**Supplementary Information**

## Appendix 1: Centres Excluded from Analyses

Table A1. Number of children with CP, multiples with CP, live births, multiple live births, and number of cohort birth years for which data were available by Centre.

| Centre | n CP | Multiples CP | Livebirths | Multiple Livebirths | Reasons for exclusion |
|---|---|---|---|---|---|
| Grenoble, France | 564 | 73 | 382,836 | 11,183 | [a] |
| Toulouse, France | 394 | 60 | 251,436 | *NA* | [a, b] |
| Edinburgh, UK | 57 | <10 | *NA* | *NA* | [a, b, c] |
| Belfast, UK | 779 | 65 | 376,968 | 637[d] | [a, c] |
| Dublin, Ireland | 799 | 72 | 405,988 | 9,870 | [a] |
| Bologna, Italy | 61 | <10 | 37,255 | *NA* | [a,b] |
| Galway, Ireland | 98 | <10 | 81,486 | *NA* | [a,b] |
| Cyprus | 29 | 10 | *NA* | *NA* | [a,b] |
| Iceland | 174 | 30 | 82,935 | 2,915 | [a] |
| Tyrol, Austria | 152 | 21 | 110,079 | 875[d] | [a] |
| Croatia | 187 | 29 | 83,404 | 2176 | [a] |

Rationale for excluding centres from analyses, according to the criteria set (see Methods):

[a] No information on multiple births denominators by GA and BW categories

[b] No information on denominators by multiplicity at birth

[c] Provides information on less than three birth cohort years

[d] Denominators by multiplicity were reported for fewer cohort years compared to the total of live births

## Appendix 2: Birth Weight Norms

In order to calculate *Standardized Birth Weight (BW) z Scores*, we referred to birth weight norms provided according to the child's gestational age and gender. These also differed between singletons and multiples. For singletons, BW norms were based on the Gardosi formula[1] applied to infant's sex specific mean weight for single births. Standardized scores for twins and multiples were calculated according to norms provided for US white male and female twins[2] and adjusted to fit European births using the same procedure described by Glinianaia et al.[3]. The reference tables for children in Sweden were different to allow for recognised differences in norms pertaining to this country[4].

1. Gardosi J, Mongelli M, Wilcox M, Chang A. AN ADJUSTABLE FETAL WEIGHT STANDARD. *ULTRASOUND Obstet Gynecol*. 1995;6(3):168-174. doi:10.1046/j.1469-0705.1995.06030168.x
2. Min SJ, Luke B, Gillespie B, et al. Birth weight references for twins. *Am J Obstet Gynecol*. 2000. doi:10.1067/mob.2000.104923
3. Glinianaia S V, Jarvis S, Topp M, et al. Intrauterine growth and cerebral palsy in twins: A European multicenter study. *TWIN Res Hum Genet*. 2006;9(3):460-466. doi:10.1375/183242706777591209
4. Kallen B. A BIRTH-WEIGHT FOR GESTATIONAL-AGE STANDARD BASED ON DATA IN THE SWEDISH MEDICAL BIRTH REGISTRY, 1985-1989. *Eur J Epidemiol*. 1995;11(5):601-606. doi:10.1007/BF01719316

## Appendix 3: Further information on the statistical approach

### *Prevalence of CP*

We presented and investigated trends in CP prevalence over time and birth type (multiples and singletons) and over categories of GA (<32 weeks GA; 32 to <36 weeks GA; ≥37 GA) and BW (<1500 g; 1500 to <2500 g; ≥ 2500 g). These categories of GA and BW are based on cut-off points that represent clinically different groups: international comparisons have relied on these categories to benchmark differences across countries and across time.

In analysing prevalence trends over time, we applied multilevel Negative Binomial regression models. In this section we provide more details on this approach. We refer to the manual by Rabe-Hesketh and Skrondal[1] for a more exhaustive and formal statistical illustration.

Our outcome of interest was the count of CP live births within catchment areas over defined time intervals. Count data such as these are distributed in ways that differ substantially from normal distributions (e.g. distributions are asymmetric). Different regressions models are available to investigate the relationship between these types of outcomes and covariates. A commonly used category of models relies on the Poisson distribution.

We had initially applied Poisson regression models to our data: However, Poisson regression assumes that the variance and the mean of an outcome are similar. This assumption is not tenable when outcomes are 'over-dispersed', i.e. display variance that is larger than the mean. **Negative Binomial regression** models generalise the Poisson model and can account for over-dispersion in the data: this is achieved by estimating an **over-dispersion parameter, dubbed *α (Alpha).*** We reported this parameter in our results together with its level of significance. Following the suggestion of an anonymous reviewer of an earlier draft, we compared Poisson and Negative Binomial models using Likelihood-Ratio tests: these indicated that the latter models provided better fit to the data. Therefore, we applied Negative Binomial regressions throughout our analyses.

We thus used **Negative Binomial regression models whereby our dependent variable was the number of CP live births in each catchment area within a year**. In epidemiological data such as ours, the significance of the count outcome is relative to the cumulative number of live births in each catchment area within a given year. The cumulative number of live births represented the number of times the event (CP live birth) could have happened within the area in a given year: this is dubbed the ***exposure***. Poisson and Negative Binomial regression models control for differences in the exposure by including an ***offset* term** in the equation: following standard statistical practice, we obtained this by calculating

the logarithm of the cumulative number of live births within a given area each year. The **independent variable** in the analyses was the continuous variable birth years, centred at the start of the study.

The **key parameters** of the models estimated were the ***intercept***, or initial status, representing the estimated prevalence of CP live births in year 0 (i.e. the start of the study, or 1990), and the ***slope***, representing average change in CP live births prevalence from one year to another. As well as the linear time trend, we investigated quadratic effects of time by including squared years in the regression. Quadratic trends describe changes that are not constant, but rather accelerate or decelerate over time.

We ran these analyses separately for different categories of birth, i.e. singletons, multiples, singletons by categories of GA, multiples by categories of GA, singletons by categories of BW, multiples by categories of BW.

We applied ***multilevel*** **Negative Binomial models** to control for variations across registers. Multilevel models allowed us to control for and estimate between-register variation in model parameters. Differences between registers were modelled in three steps:

(1) In the initial model, we allowed between-register variation in the prevalence of CP live births at the start of the study (i.e. cross-centre variation around the *intercept*).

(2) A second model included between-register variation in the rate of change (the *slope*) of CP prevalence: This model allowed registers to vary in their trends of CP prevalence (i.e. centres could display negative as well as positive trends).

(3) A third model included a register-level covariance between intercept (initial status) and slope (rate of change): Covariances would indicate that the way in which prevalence changes over the study period is related to the initial prevalence.

We compared changes in the model fit of these models using the *Likelihood-Ratio* $\chi^2$ *test*, with a threshold of $p < .005$

As well as allowing us to take into account and model cluster-level effects (e.g. between-register variation), multilevel models fulfil the tasks of: (a) adjusting for imbalances in sampling (e.g. whereby some registers provided more yearly data than others); (b) adjusting for repeat sampling (e.g. whereby more observations were provided by the same registers. For these reasons, some authors[2] recommend multilevel models as the default option whenever the variables of interest are clustered.

***Outcomes among persons with CP***

In analyses that involved categorical outcomes (e.g. level of motor severity among individuals with CP), we applied multilevel logistic regressions[1]. The multilevel approach allowed us to control for between-centre variations in the outcome of interest.

In these models, we first included type of birth (dummy coded to represent multiples vs. singletons) and time (birth year, centred at the start of the study) as covariates. We tested for linear as well as quadratic time trends, as well as for interactions between time and type of birth, retaining these terms only if the models provided a significant improvement of model fit, according to the *Likelihood-Ratio* $\chi^2$ *test* with a threshold of $p < .005$.

In a second step, we also controlled for dummy variables representing GA categories (Extremely & Very Preterm, Moderately Preterm, vs. Term) and standardized *z* BW scores. In this step, we also tested interactions between GA and *z* BW scores and the time variables in order to test varying trends.

All statistical analyses were performed using Stata 13 software[3].

*References*:

1. Rabe-Hesketh S, Skrondal, A. *Multilevel and longitudinal modeling using Stata: Categorical Responses, Counts, Survival (Volume II).* College Station, TX: STATA press. 2012.
2. McElreath R. *Statistical rethinking: A Bayesian course with examples in R and Stan*. Abingdon, UK. CRC press; 2020.
3. StataCorp. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP. 2013

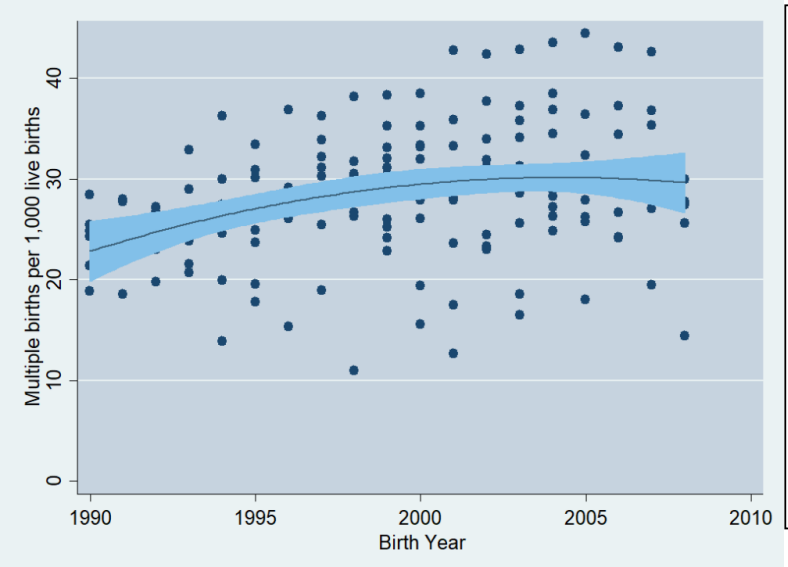
## Appendix 4: Estimated changes in prevalence of multiple births on live births

*Table A4.1. Multilevel Negative Binomial regressions coefficients of the total of multiple births on the total of live births per year. Model's Wald $\chi^2(2) = 64.39$, $p < .0001$.*

| | | IRR (95% CI) |
|---|---|---|
| **Initial Status** | Intercept | 0.019* (0.016 to 0.024) |
| | | **IRR (95% CI)** |
| **Rate of change** | Year (Linear) | 1.058* (1.041 to 1.075) |
| | Year (Quadratic) | 0.998* (0.997 to 0.999) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -6.579* (-7.181 to -5.977) |
| **Variance components** | | **Variance (95% CI)** |
| Lev.2 (Centres) | Initial status | 0.110 (0.042 to 0.283) |
| | Rate of change | 0.001 (0.001 to 0.001) |
| | Covariance | -0.005 (-0.011 to 0.001) |

* $p < .005$

*Figure A3.1: Estimated prevalence of multiple births per 1,000 live births by birth year with 95% Confidence Intervals.*




Note: the dots represent prevalence reported by SCPE registers. The line represents a fitted quadratic trend. The grey-shaded area represents 95% Confidence Intervals of the fitted quadratic trend.

## Appendix 5. Models of rate of change in CP prevalence by GA and type of birth

*Table A5.1. Multilevel Negative Binomial regression coefficients of the total number of **CP single births with GA < 32 weeks** on single live births of the same GA. Model's Wald $\chi^2(1) = 21.38$, $p < .0001$.*

| | | **IRR (95% CI)** |
|---|---|---|
| **Initial Status** | Intercept | 0.083* (0.062 to 0.111) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.963* (0.945 to 0.979) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -4.534* (-7.309 to -1.758) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.147 (0.054 to 0.401) |
| | Rate of change | NA |
| | Covariance | NA |

* $p < .005$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

*Table A5.2. Multilevel Negative Binomial regression coefficients of the total number of **CP single births with GA 32 to 36 weeks** on single live births of the same GA. Model's Wald $\chi^2(1) = 17.50$, $p < .0001$.*

| | | **IRR (95% CI)** |
|---|---|---|
| **Initial Status** | Intercept | 0.009* (0.007 to 0.012) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.962* (0.945 to 0.980) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -4.047* (-6.075 to -2.018) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.076 (0.019 to 0.297) |
| | Rate of change | NA |
| | Covariance | NA |

* $p < .005$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

*Table A5.3. Multilevel Negative Binomial regression coefficients of the total number of **CP single births with GA ≥ 37 weeks** on single live births of the same GA. Model's Wald $\chi^2(1) = 0.29$, $p = .59$.*

| | | |
|---|---|---|
| | | **IRR (95% CI)** |
| **Initial Status** | Intercept | 0.001* (0.001 to 0.002) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.991 (0.959 to 1.024) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -5.575* (-8.305 to -2.845) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.308 (0.095 to 1.000) |
| | Rate of change | 0.002 (0.001 to 0.007) |
| | Covariance | -0.024 (-0.052 to 0.005) |

* $p < .005$

*Table A5.4. Multilevel Negative Binomial regression coefficients of the total number of **CP multiple births with GA <32 weeks** on multiple live births of the same GA. Model's Wald $\chi^2(1) = 14.62$, $p = .0001$.*

| | | |
|---|---|---|
| | | **IRR (95% CI)** |
| **Initial Status** | Intercept | 0.089* (0.065 to 0.123) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.952* (0.928 to 0.976) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -3.779 (-7.104 to -0.454) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.060 (0.006 to 0.557) |
| | Rate of change | NA |
| | Covariance | NA |

* $p < .005$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

*Table A5.5. Multilevel Negative Binomial regression coefficients of the total number of **CP multiple births with GA 32 to 36 weeks** on multiple live births of the same GA. Model's Wald $\chi^2(1) = 0.10$, $p = .7535$.*

| | | |
|---|---|---|
| | | **IRR (95% CI)** |
| **Initial Status** | Intercept | 0.006* (0.003 to 0.009) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.994 (0.961 to 1.029) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -15.346 (-1269 to 1238) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.150 (0.0266 to 0.850) |
| | Rate of change | NA |
| | Covariance | NA |

* $p < .005$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

*Table A5.6. Multilevel Negative Binomial regression coefficients of the total number of **CP multiple births with GA ≥ 37 weeks** on multiple live births of the same GA. Model's Wald $\chi^2(1) = 0.77$, $p = .380$.*

| | | |
|---|---|---|
| | | **IRR (95% CI)** |
| **Initial Status** | Intercept | 0.002* (0.001 to 0.004) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.981 (0.939 to 1.024) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -3.464 (-11.34 to 4.413) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.013 (0.000 to 50.901) |
| | Rate of change | NA |
| | Covariance | NA |

* $p < .00$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

## Appendix 6. Models of rate of change in CP prevalence by BW and type of birth

*Table A6.1. Multilevel Negative Binomial regression coefficients of the total number of **CP single births with BW < 1500 g** on single live births of the same BW. Model's Wald $\chi^2(1) = 20.87$, $p < .0001$.*

| | | |
|---|---|---|
| | | **IRR (95% CI)** |
| **Initial Status** | Intercept | 0.071* (0.053 to 0.095) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.965* (0.950 to 0.980) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -4.093* (-5.974 to -2.213) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.173 (0.068 to 0.439) |
| | Rate of change | NA |
| | Covariance | NA |

* $p < .005$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

*Table A6.2. Multilevel Negative Binomial regression coefficients of the total number of **CP single births with BW 1500 to 2499 g** on single live births of the same BW. Model's Wald $\chi^2(1) = 18.88$, $p < .0001$.*

| | | |
|---|---|---|
| | | **IRR (95% CI)** |
| **Initial Status** | Intercept | 0.013* (0.010 to 0.017) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.972* (0.959 to 0.984) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -15.728 (-840 to -809) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.166 (0.065 to 0.422) |
| | Rate of change | NA |
| | Covariance | NA |

* $p < .005$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

*Table A6.3. Multilevel Negative Binomial regression coefficients of the total number of **CP single births with BW ≥ 2500 g** on single live births of the same BW. Model's Wald $\chi^2(1) = 1.08$, $p = 0.299$.*

| | | |
|---|---|---|
| | | **IRR (95% CI)** |
| **Initial Status** | Intercept | 0.001* (0.001 to 0.002) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.983 (0.953 to 1.015) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -4.621* (-5.785 to -3.457) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.325 (0.101 to 1.043) |
| | Rate of change | 0.002 (0.001 to 0.007) |
| | Covariance | -0.023 (-0.053 to 0.007) |

* $p < .005$

*Table A6.4. Multilevel Negative Binomial regression coefficients of the total number of **CP multiple births with BW < 1500 g** on mulitple live births of the same BW. Model's Wald $\chi^2(1) = 19.87$, $p < .0001$.*

| | | |
|---|---|---|
| | | **IRR (95% CI)** |
| **Initial Status** | Intercept | 0.078* (0.055 to 0.109) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.949* (0.927 to 0.971) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -13.511 (-1074 to 1047) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.145 (0.046 to 0.455) |
| | Rate of change | NA |
| | Covariance | NA |

* $p < .005$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

*Table A6.5. Multilevel Negative Binomial regression coefficients of the total number of **CP multiple births with BW 1500 to 2499 g** on multiple live births of the same BW. Model's Wald $\chi^2(1) = 0.73$, $p = .392$.*

| | | |
|---|---|---|
| | | **IRR (95% CI)** |
| **Initial Status** | Intercept | 0.008* (0.005 to 0.011) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.989 (0.964 to 1.014) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -6.580 (-57.525 to 44.365) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.070 (0.016 to 0.313) |
| | Rate of change | NA |
| | Covariance | NA |

* $p < .005$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

*Table A6.6. Multilevel Negative Binomial regression coefficients of the total number of **CP multiple births with BW ≥ 2500 g** on multiple live births of the same BW. Model's Wald $\chi^2(1) = 4.01$, $p = .045$.*

| | | |
|---|---|---|
| | | **IRR (95% CI)** |
| **Initial Status** | Intercept | 0.003* (0.002 to 0.005) |
| | | **IRR (95% CI)** |
| **Rate of change** | Birth year | 0.958 (0.919 to 0.999) |
| | | **IRR (95% CI)** |
| | Ln Alpha | -1.176* (-2.259 to -0.093) |
| **Variance components** | | **Variance (95% CI)** |
| Lev. 2 (Centres) | Initial status | 0.000 (0.000 to 0.000) |
| | Rate of change | NA |
| | Covariance | NA |

* $p < .005$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

## Appendix 7. Logistic regression of severe motor impairment on time (year) and type of birth

*Table A7.1. Coefficients of multilevel logistic regression of severe motor impairment on time (year) and type of birth (single vs. multiple birth). Model's Wald $\chi^2(5) = 29.28$, $p = .0001$.*

| | | **OR (95% CI)** |
|---|---|---|
| **Initial Status** | Intercept | 0.88 (0.72 to 1.08) |
| | Single birth | *Reference* |
| | Multiple birth | 0.91 (0.78 to 1.05) |
| | GA < 32 ww | 1.25* (1.11 to 1.40) |
| | GA 32 to 36 ww | 1.01 (0.89 to 1.15) |
| | GA 37+ ww | *Reference* |
| | zBW | 0.97 (0.94 to 1.00) |
| | | **OR (95% CI)** |
| **Rate of change** | Year | 0.98* (0.97 to 0.99) |
| **Variance component** | | **Variance (95% CI)** |
| L2 (Centres) | Initial status | 0.07 (0.02 to 0.20) |
| | Rate change | NA |
| | Covariance | NA |

* $p < .005$

*Note: comparisons of models using the Likelihood Ratio test indicated that estimating the centre-level variance around the rate of change and the centre-level covariance of intercept and rate of change did not improve model fit (at $p < .005$).*

*Table A7.2. Coefficients of multilevel logistic regression of severe motor impairment on time (year) and type of birth (single vs. multiple birth) and an interaction term time BY type of birth. Model's Wald $\chi^2(6) = 29.54$, $p = .0001$.*

| | | **OR (95% CI)** |
|---|---|---|
| **Initial Status** | Intercept | 0.87 (0.71 to 1.07) |
| | Single birth | *Reference* |
| | Multiple birth | 0.98 (0.71 to 1.34) |
| | GA < 32 ww | 1.25* (1.11 to 1.40) |
| | GA 32 to 36 ww | 1.01 (0.89 to 1.15) |
| | GA 37+ ww | *Reference* |
| | zBW | 0.97 (0.94 to 1.00) |
| | | **OR (95% CI)** |
| **Rate of change** | Year | 0.98 (0.97 to 1.00) |
| | Single birth | *Reference* |
| | Multiple birth | 0.99 (0.96 to 1.02) |
| **Variance components** | | **Variance (95% CI)** |
| L2 (Centres) | Initial status | 0.07 (0.02 to 0.20) |
| | Rate change | NA |
| | Covariance | NA |

* $p < .005$

*Note: the comparison between the latter and the former model confirmed that the inclusion of an interaction term (time BY type of birth) did not improve fit of the model, LR $\chi^2(1) = 0.26$, $p = .61$.*

## Appendix 8. Estimated changes in the number of CP live births by GA and BW categories.

In this section we report the estimated number of events, i.e. number of CP live births, per 1000 live births, according to the multilevel Negative Binomial regression models we had run (see Table 3 in the main text). By doing so, we wish to provide elements to consider the clinical significance of our findings. The estimated average incidence of CP by categories of GA and by year are reported in Table A8.1. The estimated average incidence of CP live births by categories of BW and by year are reported in Table A8.2.

These statistics indicate that incidence is estimated to be higher in more at-risk categories of low GA or low BW births. However, the estimated incidence of CP decreased more dramatically among multiples as well as singletons in the lowest GA and lowest BW groups.

**For example, the estimated incidence of CP livebirths among multiples changed from approximately 89 per 1000 live births in 1990, to approximately 36 per 1000 live births in 2008**. Between the same two birth years the incidence of CP among singletons born less than 32 weeks GA changed from 91 per 1000 livebirths to approximately 45 per 1000 live births.

*Table A8.1. Predicted incidence of CP live births per 1000 live births by categories of GA and by Singletons and Multiples, according to multilevel Negative Binomial models estimated.*

| | EXTREMELY/VERY PRETERM | | MODERATELY PRETERM | | TERM | |
|---|---|---|---|---|---|---|
| **BIRTH YEAR** | Singletons | Multiples | Singletons | Multiples | Singletons | Multiples |
| **1990** | 91.43 | 89.09 | 9.25 | 5.88 | 1.50 | 2.53 |
| **1991** | 87.85 | 88.89 | 8.65 | 5.79 | 1.34 | 2.48 |
| **1992** | 84.61 | 84.64 | 8.33 | 5.76 | 1.29 | 2.43 |
| **1993** | 81.49 | 80.60 | 8.01 | 5.73 | 1.26 | 2.38 |
| **1994** | 78.49 | 76.74 | 7.70 | 5.69 | 1.22 | 2.34 |
| **1995** | 75.60 | 73.07 | 7.41 | 5.66 | 1.19 | 2.29 |
| **1996** | 72.81 | 69.58 | 7.13 | 5.63 | 1.16 | 2.25 |
| **1997** | 68.37 | 65.66 | 6.88 | 5.65 | 1.12 | 2.21 |
| **1998** | 65.85 | 62.52 | 6.62 | 5.62 | 1.11 | 2.17 |
| **1999** | 63.24 | 58.35 | 6.51 | 5.64 | 1.05 | 2.13 |
| **2000** | 60.84 | 53.56 | 6.40 | 5.66 | 1.06 | 2.09 |
| **2001** | 58.60 | 51.00 | 6.16 | 5.63 | 1.05 | 2.05 |
| **2002** | 56.44 | 48.56 | 5.93 | 5.60 | 1.04 | 2.01 |
| **2003** | 54.36 | 46.24 | 5.70 | 5.57 | 1.03 | 1.97 |
| **2004** | 52.36 | 44.03 | 5.48 | 5.54 | 1.02 | 1.93 |
| **2005** | 50.43 | 41.92 | 5.27 | 5.51 | 1.01 | 1.89 |
| **2006** | 48.57 | 39.92 | 5.07 | 5.48 | 1.00 | 1.86 |
| **2007** | 44.88 | 38.00 | 4.71 | 5.24 | 1.00 | 1.82 |
| **2008** | 49.65 | 35.91 | 4.56 | 4.44 | 0.83 | 1.79 |

*Table A8.2. Predicted incidence of CP live births per 1000 live births by categories of BW and by Singletons and Multiples, according to multilevel Negative Binomial models estimated.*

| | EXTREMELY/VERY LOW BIRTH WEIGHT | | MODERATELY LOW BIRTH WEIGHT | | NORMAL BIRTH WEIGHT | |
|---|---|---|---|---|---|---|
| **BIRTH YEAR** | Singletons | Multiples | Singletons | Multiples | Singletons | Multiples |
| **1990** | 76.79 | 77.26 | 13.63 | 7.57 | 1.56 | 3.14 |
| **1991** | 74.54 | 76.86 | 12.75 | 7.53 | 1.38 | 3.01 |
| **1992** | 71.92 | 72.95 | 12.39 | 7.45 | 1.33 | 2.89 |
| **1993** | 69.39 | 69.24 | 12.04 | 7.37 | 1.28 | 2.77 |
| **1994** | 66.95 | 65.72 | 11.70 | 7.29 | 1.23 | 2.66 |
| **1995** | 64.59 | 62.37 | 11.37 | 7.21 | 1.19 | 2.55 |
| **1996** | 62.32 | 59.20 | 11.04 | 7.13 | 1.15 | 2.45 |
| **1997** | 59.09 | 58.55 | 10.96 | 7.06 | 1.12 | 2.35 |
| **1998** | 57.01 | 55.57 | 10.65 | 6.98 | 1.09 | 2.25 |
| **1999** | 56.20 | 51.15 | 10.78 | 7.04 | 1.03 | 2.16 |
| **2000** | 54.01 | 46.98 | 10.83 | 6.95 | 1.04 | 2.07 |
| **2001** | 52.11 | 44.59 | 10.53 | 6.87 | 1.01 | 1.99 |
| **2002** | 50.27 | 42.32 | 10.23 | 6.79 | 0.99 | 1.90 |
| **2003** | 48.51 | 40.17 | 9.94 | 6.72 | 0.98 | 1.83 |
| **2004** | 46.80 | 38.12 | 9.66 | 6.65 | 0.96 | 1.75 |
| **2005** | 45.15 | 36.18 | 9.38 | 6.57 | 0.94 | 1.68 |
| **2006** | 43.56 | 34.34 | 9.12 | 6.50 | 0.93 | 1.61 |
| **2007** | 39.71 | 32.59 | 8.51 | 6.29 | 0.92 | 1.55 |
| **2008** | 46.73 | 30.50 | 9.26 | 5.89 | 0.81 | 1.48 |

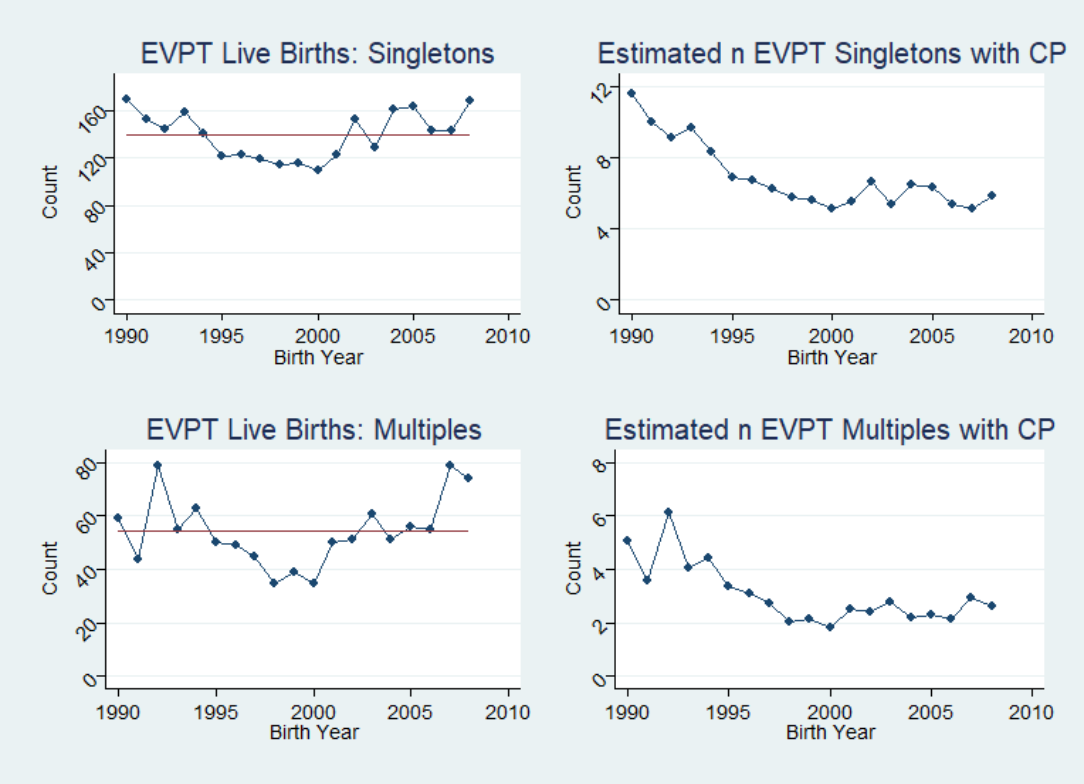
The clinical significance of these incidence rates and their change over time needs to be assessed considering the differences in the count of singletons and multiples across GA and BW categories. The impact of a considerable decrease in the CP incidence among lowest GA groups, for example, must be gauged considering that lower GA live births are fewer compared to others.

In order to illustrate this point, we took as an example the estimated number of CP births in Gothenburg (Göteborg), Sweden, a centre that captured a medium sized catchment area over the whole study period. The total live births recorded in the area was approximately 25 000 in 1990, decreased to over 17 000 in 1998, and increased again to 25 000 in 2007 and 2008.

In this centre, the average of extremely or very preterm (EVPT) single live births between 1990 and 2008 was 139 live births: The estimated number of singletons with CP in this category of preterm babies decreased from n=12 in 1990 to n=6 in 2008, see Figure A8.1. **The average number of multiple live births in the same category of prematurity was 54 over the study period: the estimated number of CP births among multiples born less than 32 weeks GA decreased from numbers ranging from n=4 to n=6 in the early 1990s**

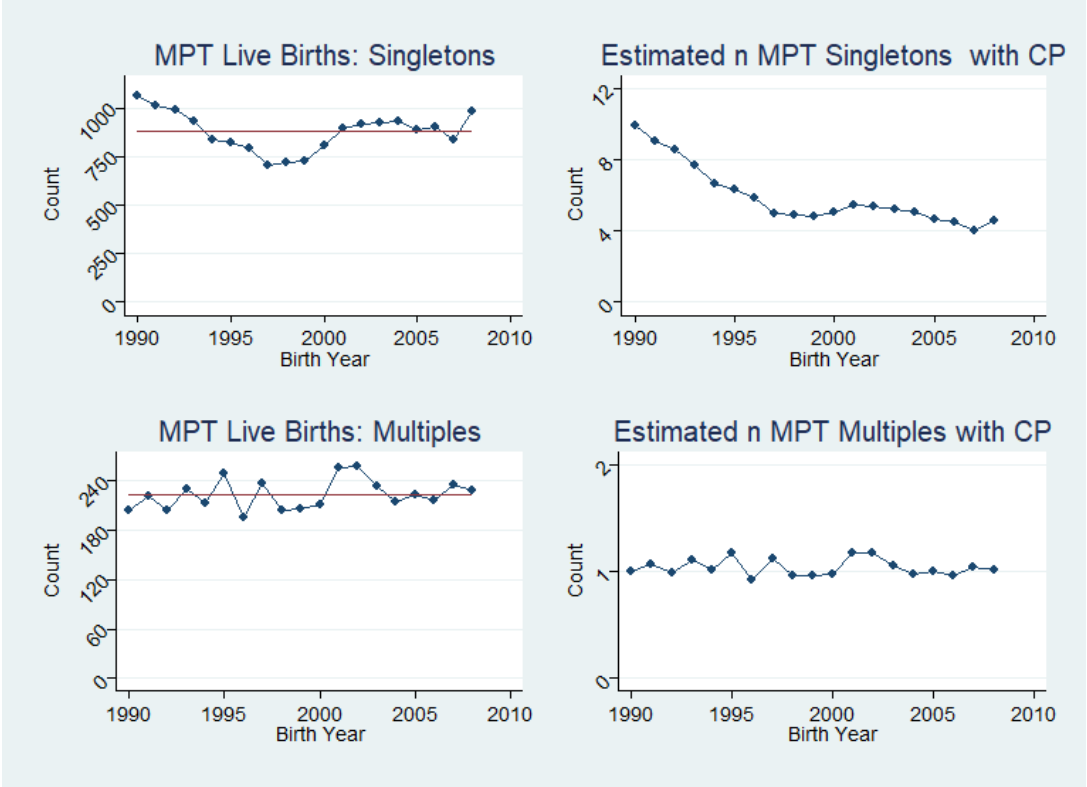
**to numbers between n=2 and n=3 by the end of the study period in 2008**, see Figure A8.1. **The fact that the models estimated did not indicate variability in the rate of change of CP prevalence among these categories of singletons and multiples (see Table 3 in the main text), indicates that similar sizeable reductions in the incidence of CP were observed across centres.**

*Figure A8.1: In the right column are reported the actual numbers of live births by single and multiple births in the Extremely and Very Preterm (EVPT) category. The red line represents the average for the study period. In the left columns are reported the estimated numbers of CP live births by singletons and multiples, respectively.*



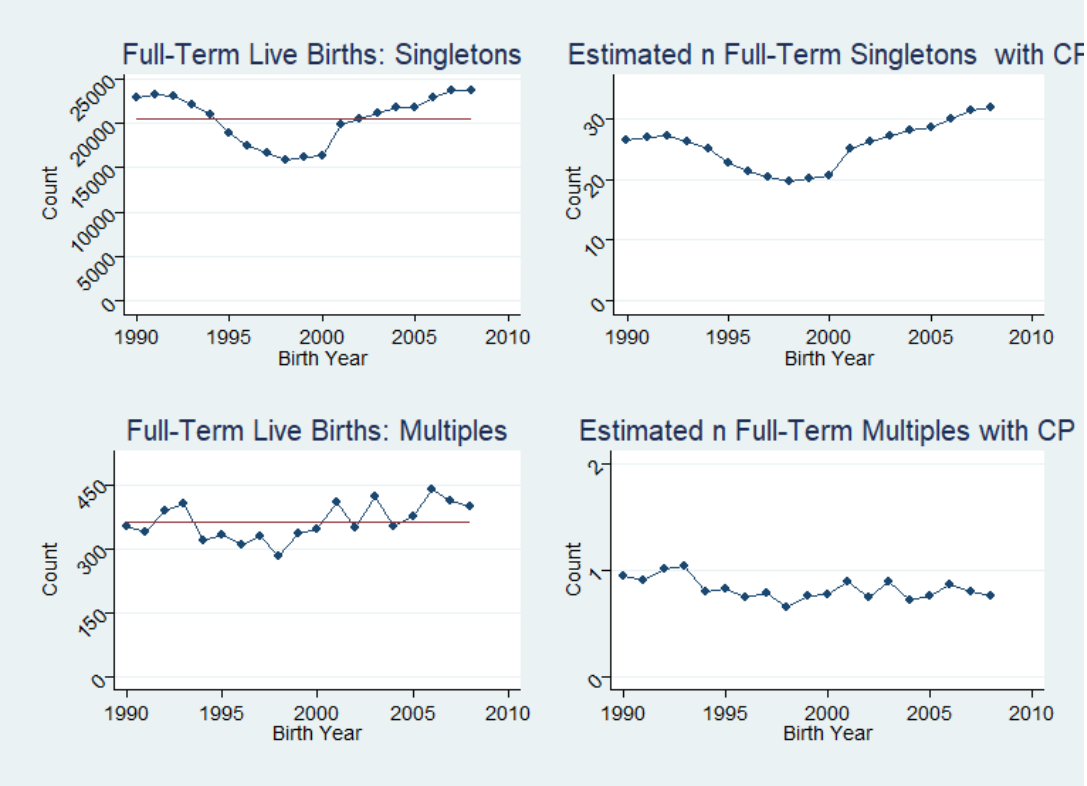

A similar, but less substantial decrease, was observed in the numbers of estimated live births with CP among the moderate preterm singletons: these decreased from n=10 in 1990, to approximately n=4 in 2008, see Figure A8.2. Since the models estimated did not indicate cross-centre variation in the rate of change of CP prevalence in this category of singletons, a similar sizeable decrease in CP incidence was estimated across other centres. In the same period, the estimated number of CP births among multiples born moderately preterm is estimated to remain approximately n=1, see Figure A8.2.

*Figure A8.2: In the right column are reported the actual numbers of live births by single and multiple births in the Moderately Preterm (MPT) category. The red line represents the average for the study period. In the left columns are reported the estimated numbers of CP live births by singletons and multiples, respectively.*




Finally, the estimated number of CP live births among singletons and multiples born at term in Gothenburg are reported in Figure A8.3. The models we ran indicated that the rate of change of CP prevalence among full-term singletons varied across centres (see Table 3 in the main text): Gothenburg was one of the centres that did not display a downward trend in this outcome. This is attested in the estimated number of CP full-term singletons, which varied according to the changes in the count of full-term singletons born in the same period (see Figure A8.3, first row). The estimated number of CP births among multiples full term did not vary substantially, remaining approximately n=1, despite a slight increase in the count of multiple livebirths (see Figure A8.3, second row).

*Figure A8.3: In the right column are reported the actual numbers of live births by single and multiple births in the born at term category. The red line represents the average for the study period. In the left columns are reported the estimated numbers of CP live births by singletons and multiples, respectively.*




**Overall, the estimated models indicated a sizeable decrease in the number of CP births among children born in categories of lowest GA and BW, and this decrease involved both singletons and multiples. This decrease was consistent across centres in this study.** Although live births of singletons and multiples in the lowest categories of GA and BW are relatively rare events, the reported decrease in CP prevalence across these categories **represented a sizeable reduction in the number of CP live births every year**. This reduction could have had significant repercussions on the need for services and support for children in the areas of interest in this study.