## Supplementary Tables & Figures

Supplementary Table 1 - Example of the GAIA classification system for the outcome small for gestational age (SGA)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Level 1 | Level 2A | Level 2B | Level 3A | Level 3B | Level 4 |
| Weight < 10th centile for GA | Weight < 10th centile for GA | Weight < 10th centile for GA | Weight < 10th centile for GA | Weight < 10th centile for GA | Baby noted to be small |
| Weight < 24 hours of birth | Weight < 24 hours of birth  | Weight < 24 hours of birth | Weight < 48 hours of birth | Weight < 48 hours of birth | No weight |
| Weight using calibrated electronic scale 10g resolution | Weight using scale with <50g resolution, tared to zero and calibrated | Weight using scale with <50g resolution, tared to zero and calibrated | Weight using scale with <50g resolution, tared to zero and calibrated | Weight using difference between adult holding and adult alone | SGA documented in medical notes |
| *GA:* Certain LMP AND 1st trimester USS OR 1st trimester USS | *GA:* Certain LMP & 1st or 2nd trimester USS OR certain LMP & 1st trimester physical exam | *GA:* Uncertain LMP & 2nd trimester USS | *GA*: Certain LMP & 3rd trimester USS ORCertain LMP & 2nd trimester fundal height OR certain LMP with birthweight OR uncertain LMP with first trimester physical exam | *GA*: Uncertain LMP & fundal height OR Uncertain LMP with newborn physical assessment OR Uncertain LMP with birthweight | *GA:* Infant examination |

Supplementary Table 2 - Search terms and results - Ovid/Medline search

|  |  |  |
| --- | --- | --- |
|  | Search Term | Hits |
| 1 | Immunization/ or immunization.mp. | 92432 |
| 2 | vaccine\*.mp | 243689 |
| 3 | 1 or 2 | 278715 |
| 4 | Safety/ or safety.mp. | 516496 |
| 5 | Pharmacovigilance or adverse event\* or AEFI or ae or sae  | 180852 |
| 6 | GAIA .mp. | 173 |
| 7 | 4 or 5 or 6 | 610057 |
| 8 | Definition or define\*.mp | 825359 |
| 9 | (maternal or pregnan\*).mp | 642231 |
| 11 | 3 AND 7 AND 8 AND 9 | 110 |

Supplementary Table 3 - Breakdown of the classification system used to describe LOC reported in this paper

|  |  |  |  |
| --- | --- | --- | --- |
| **Event Meets Case Definition:** | **Reported case with insufficient evidence to classify** | **Not a case** | **Insufficient information to distinguish between levels 4 and 5** |
| Level 1: Criteria as specified in the CD | Level 4 | Level 5 | Unclassifiable  |
| Level 2: Criteria as specified in the CD |   |   |  |
| Level 3: Criteria as specified in the CD |   |   |  |

Supplementary Table 4 Level of confidence assessments for each of the outcomes across all studies combined.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Definition** | **Total Cases** | **Studies (n)** | **Level 1 (%)** | **Level 2 (%)** | **Level 3 (%)**  | **Level 4 (%)** | **Level 5 (%)** | **Missing data or** **Unclassifiable (%)** |
| Stillbirth  | 1194 | 3 | 298 (25.0) | 33 (2.8) | 363 (30.4) | 500 (41.9) | 0 (0.0) | 0 (0.0) |
| Neonatal death | 813 | 2 | 760 (93.5) | 50 (6.2) | 1 (0.1) | 2 (0.2) | 0 (0.0) | 0 (0.0) |
| Congenital microcephaly | 228 | 2 | 25 (11.0) | 56 (24.6) | 27 (11.8) | 61 (26.8) | 0 (0.0) | 59 (25.9) |
| Low birthweight | 2173 | 2 | 329 (15.1) | 913 (42.0) | 897 (41.3) | 2 (0.1) | 0 (0.0) | 32 (1.5) |
| Preterm birth | 2192 | 4 | 553 (25.2) | 485 (22.1) | 1129 (51.5) | 0 (0.0) | 0 (0.0) | 25 (1.1) |
| Respiratory distress | 126 | 1 | 75 (59.5) | 21 (16.7) | 0 (0.0) | 22 (17.5) | 0 (0.0) | 8 (6.3) |
| Small for gestational age | 1592 | 2 | 116 (7.3) | 344 (21.6) | 376 (23.6) | 719 (45.2) | 2 (0.1) | 35 (2.2) |
| Neonatal infections | 1065 | 2 | 147 (13.8) | 485 (45.5) | 150 (14.1) | 283 (26.6) | 0 (0.0) | 0 (0.0) |
| Fetal growth restriction | 132 | 1 | 85 (64.4) | 14 (10.6) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 33 (25.0) |
| Non-reassuring fetal status | 113 | 1 | 2 (1.8) | 15 (13.3) | 17 (15.0) | 0 (0.0) | 0 (0.0) | 79 (69.9) |
| Dysfunctional labour | 126 | 1 | 42 (33.3) | 1 (0.8) | 0 (0.0) | 0 (0.0) | 31 (24.6) | 52 (41.3) |
| Hypertensive Disorders | 181 | 2 | 124 (68.5) | 24 (13.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 33 (18.2) |
| Pathways to preterm labour | 126 | 1 | 56 (44.4) | 3 (2.4) | 2 (1.6) | 0 (0.0) | 0 (0.0) | 65 (51.6) |

\* Watson et al, 2021 assessed LOC by an abstractor, the principal investigator and ABC case-logic. The results of the abstractor assessment are presented.

Supplementary Table 5 - Classification system for the GAIA outcome low birthweight

|  |  |  |  |
| --- | --- | --- | --- |
| Level 1 | Level 2 | Level 3 | Level 4 |
| Newborn infant weighed within 24h of birth | Newborn infant weighed within 24h of birth | Newborn infant weighed within 48h of birth | Newborn infant weighed within 48h of birth |
| AND | AND | AND | AND |
| Weight using calibrated electronic scale 10g resolution | Weight using scale with <50g resolution, tared to zero and calibrated | Weight measured using dial/spring/color-coded scale | Proxy measure of birthweight used |
| AND | AND | AND | AND |
| Scale calibrated once per year | Scale calibrated once per year | Weight recorded as <2500g | Weight category assessed as <2500g |
| AND | AND |  |  |
| Scale placed on a level hard surface | Scale tared to zero grams |  |  |
| AND | AND |  |  |
| Scale tared to zero grams | Weight recorded as <2500g |  |  |
| AND |  |  |  |
| Weight recorded as <2500g |  |  |  |

Supplementary Table 6 - Antenatal Stillbirth GAIA Classification System

|  |  |  |  |
| --- | --- | --- | --- |
| Level 1 | Level 2 | Level 3 | Level 4 |
| GA within predefined range for stillbirth (Level 1 or 2) | GA within predefined range for stillbirth (Level 1 or 2) | GA within predefined range for stillbirth (Level 2 or 3) | Information insufficient to assess GA |
| Delivery of an infant with no signs of life:No spontaneous movements, no heartbeat, no respirations, APGAR 0 at 1 and 5 mins)Determined by physical examination after delivery | Delivery of an infant with no signs of life:No spontaneous movements AND no heartbeat AND no respirations AND APGAR 0 at 1 and 5 mins)Determined by physical examination after delivery | Delivery of an infant with no signs of life:REPORTED TO HAVENo spontaneous movements AND no heartbeat AND no respirations AND APGAR 0 at 1 and 5 mins) | Report of stillbirth but not available for physical examination after birth |
| AND | AND | AND |  |
| Prenatal USS documenting lack of fetal cardiac activity or movement PRIOR to the onset of labourORAuscultation for fetal heart tones showing lack of FHB PRIOR to the onset of labour | Maternal report of lack of fetal movements for at least 24hours before labourORMaternal physical examination confirming lack of fetal movementORAuscultation for fetal heart tones showing lack of FHB PRIOR to the onset of labour | Maternal report of lack of fetal movements for at least 24hoursORReport of auscultation for fetal heart tones showing lack of FHB  |  |
| AND | AND | AND |  |
| Maternal report of lack of fetal movements for at least 24hoursORMaternal physical examination confirming lack of fetal movementORRadiology findings consistent with intrauterine fetal death | Attended delivery followed by examination after birth consistent with antepartum deathORPathology report consistent with antepartum death | Non-attended delivery followed by a examination after birth consistent with antepartum deathOR Verbal history by a trained healthcare provider, non-medical witness or the mother of a fetus born with no signs of life or unresponsive to resuscitation efforts immediately after birth AND with physical features consistent with antepartum death |  |
| AND |  |  |  |
| Attended delivery followed by examination after birth consistent with antepartum deathORPathology report consistent with antepartum death |  |  |  |

Supplementary Table 7 Dysfunctional Labor – Second Stage of Labor – Nulliparous Women

|  |  |
| --- | --- |
| Level 1 | Level 2 |
| Full dilation of the cervix | Full dilation of the cervix |
| AND | AND |
| Onset of the active stage (active maternal pushing OR visible head) | No delivery within 3 hours of full dilationORuse of instrumental delivery for dystociaORC-section for indication of dystocia |
| AND |  |
| Pushing for > 2hoursORuse of instrumental delivery for dystociaORC-section for indication of dystocia |  |

Supplementary Table 8 Dysfunctional Labour – Second Stage of Labour – Multiparous Women

|  |  |
| --- | --- |
| Level 1 | Level 2 |
| Full dilation of the cervix | Full dilation of the cervix |
| AND | AND |
| Onset of the active stage (active maternal pushing OR visible head) | No delivery within 3 hours of full dilationORuse of instrumental delivery for dystociaORC-section for indication of dystocia |
| AND |  |
| >1 hour pushingOR use of instrumental delivery for dystociaORC-section for indication of dystocia |  |

Supplementary Table 9 - Levels of confidence assigned for each definition in each of the studies.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Case Definitions** |  **Cases Assessed** | **Level 1 %** | **Level 2 %** | **Level 3 %** | **Level 4 %** | **Level 5 %** | **Un-assess-able %** | **Missing %** |
| Stuurman et al 2018 | Preterm birth | 72 | 11.1 | 19.4 | 69.4 | 0.0 | 0.0 | 0.0 | 0 |
| Neonatal death | 62 | 19.4 | 80.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0 |
| Neonatal invasive bloodstream infections  | 63 | 41.3 | 50.8 | 7.9 | 0.0 | 0.0 | 0.0 | 0 |
| Stillbirth  | 37 | 10.8 | 13.5 | 40.5 | 35.1 | 0.0 | 0.0 | 0 |
| Kochhar et al 2019 | Preterm birth | 64 | 0.0 | 25.0 | 75.0 | 0.0 | 0.0 | 0.0 | 0 |
| Stillbirth  | 24 | 20.8 | 8.3 | 0.0 | 70.8 | 0.0 | 0.0 | 0 |
| Hypertension | 56 | 96.4 | 3.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0 |
| GA assessment (enabling term) | 755 | 1.2 | 54.4 | 44.4 | 0.0 | 0.0 | 0.0 | 0 |
| Stuurman et al 2021 | Low birthweight | 2050 | 12.6 | 44.5 | 42.7 | 0.1 | 0.0 | 0.0 | 0 |
| Preterm birth | 1914 | 23.7 | 23.4 | 53.0 | 0.0 | 0.0 | 0.0 | 0 |
| Small for gestational age | 1467 | 4.2 | 23.1 | 23.7 | 49.0 | 0.0 | 0.0 | 0 |
| Stillbirth  | 1133 | 25.5 | 2.3 | 30.7 | 41.5 | 0.0 | 0.0 | 0 |
| Antepartum stillbirth | 807 | 34.6 | 1.1 | 31.7 | 32.6 | 0.0 | 0.0 | 0 |
| Intrapartum stillbirth  | 326 | 3.1 | 5.2 | 28.2 | 63.5 | 0.0 | 0.0 | 0 |
| Neonatal death | 751 | 99.6 | 0.0 | 0.1 | 0.3 | 0.0 | 0.0 | 0 |
| Neonatal infections -bloodstream | 783 | 13.9 | 51.3 | 7.2 | 27.6 | 0.0 | 0.0 | 0 |
| Respiratory infection | 155 | 6.5 | 30.3 | 51.6 | 11.6 | 0.0 | 0.0 | 0 |
| Meningitis | 64 | 3.1 | 6.3 | 14.1 | 76.6 | 0.0 | 0.0 | 0 |
| Congenital microcephaly | 120 | 10.0 | 34.2 | 16.7 | 39.2 | 0.0 | 0.0 | 0 |
| Watson et al 2021 | GA assessment (enabling term) - neonatal records | 624 | 47.8 | 10.4 | 23.6 | 0.0 | 0.0 | 18.3 | 0.0 |
| GA assessment (enabling term) - maternal records | 622 | 77.8 | 15.8 | 4.2 | 0.2 | 0.0 | 2.1 | 0.0 |
| Preterm birth | 142 | 64.8 | 5.6 | 12.0 | 0.0 | 0.0 | 17.6 | 0.0 |
| Low birthweight | 123 | 56.9 | 0.0 | 17.1 | 0.0 | 0.0 | 26.0 | 0.0 |
| Small for gestational age | 125 | 43.2 | 4.0 | 23.2 | 0.0 | 1.6 | 27.2 | 0.8 |
| Respiratory distress | 126 | 59.5 | 16.7 | 0.0 | 17.5 | 0.0 | 6.3 | 0.0 |
| Microcephaly | 108 | 12.0 | 13.9 | 6.5 | 13.0 | 0.0 | 30.6 | 24.1 |
| Preterm labour | 126 | 44.4 | 2.4 | 1.6 | 0.0 | 0.0 | 51.6 | 0.0 |
| Fetal growth restriction | 132 | 64.4 | 10.6 | 0.0 | 0.0 | 0.0 | 25.0 | 0.0 |
| Pre-eclampsia | 125 | 56.0 | 17.6 | 0.0 | 0.0 | 0.0 | 26.4 | 0.0 |
| Non-reassuring fetal status | 113 | 1.8 | 13.3 | 15.0 | 0.0 | 0.0 | 69.9 | 0.0 |
| Dysfunctional labour | 126 | 33.3 | 0.8 | 0.0 | 0.0 | 24.6 | 41.3 | 0.0 |