and surveillance of congenital anomalies. Available at: www.eurocat-network.eu/. Accessed January 15, 2013
25. Pihkala J, Hakala T, Voutilainen P, Raivio K. Characteristic of recent fetal growth curves in Finland [in Finnish]. *Duodecim*. 1989;105(18):1540–1546
26. Goldaber KG, Gilstrap LC III, Leveno KJ, Dax JS, McIntire DD. Pathologic fetal acidemia. *Obstet Gynecol*. 1991;78(6):1103–1107
27. Kwee A, van der Hoorn-van den Beld CW, Veerman J, Dekkers AH, Visser GH. STAN S21 fetal heart monitor for fetal surveillance during labor: an observational study in 637 patients. *J Matern Fetal Neonatal Med*. 2004;15(6):400–407
28. Sund R. Quality of the Finnish hospital discharge register: A systematic review. *Scand J Public Health*. 2012;40(6):505–515
29. Gissler M, Teperi J, Hemminki E, Meriläinen J. Data quality after restructuring a national medical registry. *Scand J Soc Med*. 1995;23(1):75–80
30. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. *J Pediatr*. 1978;92(4):529–534
31. Gissler M, Shelley J. Quality of data on subsequent events in a routine Medical Birth Register. *Med Inform Internet Med*. 2002;27(1):33–38
32. Honein MA, Kirby RS, Meyer RE, et al; National Birth Defects Prevention Network. The association between major birth defects and preterm birth. *Matern Child Health J*. 2009;13(2):164–175
33. Kramer MS, Demissie K, Yang H, Platt RW, Sauvé R, Liston R; Fetal and Infant Health Study Group of the Canadian Perinatal Surveillance System. The contribution of mild and moderate preterm birth to infant mortality. *JAMA*. 2000;284(7):843–849
34. Paneth N, Hong T, Korzeniewski S. The descriptive epidemiology of cerebral palsy. *Clin Perinatol*. 2006;33(2):251–267
35. Andersen GL, Romundstad P, De La Cruz J, et al. Cerebral palsy among children born moderately preterm or at moderately low birthweight between 1980 and 1998: a European register-based study. *Dev Med Child Neurol*. 2011;53(10):913–919
36. Oskoui M, Coutinho F, Dykeman J, Jetté N, Pringsheim T. An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. *Dev Med Child Neurol*. 2013;55(6):509–519
37. Jacobsson B, Ahlin K, Francis A, Hagberg G, Hagberg H, Gardosi J. Cerebral palsy and restricted growth status at birth: population-based case-control study. *BJOG*. 2008;115(10):1250–1255
38. Maunu J, Lehtonen L, Lapinleimu H, et al; PIPARI Study Group. Ventricular dilatation in relation to outcome at 2 years of age in very preterm infants: a prospective Finnish cohort study. *Dev Med Child Neurol*. 2011;53(1):48–54
39. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008;371(9606):75–84
40. Romero R, Quintero R, Oyarzun E, et al. Intraamniotic infection and the onset of labor in preterm premature rupture of the membranes. *Am J Obstet Gynecol*. 1988;159(3):661–666
41. Wu YW, Colford JM Jr. Chorioamnionitis as a risk factor for cerebral palsy: a meta-analysis. *JAMA*. 2000;284(11):1417–1424
42. Shatrov JG, Birch SC, Lam LT, Quinlivan JA, McIntyre S, Mendz GL. Chorioamnionitis and cerebral palsy: a meta-analysis. *Obstet Gynecol*. 2010;116(2 pt 1):387–392
43. Leone A, Ersfeld P, Adams M, Schiffer PM, Bucher HU, Arlettaz R. Neonatal morbidity in singleton late preterm infants compared with full-term infants. *Acta Paediatr*. 2012;101(1):e6–e10
44. Antenatal corticosteroid treatment for women at risk of preterm birth. Working group set up by The Finnish Medical Society Duodecim and The Finnish Society of Perinatology. Helsinki: Finnish Medical Society Duodecim; 2009. Available at: www.kaypahoito.fi. Accessed January 22, 2014

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