Decreasing prevalence and severity of cerebral palsy in Norway among children born 1999 to 2010 concomitant with improvements in perinatal health

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ABSTRACT

Background: The aim of our study was to explore if the prevalence and clinical characteristics of cerebral palsy (CP), concomitant with perinatal health indicators in the general population, remained unchanged for children born in Norway between 1999 and 2010.

Methods: This national multi-register cohort study included 711,174 children recorded in the Medical Birth Registry of Norway. Among these, 707,916 were born alive, and 1664 had a validated diagnosis of CP recorded in the Cerebral Palsy Registry of Norway and/or the Norwegian Patient Registry. Prevalence per 1000 live births as a function of birth year was analyzed using logistic regression with fractional polynomials to allow for non-linear trends. Chi-square statistics were used to estimate trends in proportions of clinical characteristics.

Results: The prevalence of CP in Norway decreased from 2.62 per 1000 live births in 1999 to 1.89 in 2010. The reduction was most evident among children with bilateral CP, in particular those with diplegia. During the study period, the proportions of children with severe motor impairments, epilepsy, intellectual impairment and reduced speech also decreased. At the same time, perinatal mortality has decreased in Norway, along with the proportion of women with preeclampsia, children born preterm or as a multiple.

Conclusion: We observed a significant decrease in the prevalence and severity of CP subtypes and associated impairments among children with CP in Norway. This coincided with
1. Introduction

Cerebral palsy (CP), the most common cause of permanent motor disabilities in children, is the result of a non-progressive injury in the immature brain that occurs before birth, during delivery or in the neonatal period, and up to two years of age. The injury may be caused by a congenital brain anomaly, infection, trauma, or acute hypoxic-ischemic insults. Known risk factors include preterm birth, restricted fetal growth, and complications during pregnancy and birth.\(^1\)\(^-\)\(^3\) Research shows that the panorama of causes has changed over time.\(^4\)\(^-\)\(^7\)

CP is categorized into subtypes based on the dominating motor disturbance and on which part of the body is affected. Further classification is regularly based on motor impairment. Associated impairments such as epilepsy, impaired ability to speak/communicate, cognitive impairments, impaired vision and/or hearing, and nutritional problems are common.\(^8\)

The prevalence of CP has been reported to vary between 1.5 and 3 per 1000 in various populations.\(^9\)\(^,\)\(^10\) Several studies have reported that the prevalence has been stable for more than fifty years.\(^6\)\(^,\)\(^9\)\(^-\)\(^12\) This has been taken as evidence that CP is mainly due to events before birth and that improvements in obstetric and neonatal care have not resulted in a measurable prevention of CP.\(^11\)\(^,\)\(^12\) However, the stable prevalence may have concealed significant changes in the causes leading to CP and to the various CP subtypes. It is also noteworthy that the prevalence of CP was stable despite a significant reduction in perinatal mortality in the developed world from around 20 per 1000 in the 1970s to less than five per 1000 in the 21st century.\(^13\) In fact, two studies by the Surveillance of Cerebral Palsy in Europe in populations born during the last two decades of the 20th century suggested slight decreases in the prevalence of CP among children born with a very low birth weight\(^14\) or moderately preterm.\(^15\) More recently, Sellier et al. showed a reduction in the prevalence of CP from 1.90 to 1.77 per 1000 live births in populations covered by 20 European registries for children born from 1980 to 2003.\(^16\) A strength of all three studies was the large number of children included, as well as the uniform and validated diagnostic criteria of the CP diagnosis and classifications. These studies attributed the decrease in prevalence of CP to improvements in obstetric and neonatal care of preterm infants towards the end of the 20th and beginning of the 21st century. However, ascertainment of cases was a challenge, and in fact, the reported overall prevalence in the Sellier et al. study was lower than in areas with a documented complete ascertainment of cases.\(^7\)\(^,\)\(^17\)\(^,\)\(^18\) Despite these findings, the debate continues whether CP may be prevented or whether it is mainly caused by antenatal factors that are less likely to be modified by obstetric and neonatal care.\(^11\)\(^,\)\(^19\)\(^,\)\(^20\)

We have recently reported high completeness and correctness of CP diagnosis codes in Norway by combining information from two national health registers, resulting in a prevalence of CP of 2.4 per 1000 for children born 1996 to 2007.\(^21\) Since then, new national guidelines have been introduced in Norway aiming to improve obstetric and neonatal care including cardiotocography (CTG), ST waveform analysis of fetal electrocardiogram (STAN), as well as therapeutic hypothermia of term born children with moderate or severe neonatal encephalopathy.\(^21\)\(^-\)\(^23\)

On this background, the aim of this study was to examine if the prevalence of CP as well as clinical characteristics have changed in Norway during the first decade of the 21st century. We also wanted to assess potential concomitant changes in other indicators of perinatal health in the general population (e.g. prevalence of preterm birth and perinatal mortality) during the same time period.

2. Method

2.1. Study design

In this register-based cohort study, all children born in Norway during 1999 to 2010 and registered in the Medical Birth Registry of Norway (MBRN) were included. The MBRN has recorded data on all births since 1967, including information on the mother’s health during pregnancy, the birth, and the child’s health after birth. Registration in the MBRN is compulsory. Data used in this study were collected from the birth notification form dated December 1, 1998.\(^22\) Children with CP were identified through the Cerebral Palsy Registry of Norway (CPRN). The CPRN is a consent-based national medical quality registry that has systematically recorded detailed clinical information on all children with CP born since 1996. In this study, data were collected for children born 1999 and onward on the CPRN Five Year Consultation Form.\(^23\) Children with postneonatally acquired CP were excluded. The completeness of the CPRN for birth years 1999 to 2010 is approximately 90%. This was ascertained by linking the CPRN with the Norwegian Patient Registry (NPR) using the 11-digit personal identification number unique to each resident.\(^17\) The NPR is a compulsory administrative registry that receives standardized data on all patients treated by the national specialist health care services, with person-identifiable data since 2008.
2.2. Study variables

Cerebral palsy was diagnosed with the International Statistical Classification of Diseases and Related Health Problems 10th revision codes (G80.0) and further classified into a CP subtype of spastic unilateral, spastic bilateral (diplegia and quadriplegia), dyskinetic, ataxic, and mixed/unspecified by a pediatrician. Gross motor function was classified according to the Gross Motor Function Classification System (GMFCS). Epilepsy was defined as present (a minimum of two unprovoked seizures after the neonatal period) or not present. Cognition was defined as either normal (IQ test above 70 or by clinical evaluation) or intellectually disabled (IQ test below 70 or by clinical evaluation). Speech ability was classified using the Viking Speech Scale and eating ability as independent, needs assistance, or partial/full tube feeding. Vision and hearing was described as normal, impaired, or severely impaired (blind i.e. <6/60 (<0.1) before correction on the best eye and loss > 70 dB before correction on the best ear, respectively). For children not registered in the CPRN, the NPR provided aggregated information on CP diagnosis by sex and birth year.

In order to assess changes in perinatal health indicators in the general population during the same time period, we accessed the Norwegian Institute of Public Health’s MBRN statistics bank. We collected aggregated data on assisted fertilization techniques (AFT), gestational age (GA), pre-eclampsia, multiple births, congenital anomalies, and perinatal mortality. GA was based on an ultrasound examination before GA week 20, and in the case where this exam was not performed it was calculated from the last menstrual period. Births occurring before GA week 28 were defined as extremely preterm, between weeks 28–36 weeks as very/moderately preterm, and births after 36 weeks as born at term. Pre-eclampsia was included if occurred before week 34. Multiple births were defined as two or more children born to the same mother at the same time. Perinatal mortality was defined as children who were either stillborn or died during the first week after birth, with a minimum birth weight of 500 g and GA week 22.

2.3. Ethics

The CPRN is approved by The Norwegian Data Protection Authority (08/01067-9/EOL). This study was approved by the Regional Committee for Medical and Health Research Ethics in Central Norway (2011/754).

2.4. Statistical analyses

Logistic regression with birth year as covariate was used to estimate time trends in the prevalence of CP and CP subtypes per 1000 live births for children born during 1999 to 2010. Non-linear trends were accounted for using fractional polynomials with birth years as covariate (Figs. 1–3). To account for the possibility of children being diagnosed with CP after the age of 7–8 years and not counted in our analyses, a worst case sensitivity analysis was performed by increasing the total number of children with CP by 10% for birth years 2009 and 2010. This percentage is five times higher than the observed percentage of children with late diagnosed CP born 1999 and 2000. To study trends in proportions of clinical characteristics, we used the linear-by-linear association test (for row × columns (r × c) tables with r > 2 and c > 2) and the Cochran–Armitage test for trend (for 2x2 tables with r = 2).29

To analyze time trends of perinatal health indicators, aggregated data were retrieved from the MBRN statistics bank for all children born in Norway during our study period. Logistic regression was used to estimate trends in prevalence of each risk factor per 1000 live births.

A p-value below 0.05 was considered statistically significant, and 95% confidence intervals (CI) are reported where relevant. Logistic regression analyses with fractional polynomials were performed using Stata 15, and other analyses using SPSS 23.

2.5. Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript. SJH and GLA had full access to the data in the study and final responsibility for the decision to submit for publication.

3. Results

In all, 711 174 children were born in Norway during 1999 to 2010. Among these, 707 916 were live births and 1664 were stillborn or died during the first week after birth, with a minimum birth weight of 500 g and GA week 22.

3.1. Prevalence of CP

The average prevalence of CP for children born in Norway 1999 to 2010 was 2.35 per 1000 live births (CI: 2.24 to 2.47). The prevalence decreased from 2.62 per 1000 in 1999 to 1.89 in 2010. This percentage is five times higher than the observed percentage of children with late diagnosed CP born 1999 and 2000. To study trends in proportions of clinical characteristics, we used the linear-by-linear association test (for row × columns (r × c) tables with r > 2 and c > 2) and the Cochran–Armitage test for trend (for 2x2 tables with c > 2).29

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2010. Assuming a linear model, the probability of a child born with CP was reduced by a factor of 0.972 per year, corresponding to a 2.8% yearly reduction (p = 0.0001). Fig. 1 illustrates the predicted CP prevalence with CIs during the study period using the non-linear model. Correspondingly, within the bilateral spastic CP group, the prevalence of diplegia decreased significantly by a factor of 0.958 per year (4.2% yearly) (p = 0.0009) assuming a linear model, while quadriplegia had a slight non-linear upside down U-shape trend, with a decrease from birth year 2007 (p < 0.0001) (Figures S2 and S3). The prevalence of unilateral spastic CP remained stable during the study period at around 0.10 per 1000 live births (p = 0.50, assuming a linear model) (Figure S1), while bilateral spastic CP decreased significantly from 1.31 per 1000 in 1999 to 0.67 in 2010 (p < 0.0001). The probability of a child being diagnosed with bilateral CP was reduced by a factor of 0.954 per year (4.6% yearly), assuming a linear model (p < 0.0001). Fig. 2 illustrates the predicted bilateral CP prevalence with CIs during the study period using the non-linear model. Correspondingly, within the bilateral spastic CP group, the prevalence of diplegia decreased significantly by a factor of 0.958 per year (4.2% yearly) (p = 0.0009) assuming a linear model, while quadriplegia had a slight non-linear upside down U-shape trend, with a decrease from birth year 2007 (p < 0.0001) (Fig. 3).

3.2. Clinical characteristics of CP

Table 1 shows that the proportion of children with CP able to walk without assistance (GMFCS level I-II) steadily increased while the proportion of children with CP able to walk only with assistance (GMFCS level III) or unable to walk (GMFCS levels IV-V) decreased over the study period (p = 0.013). Table 1 also shows that among children with CP there has been a decrease in the proportion recorded with epilepsy (p < 0.0001), intellectual disability (p < 0.0001), and with difficult to understand or no speech (Viking Speech Scale III-IV) (p = 0.023). However, there were no changes over time in the proportion of children with CP who had impaired eating abilities (p = 0.153), vision (p = 0.073), and/or hearing (p = 0.33) (Table 1).

3.3. Changes in perinatal health indicators in the general population

Perinatal mortality in Norway decreased from 7.6 per 1000 in 1999 to 5.1 in 2010 (p < 0.0001). The prevalence of extremely preterm born children decreased from 5.0 per 1000 births in 1999 to 3.6 in 2010 (p < 0.0001). Children born very/moderately preterm also decreased from 59.1 per 1000 births in 1999 to 54.9 in 2010 (p < 0.0001). The prevalence of multiple births decreased from 18.1 per 1000 births in 1999 to 16.7 in 2010 (p = 0.017). Despite a significant increase in the prevalence of children born after AFT from 18.4 per 1000 births in 1999 to 33.7 in 2010 (p < 0.0001), the prevalence of multiple births born after AFT decreased from 8.3 per 1000 in 1999 to 6.6 in 2010 (p < 0.0001). The prevalence of congenital anomalies increased from 39.8 per 1000 births in 1999 to 46.8 in 2010 (p < 0.0001), while the prevalence of preeclampsia decreased from 43.7 per 1000 births in 1999 to 33.5 in 2010 (p < 0.0001).

4. Discussion

4.1. Main findings

We found a marked decline in the overall prevalence of CP in Norway among children born 1999 to 2010. This reduction was
Table 1 – Summary of clinical characteristics among children with cerebral palsy born in Norway from 1999 to 2010.

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<td>91 (93.8)</td>
<td>90 (96.8)</td>
</tr>
<tr>
<td>Impaired</td>
<td>4 (4.3)</td>
<td>5 (5.2)</td>
<td>10 (1.0)</td>
<td>5 (5.4)</td>
<td>4 (4.4)</td>
<td>2 (1.9)</td>
<td>2 (1.9)</td>
<td>5 (4.5)</td>
<td>1 (1.1)</td>
<td>2 (1.9)</td>
<td>3 (3.1)</td>
<td>3 (3.2)</td>
</tr>
<tr>
<td>Severely impaired</td>
<td>4 (4.3)</td>
<td>4 (4.1)</td>
<td>1 (1.1)</td>
<td>2 (2.2)</td>
<td>2 (2.2)</td>
<td>5 (2.9)</td>
<td>3 (2.9)</td>
<td>2 (1.8)</td>
<td>1 (1.1)</td>
<td>3 (2.8)</td>
<td>3 (3.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Total number of children with CP</td>
<td>156</td>
<td>155</td>
<td>151</td>
<td>129</td>
<td>138</td>
<td>147</td>
<td>152</td>
<td>142</td>
<td>122</td>
<td>134</td>
<td>120</td>
<td>118</td>
</tr>
</tbody>
</table>

GMFCS = Gross Motor Function Classification System.
CP = cerebral palsy.
most evident for children with bilateral spastic CP, in particular those with diplegia. There was also a trend towards a decrease in the prevalence of children with quadriplegic and dyskinetic CP from 2007 and onwards. The prevalence of unilateral CP remained stable. We also found a decrease in the proportion of children with CP and more severe gross motor impairments, epilepsy, intellectual disability, and with limited speech. During the study period, there were significant improvements in perinatal health indicators in the general Norwegian population including a decrease in perinatal mortality, as well as in the prevalence of preterm born children, preeclampsia, and multiple births.

### 4.2. Strengths and limitations

To our knowledge, this is the first study to combine information on children with CP, as well as perinatal health information on the general population, from three nationwide population-based health registers to explore trends in prevalence rates and clinical characteristics. The CP diagnosis codes in the CPRN and NPR have been validated to ensure completeness and correctness of the CP population in Norway, confirmed at a minimum age of 5 years. This included a comparison of the CP diagnosis codes recorded only in the NPR with the proportion recorded in the CPRN, which did not indicate selection bias. An additional potential selection bias may have occurred if a large proportion of children are diagnosed with CP after 7–8 years of age, thereby leading to an erroneously low prevalence in children born 2009 and 2010. However, after performing a worst case sensitivity analysis by increasing the total number of children with CP by 10% for these birth years, the results remained nearly unchanged. Conversely, there is also the possibility that a child currently registered in the CPRN may have been misdiagnosed with CP, and will be removed from the registry at a later age. Misdiagnoses, in particular progressive disorders, are more likely to be discovered with increasing age and would be expected to be more common in the later part of the study period. This would lead to an erroneously high prevalence in the later years. Thus, we consider it most unlikely that our main findings have been affected by selection bias.

The proportions of missing data for clinical characteristics recorded only in the CPRN varied during the study period, and some caution should be taken when interpreting the trends in clinical characteristics. On the other hand, children with a more severe CP subtype and associated impairments are more likely to be assessed and registered earlier and more thoroughly than children with less severe CP and associated impairments. We therefore consider it unlikely that underreporting of severe cases explains the decrease in the proportion of children with more severe impairments. Moreover, it may be considered reassuring that there was no change in the prevalence of unilateral CP, normally having less severe impairments than children with bilateral or dyskinetic CP.

### 4.3. Comparison of other studies

Similar to our study, a reduction in the prevalence of CP for neonatal survivors was found for children born in Victoria, Australia between 1993 and 2006, including a reduction in bilateral CP and the severity of motor and associated impairments. The authors concluded that this might have been attributed to improvements in perinatal care, as well as neuroprotective strategies for HIE. In 2016, Durkin et al. reported a decline in the population prevalence of 8 year old children with CP living within four areas in the US from 3.5 per 1000 in 2006 to 2.9 in 2010. Although they were not able to directly associate this decline with an improvement of obstetric and neonatal care, it is the first report of decline in the prevalence of CP from the US. Additionally, three consecutive studies performed in a smaller population in Western Sweden reported a nonsignificant decrease in the prevalence of CP in liveborn children from 1999 to 2002 (2.18 per 1000), 2003 to 2006 (2.18 per 1000), and 2007 to 2010 (1.96 per 1000). The decrease in the latter study was a result of a reduction in all CP subtypes, including children born with HIE at or near term. This was attributed to the introduction of therapeutic hypothermia in 2007 and/or improvements in obstetric care in Sweden. Lastly, a study performed in Okinawa, Japan also reported a decrease in the prevalence of CP in liveborn children from 1988 to 2007. The decrease was accredited to a reduction of preterm born children or with a low birth weight between 1998 and 2007. The study also reported a decline in neonatal mortality, indicating improved access to perinatal interventions.

### 4.4. Interpretation

The decrease in the prevalence of CP and improved clinical picture, along with a decrease in perinatal mortality and in the proportion of preterm born children may be explained by general improvements in obstetric and neonatal care during the last 20 years in Norway. This interpretation is supported by the decrease in perinatal morbidity during the same time period. The decrease in diplegia is consistent with the decrease in the prevalence among children born preterm, which may be in part ascribed to the decrease in the occurrence of preeclampsia, or in the reduction of multiple births, mainly a result of improved AFT. However, the overall estimated reduction in children born preterm can only account for approximately nine of the ~32 fewer children with CP born 2009 and 2010 as compared to those born 1999 to 2000. We therefore consider that other improvements in obstetric and neonatal care have had a major impact on the reduction in the prevalence of CP. This interpretation is supported by the decrease in quadriplegia and dyskinetic CP, considered to be the result of HIE injuries at birth, during the latter part of the study. Although we are unable to assess which treatments may be responsible for the improved outcome, it is noteworthy that therapeutic hypothermia was introduced in Norway in 2007, which is the year when a decrease in the more severe CP subtypes become most evident. Congenital anomalies are common among children with CP, and we have recently shown that these children have more severe motor and associated impairments compared with children with other or unknown causes. A reduction in the proportion of children with congenital anomalies could therefore also explain the reduction in CP. On the other hand, data acquired from the MBRN suggested a slight increase in the number of children with congenital anomalies in the general population,
indirectly lending support to our interpretation that the decrease is due to overall improved care. During the study period, the proportions of women with high maternal age, overweight and multiple births who smoked cigarettes at the beginning of pregnancy have increased, while the prevalence of smoking at the beginning of pregnancy and multiple births have decreased in Norway. Although a recent study from Australia suggested a reduced risk for CP in mothers who smoked cigarettes at the beginning of pregnancy, high maternal age, overweight and multiple births are all factors associated with increased risk for CP.

We found that the prevalence of CP declined for children born in Norway from 2.62 per 1000 in 1999 to 1.89 in 2010. Our results indirectly lend support to our interpretation that the decrease is due to overall improved care. During the study period, the proportions of women with high maternal age, overweight and multiple births who smoked cigarettes at the beginning of pregnancy have increased, while the prevalence of smoking at the beginning of pregnancy and multiple births have decreased in Norway. Although a recent study from Australia suggested a reduced risk for CP in mothers who smoked cigarettes at the beginning of pregnancy, high maternal age, overweight and multiple births are all factors associated with increased risk for CP.

We thank our colleagues at the habilitation centers, who contributed to revisions and final approval of the manuscript.

5. Conclusion

We found that the prevalence of CP declined for children born in Norway from 2.62 per 1000 in 1999 to 1.89 in 2010. Our results also show that there was a substantial improvement in the severity of clinical characteristics over time as prevalence for bilateral CP decreased, along with a decrease in the proportion of children with severe motor impairments, epilepsy, intellectual disability, and difficult to understand or no speech. At the same time, there have been fewer pregnancies with pre-eclampsia, children born preterm or as a multiple, as well as fewer perinatal deaths of children born in Norway. This may be explained by improvements in obstetric and neonatal care in Norway during the first decade of the 21st century.

Contributors

SJH, TV, IJB and GLA designed the study. SJH performed the data collection. SJH and SL performed the data analyses. SJH drafted the manuscript. All authors interpreted the data, and contributed to revisions and final approval of the manuscript.

Declaration of interests

The authors have no conflicts of interest to disclose.

Acknowledgements

We thank our colleagues at the habilitation centers, who obtained a CPRN signed consent form and provided the clinical data for children with CP. We also would like to acknowledge the research funding provided by the Vestfold Hospital Trust.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejpn.2018.05.001.

References

18. Ravn SH, Flachs EM, Uldall P. Cerebral palsy in eastern
Denmark: declining birth prevalence but increasing numbers
19. Nelson KB, Blair E. Prenatal factors in singletons with cerebral
20. Silvert M. Claim that events before birth cause cerebral palsy
is disputed. BMJ 2000;320(7250):1625.
helsedirektoratet.no/retningslinjer/et-trygt-fodetilbud-
kvalitetskrav-til-fodselsomsorgen. [Accessed 13 March 2018]
[Norwegian].
22. The Norwegian Directorate of Health. National professional
guidelines for competence and quality in newborn intensive care
nyfodtintensivavdelinger-kompetanse-og-kvalitet. [Accessed
13 March 2018] [Norwegian].
23. Kessler J, Moster DAG, Albrechtsen S. Intrapartum monitoring
of high-risk deliveries with ST analysis of the fetal
electrocardiogram: an observational study of 6010 deliveries.
24. The Cerebral Palsy Registry of Norway. CPRN Five Year
Consultation Form. 2007. https://www.siv.no/seksjon/CP-
registreret/Documents/CPRN-registration_at_5_years.pdf.
[Accessed 6 November 2017].
25. Surveillance of Cerebral Palsy in Europe (SCPE). SCPE network-
resources/42-gross-motor-function-classification-system-
expanded-revised-gmfcs-e-r. [Accessed 9 November 2017].
27. Pennington L, Mjøen T, da Graça Andrada M, Murray J. Viking
speech Scale. 2010. http://www.scpenetwork.eu/assets/SCPE-
Tools/VSS/Viking-Speech-Scale-2011-Copyright.pdf.
[Accessed 9 November 2017].
28. Fagerland MW, Eide GE, Laake P. Linear regression. In:
Veierød MB, Lydersen S, Laake P, editors. Medical statistics in
clinical and epidemiological research. Oslo: Gyldendal
29. Fagerland MW, Lydersen S, Laake P. Statistical analysis of
contingency tables. 1 ed. Boca Raton, FL: Chapman & Hall/CRC;
2017.
30. Reid SM, Meehan E, McIntyre S, Goldsmith S, Badawi N,
Reddihough DS. Temporal trends in cerebral palsy by
impairment severity and birth gestation. Dev Med Child Neurol
31. Durkin MS, Benedict RF, Christensen D, et al. Prevalence of
cerebral palsy among 8-year-old children in 2010 and
preliminary evidence of trends in its relationship to low
in the prevalence of cerebral palsy in children born
between 1988 and 2007 in Okinawa, Japan. Brain Dev
and the severity of impairments for cerebral palsy. Dev Med
34. Norwegian Institute of Public Health. Medical birth registry and
Available from: http://statistikk.fhi.no/mfr/ [Norwegian].
35. Statistics Norway. Statistical Yearbook 2013, Table 110:
proportion overweight, with body mass index (BMI) 27 or higher.
16–79 years. Percent. Oslo - Kongsvinger: Statistics Norway;
2013 [Norwegian].
Development of social and demographic differences in
maternal smoking between 1999 and 2014 in Norway. Nicotine
37. Walstab J, Bell R, Reddihough D, Brennecke S, Bessell C,
Beischer N. Antenatal and intrapartum antecedents of
38. Thorngren-Jerneck K, Herbst A. Perinatal factors associated
population: risk factors and neuroimaging findings. Pediatrics
pregnancy BMI and risk of cerebral palsy in offspring.
Pediatrics 2016;138(4).
outcomes, and etiologies of perinatal stroke in Taiwan:
comparisons between ischemic, and hemorrhagic stroke
based on 10-year Experience in A Single Institute. Pediatr
42. Cole I, Dewey D, Letourneau N, et al. Clinical characteristics,
risk factors, and outcomes associated with neonatal
hemorrhagic stroke: a population-based case-control study.