

Antenatal and Perinatal Risk Factors for Cerebral Palsy in Scotland

Sandra R Bonellie ^a, Dorothy Currie ^b, James Chalmers ^c

a Lecturer, Centre for Mathematics and Statistics, Napier University, Edinburgh

b Senior Research Fellow, Child and Adolescent Health Research Unit,

Department of PESLS, The University of Edinburgh

c Consultant in Public Health Medicine, Information and Statistics Division, NHS
Scotland

Address for correspondence

S R Bonellie
Centre for Mathematics and Statistics
Napier University
10 Colinton Road
Edinburgh
EH10 5DT

Phone: 0131 455 2474

Fax: 0131 455 2651

e-mail: s.bonellie@napier.ac.uk

Summary

The Scottish Register for Children with a Motor Deficit of Central Origin was established in 1990 as part of a Scottish Office funded project. It contains information on children with cerebral palsy (CP) born between 1984 and 1990. This paper reports findings from a study, funded by the Chief Scientists Office, which linked the information from the register with the birth records for the children and concentrates on singleton births.

Successful links to the birth records were established for 88% of the children with CP on the register, giving a group of 512 singleton births that resulted in registered CP cases. The link between low gestational age and an increased risk of CP is well established and was confirmed using these data. In order to establish a clearer picture of other risk factors, the data were subdivided into three gestational age groups, under 32 weeks gestation, 32-36 weeks gestation and 37 weeks and over. The rates of registered cases of CP per thousand live births in each of these groups were 41.9, 5.6 and 0.7 respectively.

The risk factors for CP were found to be different in the different gestational age groups. Breech, forceps and emergency caesarean section delivery were all risk factors in the term group. In addition there was evidence that young or old maternal age was a risk factor for this group. For the middle group the risk of CP was lower if the mother suffered from pre-eclampsia. The only mode of delivery associated with an increased risk for this group was emergency caesarean section. For the most preterm group the usual pattern of an increased risk with low birthweight for gestational age was reversed. This effect is most probably explained by the increased risk of stillbirth or neonatal death in the low birthweight, low gestational age babies.

Introduction

Cerebral palsy (CP) is the most common cause of severe disability in children with a prevalence of approximately 2 per 1000 neonatal survivors in the UK,¹ with similar rates reported from other developed countries^{2,3}.

CP results from damage to the immature brain. Although postnatal causes, for example infection or trauma, are believed to account for a small proportion of cases, the majority of CP cases are thought to have their origin in the prenatal period,⁴ and investigation of the possible prenatal antecedents of CP is the focus of much current research.

The increased risk of CP associated with low birthweight and short gestation has been extensively studied. Rates of CP in low birthweight babies are many times higher than in normal (>2500g) birthweight babies⁵. Gestational age is also a major risk factor for CP⁶. Although only about 5% of births are preterm (< 37 weeks gestation) about 40-50% of all CP births are preterm⁷. More recently there had been an increasing interest in inappropriate fetal growth patterns as a risk factor for CP however few studies have been able to compare weight for gestational age patterns between CP children and the normal population⁸.

As well as the recognised association of CP with low birthweight and early gestational age many other factors have been recognised as potential antecedents of CP. For example, maternal factors, both demographic and obstetric, have been found to have an association. However, much of the research into these factors has involved preterm babies only. Investigation of the factors affecting CP risk is complicated by the inter-relationship between factors. For example, birthweight and gestational age are highly correlated and other potential risk factors are often more common in light and/or preterm infants.

Research into factors associated with CP is further limited by the rarity of the disorder. At only 1 to 2 cases per thousand neonatal survivors prospective studies are difficult and many studies are small, based on only a few tens of individuals. Most work has been done on a case-control basis. Since gestational age or birthweight is often used to match controls information on the effect of these variables themselves on the risk of CP may be lost.

The number of risk factors for which information is available is limited in most studies. This is in part because each study is carried out in isolation, with the aim of investigating a particular set of potential risk factors but in part is also because having access to information on multiple risk factors in an individual study is relatively rare.

Denominator data for prevalence rates is often difficult to obtain. The present study uses a retrospective cohort of births in Scotland to assess CP rates and identify risk factors for CP in this population that are of antenatal or perinatal origin. A data set was obtained by linkage of the records for children from the Scottish Register of Children with a Motor Deficit of Central Origin to their mothers' records for the birth (SMR2). SMR2 contains routinely recorded information on many previously recognised prenatal and perinatal risk factors for CP and is known to include 98% of all the births in Scotland.

This data set overcomes many of the problems associated with research into risk factors for CP; it has a reasonably large number of cases of CP, appropriate denominator data, and information on many previously recognised birth-related risk factors for CP. The effects of these factors on CP risk individually, and more importantly in combination with each other, were assessed. The size of this cohort permits its subdivision into term and preterm cohorts to assess independently the risk factors for each group with data sets that are directly comparable.

Methods

Compiled between 1990 and 1996 as part of a Scottish Office funded project ⁹, the Scottish Register of Children with a Motor Deficit of Central Origin includes children in Scotland born between 1984 and 1990 inclusive. European guidelines on standardisation of classification of CP were introduced after the formation of the register ¹⁰. The guidelines classify CP into four main types – spastic hemiplegic, spastic bilateral, ataxic and dyskinetic. All records of children with CP on the Scottish Register of Children with a Motor Deficit of Central Origin were assessed and classified into one of these types. Cases not considered to be CP were excluded from the study, as were instances where the diagnosis had been made before the child was two years old, cases where CP was associated with a particular syndrome, for example Downs and cases where the CP symptoms were considered to be of post-natal origin. An attempt was then made to establish a link between each of the remaining cases and the SMR2 forms. Variables were obtained or were derived from information on both the SMR2 forms and from the register. These are listed in

Error! Reference source not found..

We were particularly interested in looking at abnormal growth, therefore rather than use actual birthweights it is more appropriate to compare results by the birthweight that would be expected for a particular gestational age and sex. Birthweights for each gestational age were divided into 5 equal groups for males and for females. Each birthweight was classified as coming from the 1st, 2nd, 3rd, 4th or 5th quintile of birthweight for gestational age and sex, using the data on all singleton births in the study.

Table 1 List of variables and their source

Variable	Source	
	SMR2	Register
Description		
Registration Details		
Diagnosis of CP		X
Type of CP		X
Maternal Factors		
Maternal Age	X	X
Carstairs's Deprivation index based on post code at birth	X	X
Parity	X	X
Antenatal Factors		
Antepartum Haemorrhage	X	
Pre-eclampsia	X	
Maternal Infection	X	
Premature rupture of the membranes	X	
Perinatal Factors		
Gestational age	X	X
Mode of delivery	X	
Problems with cord at birth	X	
Postnatal Factors		
Birthweight	X	X
Sex	X	X
Apgar score at 5 mins	X	

Deprivation scores were obtained from the postcodes of the mothers' residences at the time of the birth using the Carstairs's index based on the 1991 census data. These were then coded by quintile.

Using the complete data set, odds ratios were obtained for each of the possible explanatory variables, using univariate analyses. Multivariable analysis for the complete data set was carried out, including interaction terms. This analysis is complicated by the relationships between the different variables. In particular many factors that appear to have a significant effect, with $p < 0.05$, on the odds of a child having CP cease to be significant when gestational age is taken into account.

The combined effects of different factors were investigated within three distinct gestational age groups namely, those born at less than 32 weeks gestation, between 32

and 36 weeks gestation and 37 weeks gestation and over. The babies born at 37 weeks gestation or more are basically born at term. The others are preterm. However there is a distinction to be made between those born before 32 weeks and those born between 32 and 36 weeks. In the former group a fairly high proportion of babies with brain damage will die and thus not survive to be diagnosed as having CP. The majority of the latter group, although preterm, are expected to survive and there are not therefore the same problems with the denominator data which occur in the very preterm group.

Results

There were a total of 920 children on the register who were born between 1984 and 1990. After the exclusions previously mentioned a total of 646 children with CP from the Scottish register were left and each child's record was electronically linked to their mother's SMR2 record for the child's birth. A total of 570 records linked successfully, of which 512 cases corresponded to singleton births. This rate of success is lower than that normally achieved using the Scottish record linkage system¹¹. This is probably explained by the fact that the data on the Scottish Register of Children with a Motor Deficit of Central Origin was collected some years after the birth data and in a different format. Information was also obtained on 43958 singleton, neonatal survivors born between 1984 and 1990. This includes those with CP. The overall prevalence rate for singletons over the seven-year period was 1.33 recorded cases of CP per 1000 neonatal survivors.

In general it was found that there was close agreement between the register and the SMR2 record for variables such as gestational age and birthweight but that information on other variables common to both was less reliable, for example parity and maternal age. Where the records failed to agree the SMR2 record was taken as the

most likely to be accurate on the basis that this record was completed shortly after the birth rather than a number of years later.

To assess if the linked individuals would be representative of the CP population as a whole a comparison was made between the linked and unlinked cases using the variables available from the register. The linked and unlinked cases were similar with respect to birthweight, gestational age and sex. The only variable that was found to be significantly different was the age of the mother, with maternal age being higher in the linked cases. This could reflect the linkage method being based in part on the soundex of child and mother's surname. It may be that younger mothers are more likely to have changed surname between birth of the child and registration thus making linkage more difficult. It was also found that, in the cases that linked, this variable was not recorded as accurately as others on the register. There is some evidence that in some instances the mother's age at time of registration rather than at time of birth has been recorded.

Univariate logistic regression was used initially to investigate the potential relationship between each variable and CP using data for all gestational ages. The results are summarised in Table 4.

Interaction terms involving gestational age were investigated for the complete data set and significant interactions were found for birthweight for gestational age, pre-eclampsia and delivery. In order to obtain a clearer picture of the relationships between the variables, the results were divided into the three gestational age groups, less than 32 weeks, 32-36 weeks and 37 weeks or more. There are distinct differences between these groups with respect to most of the available variables as well as differences with respect to the rate of CP cases and the type of CP. These are summarised in Table 3.

Table 2 Univariate odds ratios for each variable

Variable	Groupings	Number of CP cases	Odds ratios with 95% confidence interval
Gestational age	24-27	27	86.68 [57.79, 130.0]
	28-31	92	60.60 [47.66, 77.05]
	32-36	113	8.38 [6.73, 10.43]
	37 or more	280	reference
Birthweight for gestational age	1 st quintile	151	1.83 [1.40, 2.40]
	2 nd quintile	99	1.21 [0.91, 1.62]
	3 rd quintile	89	1.08 [0.80, 1.46]
	4 th quintile	89	1.08 [0.80, 1.46]
	5 th quintile	82	reference
Sex	Male	291	1.24 [1.04, 1.48]
	Female	221	reference
Age of mother	Teenage	76	1.69 [1.32, 2.17]
	20-24	394	reference
	35 and over	42	1.37 [0.99, 1.88]
Deprivation	1 st quintile	87	1.08 [0.80, 1.46]
	2 nd quintile	90	1.13 [0.84, 1.53]
	3 rd quintile	95	1.18 [0.88, 1.60]
	4 th quintile	116	1.44 [1.08, 1.92]
	5 th quintile	80	reference
Parity	Null parity	276	reference
	1 or more	236	0.69 [0.58, 0.82]
Antepartum Haemorrhage	Yes	58	2.87 [2.16, 3.82]
	No	454	reference
Pre-eclampsia	Yes	75	1.32 [1.03, 1.68]
	No	437	reference
Premature rupture of the membranes	Yes	39	3.89 [2.81, 5.40]
	No	473	reference
Cord problems	Yes	26	1.04 [0.70, 1.55]
	No	486	reference
Maternal Infection	Yes	73	2.19 [1.71, 2.80]
	No	439	reference
Delivery	Normal	283	reference
	Forceps	52	7.52 [4.72, 11.98]
	Breech	19	1.17 [0.87, 1.57]
	Elective CS	31	1.60 [1.10, 2.31]
	Emergency CS	127	4.00 [3.24, 4.93]

Table 3 Percentage with each characteristic by gestational age groups

Variable (number of missing observations)	Gestational Age in weeks		
	< 32	32-36	≥37
Number of births	2843	20030	416675
Age of mother (2)			
% of teenage mothers	15.4	13.6	9.2
% of mothers 35 or over	8.4	7.9	6.5
Parity (124)			
% null parous	51.8	50.7	44.1
Sex (5)			
% male	53.1	54.8	51.2
Apgar score (3552)			
% less than 7	18.64	4.13	1.26
Antepartum haemorrhage ^a			
% with	26.1	14.2	3.7
Maternal Infection ^a			
% with	22.6	15.7	6.6
Premature rupture of the membranes ^a			
% with	14.7	9.4	1.6
Pre-eclampsia ^a			
% with	16.1	16.1	11.3
Problem with cord ^a			
% with	2.5	3.3	5.0
Mode of delivery (228)			
% normal	42.9	60.6	75.0
% forceps	5.0	9.0	11.8
% breech	8.6	1.7	0.6
% elective CS	10.9	8.7	4.9
% emergency CS	32.6	20.0	7.7
Deprivation score (35443)			
% first quintile	16.2	16.9	20.3
% second quintile	17.3	18.3	19.9
% third quintile	19.1	19.9	20.0
% fourth quintile	23.3	21.5	20.0
% fifth quintile	24.1	23.5	19.8
Cerebral Palsy ^a			
Rate per 1000 births	41.9	5.6	0.7
Type of Cerebral Palsy ^a			
% Spastic Bilateral	61.3	56.6	36.8
% Spastic Hemiplegic	17.6	24.8	31.8
% Ataxic	4.2	4.4	8.2
% Dyskinetic	14.3	12.4	16.1

^a Not applicable

In general, the pregnancies of short gestation are more likely to have had some form of complication than those at normal gestation. Only 42.9% of the deliveries of

the babies with gestational age less than 32 weeks were normal, compared to 75% for those who went to term. Mothers of preterm babies were more likely to be either teenagers or 35 or over and more at greater risk of belonging to the most deprived quintile.

Univariate analysis within the gestational age groups reduced the number of variables which appeared to be significant predictors of CP. For the most preterm babies (<32 weeks) only gestational age and birthweight for gestational age were clearly significant. The age of the mother was marginally significant, ($p=0.0509$). For the middle group gestational age, birthweight for gestational age, antepartum haemorrhage and mode of delivery were all significant. Those born by breech delivery or emergency caesarean section had higher odds of having CP than those with normal deliveries.

For the term group more factors remained significant when considered on their own. In this group birthweight for gestational age, sex of the baby, age of the mother, deprivation score, parity and mode of delivery were all significant. None of the pregnancy complications however were even marginally significant.

Overall and for each of the groups except the lowest gestational ages, Apgar score was a positive predictor of CP. However this information was missing for about 3500 cases. Although this is less than 1% of the total a higher percentage of cases were missing for children with low gestational ages. For this reason Apgar score was not included in the multivariable analysis. It seems likely that the information on Apgar score is not missing at random but that it has not been recorded or obtained in a situation where the baby requires immediate medical attention. If this scenario is correct, it is likely that many of the missing scores are low. A model, which included

a category for missing for this variable, confirmed that there was a higher rate of CP among those with missing Apgar scores.

The indicator of the level of deprivation was missing for approximately 8% of the cases. By comparing the distribution of deprivation scores with those of the complete population there is no evidence that the observations are anything other than missing at random. However, because of the scale of the problem, deprivation was also excluded from the multivariable analysis.

Multivariable logistic models were then fitted to each of the gestational age groups separately. The results are shown in Table 5. In each case gestational age was fitted as a continuous variable and the first quintile for birthweight for gestational age corresponds to the lightest babies for that gestational age. Gestational age, birthweight and sex were included in all models.

For term babies, those in the first quintile were more than two and half times more likely to have CP than the heaviest babies in the fifth quintile. With the exception of an elective caesarean section those who had other than a normal delivery were more likely to have CP. The only other significant variable was the age of the mother with both the youngest and the oldest mothers having an increased risk of having a baby with CP. There was no significant difference between males and females for this group. Nor was gestational age significant, although for both variables the odds ratios are consistent with an increased risk for males and a decreased risk for gestational age. There were no cases of CP recorded at gestational ages in excess of 42 weeks.

For the middle group, with gestational age from 32-36 weeks, the significant variables were gestational age, birthweight for gestational age, mode of delivery and the occurrence of pre-eclampsia. As before, the babies with the lowest birthweights for gestational age were at higher risk of having CP. The only mode of delivery that

showed an increased risk was an emergency caesarean section. The occurrence of pre-eclampsia appears to have a protective effect on this group with the odds of having CP halved for those whose mothers had pre-eclampsia.

For the most preterm babies the only significant factors were gestational age, birthweight for gestational age and the age of the mother. Unlike the other gestational age groups it appears to be the heaviest babies that are at increased risk with the heaviest babies being more than twice as likely to have CP than the lightest ones. The effect of the mother's age is also the opposite to that observed for the term births. The oldest mothers appear to have a decreased risk of having a baby with CP.

Discussion

The availability of central electronic records of almost all births in Scotland and the ability to link those birth records with children on a cerebral palsy register has produced a powerful data resource for the investigation of the antecedents of CP. Much research into CP risks is based on limited numbers of high-risk births, and the ability to look at risk factors for all CP births, as is possible in Scotland, is unusual. In addition, having a data set that is large enough to allow division into term and preterm births allows the risk factors for these to be assessed separately and compared directly without the problems of comparing results from completely independent studies.

The overall rate of registered cases of CP is lower than has been found in other studies based on similar registers^{1 3}. In addition there are year-to-year differences in the rate of registered cases of CP with a sharp drop in 1990. It is therefore likely that ascertainment of cases is not complete on the register. However there is no reason to suppose that the level of ascertainment is affected by factors being studied so that it is

reasonable to look at the relative effects of the different factors even if the absolute prevalence cannot be calculated.

The one exception to this is deprivation. A previous study, using data from the cerebral palsy register in Oxford, found some evidence of higher rates of CP in the most deprived areas¹². In the Scottish data, the opposite effect has been observed with the rate of CP in the most deprived quintile lower than in the other categories. This may well result from the under-reporting of cases in more deprived areas.

Apgar score, which gives an indication of the intrauterine environment, has been associated with increased rates of CP in term babies, but not in preterm babies when adjustment is made for gestational age and birthweight¹³. In support of previous work univariate analysis of Apgar score was not associated with CP risk in the most extreme preterm births, but was a strong predictor of CP in other births. In this data set however there are many missing Apgar scores in the very preterm babies. Thus Apgar may have an effect on risk in these births but data shortcomings do not permit this to be assessed, alternatively this may not be a discriminative feature for CP in preterm babies as so many have low Apgar scores for a wide variety of reasons.

As in many previous studies maternal, antenatal and perinatal factors were all shown to have effects on CP risk in this population. However, attempting to interpret these effects when there are known interrelationships between the variables involved is not simple. Birthweight and gestational age are major predictors of CP risk in this population, as has been found in all studies. Assessment of the effect of other risk factors must involve adjustment for these two variables.

Many of the risks associated with an increase in CP rate are well-documented risks for preterm delivery. Risks for preterm birth which have also been shown to have associations with CP are pre-eclampsia, premature rupture of the membrane, young

maternal age, low socio-economic status and maternal infection¹⁴. The relationship of these factors with preterm birth is clearly shown in this data set when it is subdivided into three groups for different gestational ages. This could explain why so many associations found with CP do not persist when information on gestational age is available. An important issue to clarify is whether each of the maternal or antenatal factors has a direct, independent effect on CP rate, or whether its effect is mediated through some subsequent event such as preterm birth or through effects on intrauterine growth or birthweight. Alternatively, some unknown event may have led both to the antenatal problem and the subsequent CP¹⁵.

In this study, when all cases of CP were considered together pregnancy complications, such as premature rupture of the membranes, maternal infection, antepartum haemorrhage and pre-eclampsia, had univariate associations with increasing CP risk, but did not have an effect when adjusted for birthweight and gestational age. This supports previous evidence that these factors do not have an independent effect on CP risk⁴ but that their effect is mediated through preterm birth, as all these factors are known associates of preterm delivery. However, in preterm births one of these maternal complications of pregnancy, pre-eclampsia, has previously been found to be protective of CP¹⁶.

Overall the associate between pre-eclampsia and CP was shown to be positive across the range of gestational ages. However in the 32-36 week group it was found that there was a decreased risk of CP for those born to mothers who suffered from pre-eclampsia. The rate for those in the most preterm group was also lower when the mother had pre-eclampsia but not significantly so. Pre-eclampsia has previously been associated with an increase in the CP rate in term babies when unadjusted for gestational age⁴. However in preterm babies it has been found to suggest decreased

rates of CP¹⁷. A number of possible explanations for this have been suggested¹⁸, one of which is that magnesium sulphate used to treat pre-eclampsia could be a protective agent⁵, although it is unlikely that this was widely used for this particular cohort of women.

There is therefore an apparent contradictory effect of pre-eclampsia in term and preterm babies. It may be that more severe pre-eclampsia results in preterm birth whereas less severe pre-eclampsia results in a poor intrauterine environment for the remainder of the pregnancy¹⁹. Preterm births caused by pre-eclampsia would not suffer from this poor environment and would only have their prematurity and birthweight as risk factors for CP. Other preterm births, not caused by pre-eclampsia, must have some other cause which may have an additional risk of CP associated with it above the gestational age and birthweight risks. Knowledge of the timing of pre-eclampsia relative to delivery, and severity of pre-eclampsia would be valuable in testing these ideas.

Previous studies have found maternal factors such as the extremes of maternal age and increasing parity have been associated with an increase in the risk of CP. These associations are all confirmed in this study, however, the relationship with parity and CP is not strong enough to persist when adjustment for gestational age is carried out.

Maternal age has frequently been associated with an increase in CP risk for the youngest and oldest mothers. In the Scottish cohort when all cases were considered this was confirmed, an effect that persisted when adjustment was made for all other factors in term births. In the middle gestational age groups there was no association with maternal age and CP, even at a univariate level. However for the most preterm group the adjusted effect of maternal age was found to be significant with mothers aged 35 and over having a decreased chance of having a baby with CP.

It is well established that the risk of CP is higher for males than for females. This is borne out in the Scottish data overall and for term babies when sex is considered on its own. However the difference in risk between males and females was not statistically significant in any of the gestational age groups when adjusted for other variables. This may be due to lack of power when the data set is subdivided.

Type of delivery has also been scrutinised for potential association with CP rates. In general for term births, there were strong relationships between the rate of CP and birth-related factors. In these babies any abnormal mode of delivery is associated with an increased rate of CP. The only exception is an elective caesarean section. The picture is different in preterm babies however, with only an emergency caesarean in the 32-36 week group showing a significantly increased risk. This, of course, does not necessarily imply that the mode of delivery has contributed to the development of CP. It may be that the child has already suffered damage in the womb and this leads to the necessity of an abnormal mode of delivery such as an emergency caesarean section. Although the number of breech births is small compared to other modes of delivery, a large effect for breech birth is noted in both the full data set and within the term births.

There are clear differences brought out by comparing subsets of the data. When the data are subdivided by gestational age, it can be seen that risk of spastic bilateral CP is much higher in low birthweight and pre-term babies than the risk of spastic hemiplegic CP, which is mainly found in normal birthweight, term babies. For the term babies it is maternal and perinatal factors that are connected with CP. It is of interest that no relationship was found between problems with the umbilical cord at birth and the occurrence of CP in any of the subsets.

For the very preterm babies it is really only gestational age and birthweight for gestational ages that are connected with an increased risk of CP. The nature of the relationship is however different from that found at other gestational ages. For these babies there is an increased risk of CP with decreasing gestational age, as before, but it is the heavier babies who have a higher rate of CP. It must be remembered that the rates are calculated in terms of neonatal survivors. For the very lightest and earliest babies the rates of stillbirth and neonatal deaths are much higher. It may well be that many of those who fail to survive have CP but this is never diagnosed. This would explain the observed anomaly.

Recent findings⁸ have also suggested that there is an increased risk of cerebral palsy for children with birthweights above the 97th centile for gestational age. Although the results presented here have not used such a fine division of birthweight for gestational age, there was no indication in this data set of such an increased risk. This may well be a result of the relatively small sample size.

Only by studying prenatal antecedents of CP can hypotheses on the timing and causes of damage leading to CP be explored. Much CP research is hampered because the populations used are from different sources, have small numbers and each study has access to only a few potential risk factors. Having many factors available and a large data set has been a valuable opportunity, and encouragingly many of the risk factors identified in quite small studies where gestational age and birthweight were available were also identified here, suggesting these effects are quite robust.

The differences in the risk factors and strengths of these factors demonstrated when the data are divided into preterm and term births indicates the critical importance of gestational age explicitly, and birthweight by implication as average birthweight is lower for these births. It is clear that a vital prerequisite for any

analysis of risk factors for CP must be the ability to adjust for birthweight and gestational age.

References

1. Pharoah POD, Cooke T, Johnson MA, King R, Mutch L. *Epidemiology of cerebral palsy in England and Scotland, 1984-9*. Archives of Disease in Childhood 1998;**79**(1):F21-F25.
2. Sciberras C, Spencer N. *Cerebral palsy in Malta 1981 to 1990*. Developmental Medicine and Child Neurology 1999;**41**(8):508-511.
3. Hagberg B, Hagberg G, Beckung E, Uvebrant P. *Changing panorama of cerebral palsy in Sweden. VIII. Prevalence and origin in the birth year period 1991-94*. Acta Paediatrica 2001;**90**(3):271-277.
4. Palmer L, Blair E, Petterson B, Burton P. *Antenatal Antecedents of Moderate and Severe Cerebral-Palsy*. Paediatric and Perinatal Epidemiology 1995;**9**(2):171-184.
5. Nelson KB, Grether JK. *Cerebral palsy in low-birthweight infants: Etiology and strategies for prevention*. Mental Retardation and Developmental Disabilities Research Reviews 1997;**3**(2):112-117.
6. Murphy DJ, Sellers S, Mackenzie IZ, Yudkin PL, Johnson AM. *Case-Control Study of Antenatal and Intrapartum Risk-Factors for Cerebral-Palsy in Very Preterm Singleton Babies*. Lancet 1995;**346**(8988):1449-1454.
7. Colver AF, Gibson M, Hey EN, Jarvis SN, Mackie PC, Richmond S. *Increasing rates of cerebral palsy across the severity spectrum in north-east England 1964-1993*. Archives of Disease in Childhood 2000;**83**(1):F7-F12.
8. Jarvis S, Glinianaia SV, Torrioli MG, Platt MJ, Miceli M, Jouk PS, et al. *Cerebral palsy and intrauterine growth in single births: European collaborative study*. Lancet 2003;**362**(9390):1106-1111.
9. Mutch L, Ronald E. *The Scottish Register of Children with a Motor Deficit of Central Origin, 1992*.
10. Cans C, Guillem P, Baille F, Arnaud C, Chalmers J, Cussen G, et al. *Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers*. Developmental Medicine and Child Neurology 2000;**42**(12):816-824.
11. Kendrick S, Clarke J. *The Scottish Record Linkage System*. Health Bulletin 1993;**51**:72-79.
12. Dolk H, Pattenden S, Johnson A. *Cerebral palsy, low birthweight and socio-economic deprivation: inequalities in a major cause of childhood disability*. Paediatric and Perinatal Epidemiology 2001;**15**(4):359-363.
13. Topp M, LanghoffRoos J, Uldall P. *Preterm birth and cerebral palsy - Predictive value of pregnancy complications, mode of delivery, and Apgar scores*. Acta Obstetrica Et Gynecologica Scandinavica 1997;**76**(9):843-848.
14. Berkowitz GS, Papiernik E. *Epidemiology of Preterm Birth*. Epidemiologic Reviews 1993;**15**(2):414-443.
15. Pharoah POD, Cooke T, Cooke RWI, Rosenbloom L. *Birth-Weight Specific Trends in Cerebral-Palsy*. Archives of Disease in Childhood 1990;**65**(6):602-606.

16. Murphy DJ. *Neonatal risk factors for cerebral palsy in very preterm babies - Reply*. British Medical Journal 1997;**314**(7094):1624-1624.
17. Topp M, Uldall P, LanghoffRoos J. *Trend in cerebral palsy birth prevalence in eastern Denmark: birth-year period 1979-86*. Paediatric and Perinatal Epidemiology 1997;**11**(4):451-460.
18. Stanley F, Blair E, Alberman E. *Cerebral Palsies: Epidemiology & Causal Pathways*. First ed: Mac Keith Press, 2000.
19. Hutton JL, Pharoah POD, Cooke RWI, Stevenson CJ. *Differential effects of preterm birth and small for gestational age on cognitive and motor development*. Archives of Disease in Childhood 1997;**76**:F75-F81.

Table 4 Univariate odds ratios for each variable

Table 5 Results from multivariable logistic regressions for each gestational age group

Variable	37 weeks or more		32-36 weeks		Less than 36 weeks	
	Number of CP cases	Odds Ratio with 95% Confidence Interval	Number of CP cases	Odds Ratio with 95% Confidence Interval	Number of CP cases	Odds Ratio with 95% Confidence Interval
Gestational Age	280	0.92 ^a [0.83,1.01]	113	0.50 ^a [0.44, 0.57]	119	0.87 ^a [0.79, 0.96]
Birthweight for gestational age						
1 st quintile	151	2.59 [1.80, 3.73]	31	2.75 [1.38, 5.46]	15	0.47 [0.25, 0.88]
2 nd quintile	99	1.22 [0.80, 1.86]	27	2.30 [1.16, 4.56]	25	0.78 [0.45, 1.35]
3 rd quintile	89	0.98 [0.63, 1.52]	23	1.93 [0.96, 3.90]	28	0.87 [0.51, 1.49]
4 th quintile	89	1.29 [0.85, 1.95]	19	1.57 [0.76, 3.24]	20	0.61 [0.34, 1.10]
5 th quintile	82	reference	12	reference	30	reference
Sex						
Male	291	1.24 [0.97,1.57]	71	1.36 [0.93,2.01]	60	0.91 [0.63,1.32]
Female	221	reference	42	reference	59	reference
Age of mother						
Teenage	38	1.53 [1.08, 2.17]		Not significant	19	0.92 [0.56, 1.53]
20 to 34	214	reference			96	reference
35 or more	28	1.70 [1.12, 2.48]			4	0.35 [0.13, 0.97]
Mode of delivery						
Normal	170	reference	51	reference		Not significant
Forceps	41	1.53 [1.09, 2.16]	6	0.83 [0.35, 1.94]		
Breech	7	4.77 [2.23, 10.20]	4	2.00 [0.71, 5.64]		
Elective CS	13	1.09 [0.62, 1.94]	9	0.95 [0.45, 2.00]		
Emergency CS	49	2.73 [1.98, 3.75]	43	1.84 [1.19, 2.84]		
Pre-eclampsia		Not significant	15	0.53 [0.30, 0.97]		Not significant

^a Increment per week