**Supplementary material**

Table A.1. Systemic damage score in the cohort of infants with hypoxic-ischemic encephalopathy

|  |  |  |
| --- | --- | --- |
| Systemic damage | Score | Definition |
| Cardiovascular | 1 | Need for inotropes |
| Pulmonary | 3 | Use of nitric oxide for pulmonary hypertension |
|  | 1 | Pulmonary hypertension and/or use of supplementary oxygen |
| Renal | 3 | Creatinine levels > 1.5 mg/dl and/or use of dialysis |
|  | 1 | Use of diuretics |
| Hepatic | 3 | alanine and/or aspartate aminotransferase transaminases > 500 UI/L |
|  | 1 | alanine and/or aspartate aminotransferase transaminases > 100 UI/L |
| Coagulopathy | 3 | Need for fresh frozen plasma and coagulation factors |
|  | 1 | Need for fresh frozen plasma |
| Hemorrhage | 3 | Need for platelet and/or red blood transfusion |
|  | 1 | Presence of hemorrhage but no need for transfusion |
| Gastrointestinal | 3 | Necrotizing enterocolitis |
|  | 1 | Gastrointestinal bleeding |

Table A.2. and Figure A.2. Temporal trends of using overlapping periods of time

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Period | Births (n) | Total HIE | Moderate HIE (n) | Severe HIE (n) | Global rate (95% CI) | Moderate HIE rate (95% CI) | Severe HIE rate (95% CI) |
| July 2010-Dec 2012 | 50,036 | 44 | 27 | 17 | 0.88  0.62-1.14 | 0.54  0.34-0.74 | 0.34  0.18-0.5 |
| Jan 2011- Dec 2013 | 57,044 | 55 | 36 | 19 | 0.96  0.71-1.22 | 0.63  0.43-0.84 | 0.33  0.18-0.48 |
| Jan 2012- Dec 2014 | 55,269 | 53 | 36 | 17 | 0.96  0.70-1.22 | 0.65  0.44-0.86 | 0.31  0.16-0.45 |
| Jan 2013- Dec 2015 | 53,586 | 49 | 34 | 15 | 0.91  0.66-1.17 | 0.63  0.42-0.85 | 0.28  0.14-0.42 |
| Jan 2014- Dec 2016 | 52,367 | 42 | 29 | 13 | 0.80  0.56-1.04 | 0.55  0.35-0.76 | 0.25  0.11-0.38 |
| Jan 2015-Dec 2017 | 50,064 | 35 | 23 | 12 | 0.70  0.47-0.93 | 0.46  0.27-0.65 | 0.24  0.10-0.38 |
| Jan 2016-Dec 2018 | 47,736 | 43 | 33 | 10 | 0.90  0.63-1.17 | 0.69  0.46-0.93 | 0.21  0.08-0.34 |
| Jan 2017-July 2019 | 39,237 | 41 | 33 | 8 | 1.04  0.73-1.36 | 0.84  0.55-1.13 | 0.20  0.06-0.35 |

HIE incidence rates are expressed as number per 1,000 births; HIE = hypoxic-ischemic encephalopathy; n = number; CI = confidence interval.



Cumulative incidence rate expressed as number of infants with HIE per 1,000 births for moderate-to-severe HIE (black line) (χ2 for trend, p=0.8), moderate HIE only (grey dashed line) (χ2 for trend, p=0.3), and severe HIE only (grey dotted line) (χ2 for trend, p=0.06).