Cerebral palsy and intrauterine growth in single births: European collaborative study

Stephen Jarvis, Svetlana V Glinianaia, Maria-Giulia Torrioli, Mary-Jane Platt, Maria Miceli, Pierre-Simon Jouk, Ann Johnson, Jane Hutton, Karla Hemming, Gudrun Hagberg, Helen Dolk, James Chalmers, on behalf of the Surveillance of Cerebral Palsy in Europe (SCPE) collaboration of European Cerebral Palsy Registers

Summary

Background Cerebral palsy seems to be more common in term babies whose birthweight is low for their gestational age at delivery, but past analyses have been hampered by small datasets and Z-score calculation methods.

Methods We compared data from ten European registers for 4503 singleton children with cerebral palsy born between 1976 and 1990 with the number of births in each study population. Weight and gestation of these children were compared with reference standards for the normal spread of gestation and weight-for-gestational age at birth.

Findings Babies of 32–42 weeks’ gestation with a birthweight for gestational age below the 10th percentile (using fetal growth standards) were 4–6 times more likely to have cerebral palsy than were children in a reference band of 1·6 to 3·1, but still significant. Those with a birthweight about 1 SD above average always had the lowest risk of cerebral palsy. A similar pattern was seen in those with a birthweight below that expected for their gestation, but risk rises when weight is well below normal. Whether deviant growth is the cause or a consequence of the disorder remains to be determined.

Introduction Cerebral palsy is the most common cause of severe physical disability in children in developed countries. The frequency of the disorder in children born at low birthweights increased sharply in about 1980, but the cause of the condition is still poorly understood.1

Results of previous studies have shown that the well known excess risk of cerebral palsy in low birthweight babies is still apparent after adjustment for gestational age. However, this increase in cerebral palsy in babies with a birthweight below that expected for their gestation seems to be attenuated, or even reversed, at gestations earlier than 34 weeks.2,4 Interpretation of studies of lower gestational ages was limited by small sample sizes. Additionally, little attempt was made to consider the inherent biases in growth standards for preterm babies, such that babies with poor intrauterine growth also tend to be born preterm. In this study, we compare our results derived from use of conventional growth standards based on birthweight, with those from standards based on estimates of fetal weight calculated from ultrasonograms in healthy babies born at term.

Perinatal mortality is increased in relation not only to poor intrauterine growth but also to excess growth as manifested by heavy weight for gestational age.5,6 Results of some analyses have suggested this risk pattern might also be true for cerebral palsy,3,7,8 but they were not able to assess whether the effect existed in babies born prematurely, and the studies tended to concentrate on babies with a low birthweight for gestation.

More than 6500 cases of cerebral palsy have been identified in babies born between 1976 and 1990 in eight European countries as part of a collaborative study that includes 13 cerebral palsy registries—the surveillance of cerebral palsy in Europe (SCPE). This large dataset allows for detailed study of the relation between cerebral palsy and intrauterine growth, as judged by birthweight for gestational age. The aim of this study was to assess deviation from normal intrauterine growth as a possible pathological factor in the origins of cerebral palsy, and to thereby illuminate the debate about antenatal versus perinatal causes of the disorder.1

Methods SCPE collaboration methodology Participating centres use a consensus definition of cerebral palsy with the following key elements: cerebral palsy is a group of disorders—ie, it is an umbrella term; it is permanent but not unchanging; it involves a disorder of movement, posture, or both, and of motor function; it is caused by a non-progressive interference, lesion, or abnormality in the developing or immature brain.9 The main inclusion criteria are: age of at least 4 years when meeting criteria for the definition of cerebral palsy (except for deaths in children aged 2–4 years). Children with recognised syndromes, brain abnormalities, or...
participants of SCPE is described in greater detail elsewhere, as are other methodological details of the SCPE collaboration.9

Participants
From cases in the SCPE register, we excluded children with cerebral palsy born outside the register catchments, and those with disease of known postnatal origin. We intended to do analyses that used birthweight (g), gestation in completed weeks (largely confirmed by ultrasonographical dating), sex, and type of cerebral palsy (bilateral or unilateral spastic, dyskinetic, or ataxic). However, not all contributing cerebral palsy registers have complete data, so within calendar years we excluded information from registers in which 20% or more of values were missing. At one register (Tübingen, Germany) only cases of bilateral spastic cerebral palsy were recorded, and these data are only included in analyses in which cerebral palsy types are separated.

Assessment of intrauterine growth
Two conventional reference standards of expected weight-for-gestation at birth were selected after review of a larger set (Hemming K, personal communication). The North of England standard10 is widely used and is based on more than 118 000 singleton births of non-malformed children (but excluding antepartum stillbirths) from the same period as the register cases, and aligns well with most published European standards. However, because Swedish babies are heavier at each gestation, a second conventional standard was used for these cases.11 Conventional standards use the assumption that the weight-for-gestation profile of babies born prematurely represents that of the healthy babies who continue to grow in utero; however, this assumption might be incorrect.11

We, therefore, used a fetal growth standard calculated from the mean term weights of babies from the North of England standard10 using the Gardosi formula.13 This method is based on estimates of fetal weights from ultrasonographical information in 392 normal pregnancies in Texas.14 For Swedish babies, we used the fetal growth standard developed by Marsal and colleagues,15 which is derived from 759 serial ultrasonographical estimates of fetal weights in 86 normal pregnancies from four centres in Denmark and Sweden.

Birthweight for gestation for each singleton case was compared with these standards separately by sex, but not by parity (as this was unknown in many cases) to derive a standard deviation score (Z score). Cases were then allocated to Z-score bands chosen to equate to conventional growth percentiles (eg, in a normal distribution the Z-score band 1·28 to <1·88 is the same as 90th to <97th percentile).

Figure 1: Prevalence of cerebral palsy by Z score of weight for gestation: effect of different growth standards
For clarity, error bars on rates are omitted here; relevant rate ratios and p values are in the table.

<table>
<thead>
<tr>
<th>Z-score band</th>
<th>&lt;=1·88</th>
<th>-1·88 to &lt;-1·28</th>
<th>-1·28 to &lt;-0·67</th>
<th>-0·67 to &lt;0·67</th>
<th>0·67 to &lt;1·28</th>
<th>1·28 to &lt;1·88</th>
<th>&gt;1·88</th>
<th>Denominator*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conventional growth standards</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestation (weeks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;28</td>
<td>0·5 (4)</td>
<td>0·2 (3)†</td>
<td>0·2 (8)†</td>
<td>1 (133)</td>
<td>1·2 (49)</td>
<td>1·0 (18)</td>
<td>1·9 (15)</td>
<td>4521</td>
</tr>
<tr>
<td>28–31</td>
<td>0·9 (21)</td>
<td>0·5 (26)†</td>
<td>0·7 (78)†</td>
<td>1·3 (399)</td>
<td>1·0 (116)</td>
<td>1·0 (97)</td>
<td>1·2 (29)</td>
<td>15539</td>
</tr>
<tr>
<td>32–36</td>
<td>3·2 (78)†</td>
<td>1·7 (97)†</td>
<td>1·3 (154)</td>
<td>1·4 (406)</td>
<td>0·5 (62)†</td>
<td>0·3 (19)†</td>
<td>0·7 (18)</td>
<td>109 555</td>
</tr>
<tr>
<td>37–38</td>
<td>7·8 (105)‡</td>
<td>2·7 (85)‡</td>
<td>1·8 (120)‡</td>
<td>1·2 (225)</td>
<td>0·7 (45)</td>
<td>0·7 (22)</td>
<td>1·4 (19)</td>
<td>373 481</td>
</tr>
<tr>
<td>39–41</td>
<td>3·6 (162)‡</td>
<td>1·8 (190)‡</td>
<td>1·5 (328)‡</td>
<td>1·7 (746)</td>
<td>0·8 (173)§</td>
<td>0·8 (80)</td>
<td>1·0 (45)</td>
<td>1 784 177</td>
</tr>
<tr>
<td>42‡</td>
<td>2·3 (10)</td>
<td>1·7 (17)</td>
<td>1·2 (26)</td>
<td>1·7 (72)</td>
<td>0·7 (16)</td>
<td>0·7 (7)</td>
<td>1·6 (7)</td>
<td>1 103 754‡</td>
</tr>
<tr>
<td>All gestations</td>
<td>3·2 (380)‡</td>
<td>1·5 (420)‡</td>
<td>1·2 (714)</td>
<td>1 (1981)</td>
<td>0·8 (461)§</td>
<td>0·7 (202)‡</td>
<td>1·1 (133)</td>
<td>2 391 027</td>
</tr>
<tr>
<td><strong>Fetal growth standards</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestation (weeks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;28</td>
<td>2·4 (13)§</td>
<td>1·3 (16)</td>
<td>1·5 (40)</td>
<td>1 (90)</td>
<td>0·9 (25)</td>
<td>1·1 (14)</td>
<td>5·9 (32)</td>
<td>4521</td>
</tr>
<tr>
<td>28–31</td>
<td>6·8 (11)‡</td>
<td>2·0 (75)‡</td>
<td>1·5 (122)</td>
<td>1·2 (727)</td>
<td>0·8 (83)</td>
<td>1·0 (37)</td>
<td>2·9 (47)</td>
<td>15 539</td>
</tr>
<tr>
<td>32–36</td>
<td>13·7 (216)‡</td>
<td>3·0 (111)‡</td>
<td>1·7 (136)</td>
<td>1·2 (263)</td>
<td>0·6 (44)§</td>
<td>0·9 (32)</td>
<td>2·0 (32)§</td>
<td>109 555</td>
</tr>
<tr>
<td>37–38</td>
<td>13·6 (148)‡</td>
<td>3·3 (83)</td>
<td>1·8 (100)</td>
<td>1·2 (182)</td>
<td>0·8 (45)</td>
<td>1·1 (29)</td>
<td>3·1 (34)‡</td>
<td>373 481</td>
</tr>
<tr>
<td>39–41</td>
<td>6·4 (242)‡</td>
<td>2·5 (222)‡</td>
<td>1·7 (324)‡</td>
<td>1·6 (629)</td>
<td>0·9 (163)</td>
<td>1·0 (87)</td>
<td>1·6 (59)§</td>
<td>1 784 177</td>
</tr>
<tr>
<td>42‡</td>
<td>6·3 (241)‡</td>
<td>2·8 (21)</td>
<td>1·9 (35)§</td>
<td>1·6 (63)</td>
<td>0·7 (14)</td>
<td>0·3 (1)</td>
<td>1·9 (7)</td>
<td>107 855‡</td>
</tr>
<tr>
<td>All gestations</td>
<td>8·4 (754)‡</td>
<td>2·5 (532)‡</td>
<td>1·7 (757)</td>
<td>1·4 (1499)</td>
<td>0·8 (352)§</td>
<td>1·0 (202)</td>
<td>2·3 (211)‡</td>
<td>2 395 128</td>
</tr>
</tbody>
</table>

Equivalent percentiles

<table>
<thead>
<tr>
<th>≤3</th>
<th>3 to &lt;10</th>
<th>10 to &lt;25</th>
<th>25 to &lt;75</th>
<th>75 to &lt;90</th>
<th>90 to &lt;97</th>
<th>&gt;97</th>
</tr>
</thead>
</table>

*Estimated from 2 395 128 known total livebirths allocated according to the gestational age distribution of Scotland 1980–92. † p<0·001. ‡ p<0·001 and >0·001. § Gestational age 43 weeks or more omitted because no North of England standard is available (16 cases in 4100 estimated births). Rates (as illustrated in figure 1) can be calculated for each cell by allocating the denominator column to the percentages in the final row. |41 weeks’ denominators may be 5–10% too low as Swedish postmature gestational age distribution differs from that in Scotland.

Rate ratios (n) of cerebral palsy by Z-score band in gestational age-groups with use of conventional and fetal growth standards
Denominators
In estimations of the Z-score band specific rate of cerebral palsy, we used the actual number of livebirths in the source population as a denominator, allocated in accordance with the percentage gestational age distribution of a reference dataset of some 800 000 Scottish singleton livebirths in 1980–92. The estimated number of births within each gestational age group (eg, 32–36 weeks) is then divided between Z-score bands, assuming a normal distribution. Rate comparisons are between Z-score bands and are not reliant on exact denominator allocation to gestational-age categories.

Statistical analysis
The rate at which cases appear in a particular Z-score band is compared with the rate in the reference band –0·67 to less than 0·67 (equivalent to the 25th to <75th percentiles). Rate ratio 99% CIs are calculated with methods described by Morris and Gardner.

Role of the funding source
The sponsor had no role in study design, data collection, data analysis, data interpretation, the writing of the report, or the decision to submit the paper for publication.

Results
After exclusion from the SCPE database of cases with known postneonatal cause, those born outside the register catchments, the Netherlands register (because there were no reliable denominators), the two French registries (>20% of data were missing for plurality, birthweight, or gestation in every year), and 2 of the 15 years in the Southern Irish register (>20% of data missing), 4622 singleton cases remained. Of these, 119 (2·6%) had missing values for gestational age, birthweight, or both. Thus, 4503 cases were included in our analysis, including 196 from the German register of bilateral spastic cerebral palsy.

Figure 1 shows weight-for-gestation specific rates of cerebral palsy expressed in Z-score bands for conventional and fetal standards. The corresponding rate ratios for risk of cerebral palsy are shown in the table.

Use of conventional standards results in an excess number of cerebral palsy cases in both light and heavy-for-gestation babies, often in a reversed J shaped pattern around an apparent optimum weight for that gestational age. For births before 32 weeks' gestation, this optimum seems to be located in the –1·88 to less than –1·28 Z-score band, but moves at later gestations to between 0·67 and less than 1·88. Post hoc rate ratio comparisons with the 0·67 to less than 1·88 optimum band (rather than the a-priori central band used in the table) showed an excess risk in the heaviest babies (≥1·88 at all gestations: rate ratio [RR] 1·44 [99% CI 1·12–1·86]).

The corresponding analysis with fetal growth standards shifts these patterns so that light-for-gestation babies at gestations of less than 32 weeks have a greater risk of cerebral palsy than when using the conventional growth standard. Optimum weight for these very preterm babies now moves above mean birthweight to a position consistent with other gestational age groups. At early gestations, SD are smaller in the fetal growth standards. Premature cases are, therefore, usually assigned to Z-score bands further away from the mean. In babies of 32–42 weeks' gestation, those with a weight below the 10th percentile were 4–6 times more likely to have cerebral palsy than were those in the 25th–75th percentile reference band (RR 3·7 [3·2–4·3] to 6·3 [4·9–8·2]). In those with a weight above the 97th percentile, the increase in risk was smaller than that for the underweight babies (1·6 [1·1–2·2] to 3·1 [1·9–5·0]), but was still significant (table).

Because the number of cases of ataxic and dyskinesia cerebral palsy was quite small, we used only two groups (term and preterm [<37 weeks’ gestation]) for analysis by type of cerebral palsy. Results are shown in figure 2. Data shown in figure 2 is based on conventional standards, and show that there is little to distinguish the patterns by type of cerebral palsy. Excess risk for heavy-for-gestation babies occurs for every cerebral palsy type at term, with optimum birthweight consistently on the heavy side of the mean. For preterm babies when using conventional growth standards, there is not such a clear optimum Z-score band, but the reversed J shaped distribution of risk is clearly present for the bilateral spastic forms of cerebral palsy.

When fetal growth standards are used for preterm babies, as in figure 2, the patterns become more consistent with those at term. Further splitting of the preterm group shows that most of the discrepancy between the patterns in figure 2 occurs in the age band of less than 32 weeks’ gestation. Meanwhile, for term babies the patterns derived from the two different types of standard are virtually identical (data not shown).

Discussion
Growth standards
Our data suggest that the risk of cerebral palsy is linked, not only to low weight-for-gestation, but also to excessively high weight-for-gestation. The main concerns about validity in the kind of analyses we have done are about the appropriateness of the estimated denominators for each weight-for-gestation category. At very low gestational age (<32 weeks’ gestation), neonatal mortality and cerebral palsy are competing outcomes, and cerebral palsy rates...
standards, we used one standard from the North of England for five countries. This standard might be slightly heavy for the Danish and Italian births (Hemming K, personal communication), and thus the true excess of cerebral palsy in babies who are heavy for gestation could be even larger than we estimate.

An optimum birthweight, as judged by a reversed J-shaped rate variation within gestational age bands has been reported for perinatal mortality.\(^5\)\(^6\) Presumably, the overall pattern of mortality risk by birthweight is the product of intrauterine growth trajectories that can be interrupted by birth at many points. This optimum does not correspond to the most frequent (ie, mean) birthweight, but is actually somewhat heavier.\(^6\)

A similar reversed J-shaped distribution of cerebral palsy risk by birthweight (unadjusted for gestation) was demonstrated in an earlier study from the north-east of England.\(^8\) A recent report from China shows an optimum "standard normal deviate" at about +1 \(Z\) score of weight-for-gestation for singleton cerebral palsy cases.\(^7\) Our new finding that this optimum is present at every gestation longer than 32 weeks (and could be the case for earlier gestations when appropriate adjustments are made for intrauterine compatriots) suggests that this is an important biological phenomenon.

Unusual intrauterine growth (both increased and decreased) seems to have a similar link to several causes of perinatal mortality,\(^6\) to other non-fatal perinatal

Figure 3: Mean male weight-for-gestation with four growth standards
Formulae for the two fetal standards use exact weeks (Gardosi) or days (Marsal) of gestation to calculate expected weights (eg, 40 completed weeks (as recorded for cases)=283·5 days=40·5 exact weeks\(^6\) gestational age).

will, therefore, be underestimated when livebirths are used as denominators. Recalculation of data in the table and figure 1 with contemporary neonatal survival rates by \(Z\) score (Hey E, personal communication), shows that allowance for selective mortality further exaggerates the reversed J patterns of cerebral palsy rates in children of gestation less than 32 weeks.

Figure 3 shows that conventional growth standards based on weight at delivery might be biased by an excess of preterm light-for-gestation babies.\(^2\)\(^,\)\(^12\) In our analysis, use of the new fetal growth standards leads to more uniformity in the shape of the J curve, especially placing optimum growth more consistently at about one SD above the mean, even for preterm babies. Such fetal standards are also likely to be based on more exact gestational age estimations. On the other hand, fetal standards propose variances of weight at low gestation (12% Marsal,\(^15\) 11% Gardosi\(^13\)) much narrower than those in many conventional standards. Recalculation of \(Z\) scores with the Gardosi mean fetal weights and North of England conventional variances produces patterns between those seen in figure 1.

Assignment of \(Z\) scores and percentiles based on \(Z\) scores assumes a normal distribution of weight-for-gestation data. To assess the extent of possible bias, we recalculated results using empirical percentiles published for the same North of England standard that we used for \(Z\) scores. Figure 4 shows that results obtained by both of these methods do not differ greatly.

Determination of gestational age carries some uncertainty, and needs to be similar in the numerator (cerebral palsy cases) and denominator (all births). Extensive use of ultrasonographical dating underpinned the estimation of gestational age, in both the conventional standards used and the obstetric centres where children with cerebral palsy in our study were born, since the early 1980s. After doing another analysis with only data from 1983 to 1990, we noted similar results to those derived from the full dataset.

Normal growth for gestation might vary between countries. In the absence of appropriate country-specific standards, we used one standard from the North of England for five countries. This standard might be slightly heavy for the Danish and Italian births (Hemming K, personal communication), and thus the true excess of cerebral palsy in babies who are heavy for gestation could be even larger than we estimate.

An optimum birthweight, as judged by a reversed J-shaped rate variation within gestational age bands has been reported for perinatal mortality.\(^5\)\(^6\) Presumably, the overall pattern of mortality risk by birthweight is the product of intrauterine growth trajectories that can be interrupted by birth at many points. This optimum does not correspond to the most frequent (ie, mean) birthweight, but is actually somewhat heavier.\(^6\)

A similar reversed J-shaped distribution of cerebral palsy risk by birthweight (unadjusted for gestation) was demonstrated in an earlier study from the north-east of England.\(^8\) A recent report from China shows an optimum "standard normal deviate" at about +1 \(Z\) score of weight-for-gestation for singleton cerebral palsy cases.\(^7\) Our new finding that this optimum is present at every gestation longer than 32 weeks (and could be the case for earlier gestations when appropriate adjustments are made for intrauterine compatriots) suggests that this is an important biological phenomenon.

Unusual intrauterine growth (both increased and decreased) seems to have a similar link to several causes of perinatal mortality,\(^6\) to other non-fatal perinatal mortality,\(^4\) to other non-fatal perinatal mortalities, and to other causes of perinatal mortality.

Figure 4: Prevalence of cerebral palsy by weight for gestation: percentile versus \(Z\)-score methods both with use of the same North of England conventional growth standard
Swedish babies are excluded. Vertical bars are SE.
outcomes, to abnormalities of the placenta, and even to spontaneous premature delivery, which suggests that slowed or increased growth is a generic response to intrauterine insult and distress.

Six other studies of the relations between intrauterine growth and risk of cerebral palsy in the USA, Sweden, Western Australia, Denmark, and England have been reported. Indeed, a small number of infants with cerebral palsy also contribute to the present analysis, as do a few from the Danish study. Otherwise, the current study is an independent dataset and is much larger than previous studies.

Of these earlier reports, only the largest study from Sweden (based on >500 cases from births in 1967–81) showed the significant inflexion in risk for heavier babies. In an earlier Swedish study confined to 116 dyskinetic cases from 1959–70, reanalysis of the published data shows that a significantly raised risk in babies greater than +2 Z scores from the mean weight was apparently overlooked. Likewise, in a review of the subject, a whole chapter is dedicated to intrauterine growth retardation as a pathway to cerebral palsy, but babies who are heavy for their gestation are not mentioned.

What is the nature of the relation between deviant growth and cerebral palsy? The link might exist in either direction (ie, abnormal growth causes cerebral palsy or vice versa) or through some confounding factor linked independently to growth and to risk of cerebral palsy.

Brain damage or maldevelopment in utero might trigger an abnormal growth pattern through endocrine or other pathways. Such abnormal growth could occur throughout pregnancy or it might immediately precede delivery. Fetal abnormalities might precipitate or even delay delivery with attendant additional risks to an already compromised infant.

Alternatively, the original cause of abnormal growth in utero might not be connected with damage to the developing brain but, because abnormal growth increases physiological vulnerability, the brain is exposed to irreparable damage during or after delivery. This issue might be clarified by studies that distinguish growth retardation from proportionate growth in small- for-gestational-age children who have cerebral palsy. For instance, Uvebrant and Hagberg in a report of risks for cerebral palsy by birthweight-for-birthlength noted that babies with cerebral palsy are comparatively thin, especially at term. On the other hand, Blair and Stanley describe a variety of morphological types with a significant increase in risk for spastic cerebral palsy, only some of which involve thinness—others have disproportionately large heads.

Topp and colleagues in their study of preterm cases state that “in general, there is no correlation between ponderal index and cerebral palsy”, while Gould in a review of low birthweight outcome studies states that “paradoxically, long-term neurological handicap appears to be higher in the proportionately small infants even though they experience fewer problems during the neonatal period”. The question remains, therefore, is deviant growth associated with cerebral lesions mainly proportionate (possibly attributable to disturbed growth regulation in an abnormal fetus?) or disproportionate (possibly due to deficient nutrition rendering the baby vulnerable to cerebral insults)?

What does seem certain is that these abnormal growth patterns indicate a process that commenced well before birth. Increasingly, evidence is pointing to endocrine pathways, infection, coagulation defects, or even a “vanishing twin” episode early in pregnancy as the primary cause in many cases of cerebral palsy. However, we do not suggest that excellent intrapartum and postpartum care cannot influence the outcome, but rather that these are palliative measures and that definitive intervention should start earlier.

Despite some reservations about the choice of appropriate denominators, the risk of cerebral palsy is linked, not only to low weight-for-gestation, but also to excessively high weight-for-gestation. It seems likely that this effect is part of a wider biological phenomenon whereby there is an optimum intrauterine weight trajectory that can be disturbed by a variety of antepartum insults.

Obstetricians should view deviations (in either direction) away from optimum growth-for-gestation as signals for fetal abnormality that warrant investigation. Growth deviations might indicate treatable, continuing conditions (eg, infections) or the need to prepare for (or prevent) mistimed delivery. Aberrant growth trajectories are more informative than single weight deviations and might give clues to the timing and nature of original insults.

Investigation of mechanisms of abnormal growth in utero could reveal whether the brain’s developmental insults are to the developing brain or to other organs (including the placenta). In the case of damage to other organs, maintenance of pregnancy or intensive extraterine support might preserve what is, until delivery, a child with an intact brain.

Contributors
All authors, other than K Hemming, participated in the original process of SCPE data definitions, collection, and harmonisation. All authors contributed to analysis design or commented on report drafts.
K Hemming and J Hutton did literature searches for and comparative analyses of conventional standards of weight for gestation. S Jarvis and S V Glinianaia did the main analyses and J S Jarvis drafted the manuscript.

Conflict of interest statement
JH acts as an expert witness on the life expectancy of people with cerebral palsy. The other authors have no conflicts of interest. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Acknowledgements
We thank participants in the SCPE collaboration: from France (C Cans, P Guillen, C Arnaud), Scotland (J Chalmers), Eire (V McManus, G Gussen (died January, 2001)), O Hensley, V Dowding, N Ireland (J Parkes, H Doli), Sweden (B Hagberg, G Hagberg), England (S Jarvis, A Colver, A Johnson, G Surman, M J Platt, P Pharoah), Germany (K Kraegeloh-Mann, R Michaelis), Denmark (M Topp, P Uldall), Italy (M G Torrioli, M Miceli), and the Netherlands (M Wichers). We also thank Ed Hey who gave valuable advice at various stages of this work.

This research was supported by European Commission funds: DGXII-BIOMED2-Contract N°BMH4-983701.

References


