Supplemental tables

Table S1: Distribution of children by child’s sex for each contributing registry

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | Total | Male | Female | Indeterminate/Unknown |
| Registry | livebirths | N | % | N | % | N | % |
| Denmark, Funena | 2,425 | 1,425 | 58.7% | 1,000 | 41.2% | 0 | 0.0% |
| Finland | 42,861 | 23,267 | 54.3% | 19,594 | 45.7% | 0 | 0.0% |
| France, Paris | 11,624 | 6,639 | 57.1% | 4,985 | 42.9% | 0 | 0.0% |
| Italy, Emilia Romagna | 5,589 | 3,334 | 59.7% | 2,253 | 40.3% | 2 | 0.0% |
| Italy, Tuscany | 4,312 | 2,582 | 59.9% | 1,727 | 40.1% | 3 | 0.1% |
| Malta | 2,718 | 1,557 | 57.3% | 1,160 | 42.7% | 1 | 0.0% |
| North Netherlandsa | 8,400 | 4,480 | 53.3% | 3,920 | 46.7% | 0 | 0.0% |
| Norway | 27,201 | 14,977 | 55.1% | 12,224 | 44.9% | 0 | 0.0% |
| Spain, Valencian Region | 7,389 | 4,206 | 56.9% | 3,182 | 43.1% | 1 | 0.0% |
| United Kingdom, Thames Valley | 3,854 | 2,209 | 57.3% | 1,641 | 42.6% | 4 | 0.1% |
| United Kingdom, EMSY | 11,288 | 6,817 | 60.4% | 4,459 | 39.5% | 12 | 0.1% |
| United Kingdom, Wessex  | 4,360 | 2,668 | 61.2% | 1,683 | 38.6% | 9 | 0.2% |
| United Kingdom, Wales | 18,177 | 10,617 | 58.4% | 7,554 | 41.6% | 6 | 0.0% |
| TOTAL | 150,198 | 84,777 | 56.4% | 65,382 | 43.6% | 39 | 0.0% |

a individual categories may not sum to total due to rounding nearest 5 in North Netherlands and Funen registries

EMSY, East Midlands and South Yorkshire

Table S2: Distribution of children by maternal age (years) b for each contributing registry

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|   | Total | <20 | 20-34 | 35+ | Unknown/Missing |
| Registry | livebirths | N | % | N | % | N | % | N | % |
| Denmark, Funena | 2,425 | 50 | 1.9% | 1,940 | 80.0% | 440 | 18.1% | 0 | 0.0% |
| Finland | 42,861 | 1,075 | 2.5% | 32,965 | 76.9% | 8,818 | 20.6% | 3 | 0.0% |
| France, Paris | 11,624 | 150 | 1.3% | 8,115 | 69.8% | 3,356 | 28.9% | 3 | 0.0% |
| Italy, Emilia Romagna | 5,589 | 77 | 1.4% | 3,418 | 61.2% | 1,986 | 35.5% | 108 | 1.9% |
| Italy, Tuscany | 4,312 | 57 | 1.3% | 2,655 | 61.6% | 1,556 | 36.1% | 44 | 1.0% |
| Malta | 2,718 | 136 | 5.0% | 2,131 | 78.4% | 450 | 16.6% | 1 | 0.0% |
| North Netherlandsa | 8,400 | 75 | 0.9% | 6,655 | 79.2% | 1,570 | 18.7% | 100 | 1.2% |
| Norway | 27,201 | 591 | 2.2% | 21,098 | 77.6% | 5,512 | 20.3% | 0 | 0.0% |
| Spain, Valencian Region | 7,389 | 225 | 3.0% | 4,693 | 63.5% | 2,221 | 30.1% | 250 | 3.4% |
| United Kingdom, Thames Valley | 3,854 | 175 | 4.5% | 2,633 | 68.3% | 1,019 | 26.4% | 27 | 0.7% |
| United Kingdom, EMSY | 11,288 | 857 | 7.6% | 7,436 | 65.9% | 2,049 | 18.2% | 946 | 8.4% |
| United Kingdom, Wessex  | 4,360 | 259 | 5.9% | 2,701 | 61.9% | 896 | 20.6% | 504 | 11.6% |
| United Kingdom, Wales | 18,177 | 1,664 | 9.2% | 13,406 | 73.8% | 3,089 | 17.0% | 18 | 0.1% |
| TOTAL | 150,198 | 5,388 | 3.6% | 109,846 | 73.1% | 32,960 | 21.9% | 2,004 | 1.3% |

a individual categories may not sum to total due to rounding nearest 5 in North Netherlands and Funen registries

b values <10 or >59 were treated as data errors and set to missing

EMSY, East Midlands and South Yorkshire

Table S3: Distribution of children by gestational age at birth (weeks) b for each contributing registry

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Total | <28 | 28-31 | 32-36 | 37+ | Unknown/Missing |
| Registry | livebirths | N | % | N | % | N | % | N | % | N | % |
| Denmark, Funen a | 2,425 | 15 | 0.5% | 65 | 2.7% | 305 | 12.6% | 2,030 | 83.7% | 10 | 0.5% |
| Finland | 42,861 | 307 | 0.7% | 869 | 2.0% | 4,424 | 10.3% | 37,189 | 86.8% | 72 | 0.2% |
| France, Paris | 11,624 | 65 | 0.6% | 213 | 1.8% | 1,159 | 10.0% | 10,183 | 87.6% | 4 | 0.0% |
| Italy, Emilia Romagna | 5,589 | 40 | 0.7% | 123 | 2.2% | 713 | 12.8% | 4,610 | 82.5% | 103 | 1.8% |
| Italy, Tuscany | 4,312 | 15 | 0.3% | 89 | 2.1% | 624 | 14.5% | 3,568 | 82.7% | 16 | 0.4% |
| Malta | 2,718 | 15 | 0.6% | 64 | 2.4% | 367 | 13.5% | 2,264 | 83.3% | 8 | 0.3% |
| North Netherlands a | 8,400 | 40 | 0.5% | 170 | 2.0% | 870 | 10.4% | 6,770 | 80.6% | 550 | 6.5% |
| Norway | 27,201 | 266 | 1.0% | 660 | 2.4% | 3,211 | 11.8% | 22,787 | 83.8% | 277 | 1.0% |
| Spain, Valencian Region | 7,389 | 114 | 1.5% | 286 | 3.9% | 1,306 | 17.7% | 5,437 | 73.6% | 246 | 3.3% |
| United Kingdom, Thames Valley | 3,854 | 44 | 1.1% | 96 | 2.5% | 542 | 14.1% | 3,129 | 81.2% | 43 | 1.1% |
| United Kingdom, EMSY | 11,288 | 160 | 1.4% | 333 | 3.0% | 1,605 | 14.2% | 8,405 | 74.5% | 785 | 7.0% |
| United Kingdom, Wessex | 4,360 | 37 | 0.8% | 93 | 2.1% | 437 | 10.0% | 3,777 | 86.6% | 16 | 0.4% |
| United Kingdom, Wales | 18,177 | 206 | 1.1% | 548 | 3.0% | 2,270 | 12.5% | 14,823 | 81.5% | 330 | 1.8% |
| TOTAL | 150,198 | 1,322 | 0.9% | 3,610 | 2.4% | 17,833 | 11.9% | 124,972 | 83.2% | 2,461 | 1.6% |

EMSY, East Midlands and South Yorkshire

a individual categories may not sum to total due to rounding nearest 5 in North Netherlands and Funen registries

b gestational age <24 were excluded from the study; values >44 were treated as data errors and set to missing

Table S4: Meta-analysis of the effect of risk factors on death <1 year in children with major congenital anomalies

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | Unadjusted | Adjusteda |
| **Risk Factor** | **Category** | Hazard Ratio (95% CI) | I2JWR (%) | I2joint (%) | Hazard Ratio (95% CI) | I2JWR (%) | I2joint (%) |
| Sex | Male | 1.00 | -- | 93.9 | 1.00 | -- | 57.0 |
|   | Female | 1.12 (0.91, 1.36) | 93.9 | 1.13 (0.97, 1.31) | 57.0 |
|  |  |  |  |  |  |  |  |
| Maternal age, years  | <20 | 1.30 (1.09, 1.54) | 51.4 | 61.5 | 1.13 (1.00, 1.28) | 0.96 | 42.4 |
|   | 20-34 | 1.00 | -- | 1.00 | -- |
|   | 35+ | 1.12 (1.00, 1.25) | 71.9 | 1.04 (0.94, 1.15) | 65.5 |
|  |  |  |  |  |  |  |  |
| Gestational Age, weeks | <28 | 14.88 (12.57, 17.62) | 64.7 | 64.0 | 15.21 (12.74, 18.15) | 67.3 | 64.5 |
|   | 28-31 | 8.39 (7.16, 9.85 | 74.9 | 8.43 (7.04, 10.10) | 80 |
|   | 32-36 | 3.88 (3.40, 4.43) | 81.6 | 3.87 (3.40, 4.41) | 80.8 |
|   | 37+ | 1.00 | -- | 1.00 | -- |

CI: confidence interval; I2JWR: Jackson-White-Riley I2 statistic for each level of a risk factor; I2joint: Jackson-White-Riley I2 statistic for all levels of a risk factor jointly.

a adjusted for all other risk factors listed and grouped birthyears (1995-2004 and 2005-2014)

Table S5: Meta-analysis of the effect of risk factors on death 1-9 years in children with major congenital anomalies

|  |  |  |
| --- | --- | --- |
|  |  | Unadjusteda |
| **Risk Factor** | **Category** | Hazard Ratio (95% CI) | I2JWR (%) | I2joint (%) |
| Sex | Male | 1.00 | -- | 17.1 |
|   | Female | 1.22 (1.07, 1.39) | 17.1 |
|  |  |  |  |  |
| Maternal age, years  | <20 | 1.58 (1.19, 2.10) | 11.6 | 7.0 |
|   | 20-34 | 1.00 | -- |
|   | 35+ | 1.23 (1.05, 1.43) | 0.9 |
|  |  |  |  |  |
| Gestational Age, weeks | <28 | 4.99 (2.94, 8.48) | 17.4 | 16.7 |
|   | 28-31 | 3.09 (2.28, 4.18) | 7.7 |
|   | 32-36 | 2.04 (1.69, 2.46) | 25.0 |
|   | 37+ | 1.00 | -- |

CI: confidence interval; I2JWR: Jackson-White-Riley I2 statistic for each level of a risk factor;

I2joint: Jackson-White-Riley I2 statistic for all levels of a risk factor jointly.

a Insufficient data for adjusted analyses