

Supplementary Table 4: Additional information about included reports

| Author Year | Main aim | Follow-up period | Lost to follow-up | Gest. Age | Hypoxia-ischemia definition | NE diagnosis | Exclusion criteria | Income Group | National NMR† | Setting | Public/private |
|---|---|------------------|-------------------|--------------------------------|--|--|---|--------------|---------------|-------------------|----------------|
| INCIDENCE: | | | | | | | | | | | |
| Yang 2019 | Incidence of NE with and without gestational hypertension | N/A | N/A | 37-42 | Any of: i) Apgar <3 at 1 min and Apgar <6 at 5min ii) > 10 min resuscitation or >2 min PPV via endotracheal tube | Neurological examination by Chinese Pediatric Society within 12hrs | Severe congenital malformations, multiple gestation, umbilical cord prolapse | UM | High | 27 hospitals | Unclear |
| INCIDENCE AND NEONATAL MORTALITY: | | | | | | | | | | | |
| Horn 2013 | Compare incidence of NE using different criteria | Until discharge | Unclear | ≥36 | Several definitions | Several definitions | Severe congenital malformations, sepsis, neonatal abstinence, chromosomal syndromes | UM | Mid | 2 SEC and 1 TER | Public |
| Moshiro 2020 | Cause of neonatal deaths | 7 days | Unclear | Term | Apgar <7 at 5 min | Thompson score after admission to NICU | Outborn | Low | High | Referral hospital | Private |
| Niaz 2021 | Risk factors and outcomes of birth asphyxia | Until discharge | 0/97 | 34-40 (in analysis only 37-40) | Apgar 5 at 5min and no improvement to more than 7/10 at 20 minutes of age (SIC), or delayed cry at 5 min | Sarnat&Sarnat, no EEG, unclear timing | Dysmorphism, congenital heart defects, chromosomal abnormalities, congenital infections, infectious and metabolic causes of NE, outborn and birth weight <1000g | LM | High | TER | Public |
| Author Year | Main aim | Follow-up period | Lost to follow-up | Gest. Age | Hypoxia-ischemia definition | NE diagnosis | Exclusion criteria | Income Group | National NMR† | Setting | Public/private |
| INCIDENCE, NEONATAL MORTALITY AND DEVELOPMENTAL OUTCOME: | | | | | | | | | | | |

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| Lally 2014 | MR biomarkers to characterize brain injury in NE | NMR = until discharge Develop. = 42 m | NMR = 0/54, Develop= 10/54 | ≥36 | Any of: i) Resuscitation at birth ii) Apgar <6 at 5 min | Thompson >5 within 6 hrs | Birth weight <1800g, severe congenital malformations | LM | High | TER | Public |
| NEONATAL MORTALITY: | | | | | | | | | | | |
| Aly 2015 | Efficacy of melatonin combined with TH | 2 weeks | 0/30 | 38-42 | Any of: i) Apgar <4 at 5 min and/or delayed first breath (45 min after birth); ii) metabolic or mixed acidosis with serum bicarbonate concentrations of < 12 mmol/l at initial blood gas analyses (SIC) | Sarnat&Sarnat <6hrs (unclear modification) | i) twin gestation; ii) maternal neuro-endocrinal disturbances including diabetes mellitus; iii) chorioamnionitis or congenital infections; iv) low birth weight <2500g; v) congenital malformations of the CNS or gastrointestinal anomalies; vi) chromosomal abnormalities; vii) moribund patient | LM | High | TER | Public |
| Bharadwaj 2012 | Whether TH reduces death and NDD at 6m. | Until discharge | 4/130 | > 37 | pH<7 or BE - 12 or more (SIC) within 1 hr and ≥2 of: (i) Apgar ≤6 at 10 min; (ii) foetal distress; (iii) assisted ventilation ≥ 10 min; (iv) organ dysfunction; (v) acute perinatal event | Sarnat&Sarnat (no EEG) <6hrs | Serious congenital anomalies, outborn, no spontaneous respiration by 20 min | LM | High | TER | Public |
| Biselele 2013 | Incidence and etiology of NE | Until discharge | Unclear | ≥36 | Any of: (i) Apgar <6 at 5 min, (ii) Resuscitation at 10 min, (iii) pH <7 and BE >16 within 1 hr | Sarnat&Sarnat (no EEG) within 24hrs | Severe congenital malformations | Low | High | TER | Public |

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| Biselele 2020 | Safety and pharmacokinetics of Imitiobin | Until discharge | Unclear | ≥ 36 | PPV with bag-and-mask ≥ 10 min | Thompson score of ≥7 at 1-3 hrs | 1) inability to insert umbilical catheter 2) major congenital or chromosomal abnormalities, 3) birth weight < 1800 g; 4) clear signs of infection, 5) moribund patients. | Low | High | 3 Public Hospitals | Public |
| Biselele 2018 | Feasibility of TH defined as arrival to hospital <6hrs | Until discharge | 0/57 | ≥ 36 | Any of i) Apgar up to 5 at 5 min or ii) need of resuscitation ≥ 10 min | Thompson score of ≥7 at < 6 hrs | Severe congenital or chromosomal malformations | Low | High | 3 Public Hospitals | Public |
| Biselele 2014 | Determine the evolution of Thompson score during first 6 hrs | Until discharge | Unclear | ≥ 36 | Any of: (i) Apgar <6 at 5 min, (ii) Resuscitation at 10 min, (iii) pH <7 and BE >16 within 1 hr | Thompson score ≥6 at < 1 hr | Congenital malformations | Low | High | TER | Public |
| Bozkurt 2020 | Evaluate the incidence and severity of acute kidney injury in newborns treated with TH | Unclear | Unclear | ≥ 36 | pH < 7 or BD ≥ 16 in cord blood, if pH 7...7.15 and/or BD 10...15.9 then any of the following was also needed: i) Apgar score < 6, ii) ventilation ≥10 min iii) evidence of organ dysfunction. | Sarnat&Sarnat <6hrs | congenital renal anomalies, major congenital anomalies, IUGR and sepsis | UM | Mid | TER | Public |
| El Shimi 2014 | Safety and efficacy of EPO | Until discharge | 1/30 | ≥ 37 | pH <7 or BE < -16 within 1 hr. If pH 7.01...7.15 or BE -10...-15.9 mmol/L or blood gas not available, both i) an acute perinatal event and ii) Apgar <6 at 10 min or assisted ventilation ≥ 10 min | Sarnat by NICHD Grade II-III | congenital renal anomalies, major congenital anomalies, IUGR and sepsis | LM | High | TER | Public |

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| Enweronu-La ryea 2019 | Temperature profile of infants with NE | Until discharge | 0/14 | ≥36 | Both: i) Bag-mask resuscitation at birth and ii) Apgar <6 at 5 min | Thompson ≥7 or seizures | birth weight < 2000 g, imminent death and infants with major congenital malformations, swift recovery | LM | High | TER | Public |
| Hassanein 2017 | Concentration of umbilical cord CD34+ stem cells | Unclear | 0/20 | ≥37 | pH of ≤7.0 and/or a BD of ≥16 within 1 hr. If pH 7.01...7.15 and/or the BD 10–15.9, additional criteria were used: i) Apgar <6 at 10min and ii)resuscitation with or without assisted ventilation 10 min (unclear if both were required) | aEEG and Sarnat | congenital or chromosomal anomalies, multiple pregnancy, or parents refused enrollment | LM | Mid | TER | Public |
| Horn 2010 | Temperature profile of a new cooling method | Until discharge | 0/5 | ≥36 | Any of: i) BD ≥ 16 within 1 hr, or ii) An abnormal intra-partum course and either Apgar < 7 at 10 min or continued respiratory support at 10 min | Clinical seizures or abnormal aEEG | Birth weight <2000g, major congenital abnormalities, active bleeding, obvious sepsis, persistent pulmonary hypertension, severe hypoglycaemia or electrolyte abnormality that did not respond to usual therapy | UM | Mid | TER | Public |

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| Horn 2012 | Temperature profile | Until discharge | 0/14 | 36-42 | pH \leq 7.0 or BD \geq 16 in cord or within 1 hr. If pH was 7.01...7.15 or BD 10...15.9 or a blood gas was not available and one of following: acute perinatal event and Apgar \leq 5 at 10min or assisted ventilation for 10 min | Sarnat NICHD grade II-III | Not reported | UM | Mid | SEC | Public |
| Kinoshita 2021 | Feasibility and effectiveness of using ice packs to reach and maintain the TH target temperature | Until discharge (but reports one death at 28d) | 26207 | \geq 35 | Not specified but reported mean Apgars, pH and BE were low | Modified Sarnat (unspecified) within 6 hrs | Not reported | UM | Mid | TER | Private |
| Martinez-Hernandez 2020 | Analyse survival and neurological condition of neonates treated with TH | Until discharge | Unclear | >34 (incl 1 born w 34) | pH \leq 7 or BD \geq 16 in cord blood, if pH 7.01...7.15 or BD 10...15.9 during 1st hr of life (SIC) or if blood sample was not available then any of: i) adverse perinatal event ii) Apgar \leq 5 at 10 min iii) ventilation at 10 min | Sarnat&Sarnat grade II-III within 6 hrs | Birth weight <1800g or major congenital malformations and chromosomal abnormalities incompatible with life | UM | Mid | TER | Unclear |
| Oliveira 2018 | Feasibility and effectiveness of TH | Until discharge | Unclear | Term | Resuscitation at birth (mean (SD) Apgar at 5 min was 4.5 (1.3)) | NICHD Sarnat Grade II-III < 6 hrs | Birth weight < 1800g, moribund condition, major life-threatening congenital malformations, cooling device not available | LM | High | 5 TERs | Public |

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| Onay 2021 | To compare the renal function of infants who received aminophylline during TH vs. TH alone | Unclear | Unclear | ≥36 | Both i) pH ≤7 or BE ≤ -16 within 1 hr and ii) Apgar <5 at 10 min or need for resuscitation at 10min | Sarnat&Sarnat stage II-III or pathologic aEEG within 6 hrs | birth weight < 2000 g, central nervous system malformation, anatomical renal anomaly, chromosomal disorders, inborn error of metabolism, maternal chorioamnionitis, stroke, or drug exposure that might lead to neonatal encephalopathy, severe or diffuse parenchymal cranial hemorrhages | UM | Mid | TER | Public |
| Prashantha 2019 | Efficacy and safety of TH | Until discharge | 11/62 | ≥36 | Inborn babies any of: i) pH <7 ii) BD ≥12 iii) Apgar <6 at 5 min iv) PPV ≥10 min. Outborn babies any of: i) no cry immediately after birth ii) required resuscitation iii) Apgar score <5 at 5min iv) need of respiratory support | NICHD Sarnat Grade II-III < 6 hrs | Birth weight < 1800g | LM | High | TER | Private |
| Shabeer 2017 | Compare efficacy and safety of different TH methods | Until discharge | Unclear | ≥35 | Any of i) pH < 7 or BD >12 from cord blood; ii) Apgar < 5 at 5 min iii) resuscitation > 10 min | NICHD Sarnat Grade II-III within 6 hrs | Birth weight <1800g | LM | High | TER | Private |

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| Shrestha 2020 | Association of Thompson score and early neonatal outcomes | Unclear (3 days?) | 0/20 | Term | pH < 7.0 within 1 hr included in review (original criteria Apgar <7 at 5min) | Thompson score day 1 | Congenital anomalies | LM | High | TER | Private |
| Tanigasalam 2016 | Effectiveness of TH on acute kidney injury | Unclear (most deaths within 5 days) | 0/120 | Term | pH ≤7 or BD ≥ 12in cord blood and ≥2 of: i) Apgar ≤5 at 10 min, ii) fetal distress, iii) assisted ventilation for at least 10 min, iv) organ dysfunction | Sarnat&Sarnat Grade II-III < 6hrs | Extramural neonates, major congenital abnormalities, absence of spontaneous respiratory efforts by 20 min or history of maternal renal failure | LM | High | TER | Public |
| Thomas 2018 | Feasibility and safety of TH | Until discharge | Unclear | ≥35 | Inborn: pH <7 or BD >12 in cord blood or Apgar <5 at 5 min or need for resuscitation for >10 min. Outborn: no cry/breathing immediately after birth or assistance for breathing soon after birth or Apgar <5 at 5 min | NICHD Sarnat Grade II-III < 6 hrs | Chromosomal disorder or major congenital anomaly | LM | High | 11 TERs | Both |
| Umran 2016 | IGF-1 levels in NE | Until discharge | Unclear | 37-41+6 | All of: i) intrapartum fetal distress; ii) Apgar score <6 at 5 min; iii) need of mask-bag ventilation or intubation | Abnormal muscle tone, level of consciousness, posture, reflexes, myoclonus, pupils, seizures evaluated in < 6hrs | Congenital abnormalities, or confirmed inborn error of metabolism | UM | High | TER | Public |

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| Variante 2017 | Correlate aEEG findings with mortality and neuroimaging findings | Until discharge | Unclear | ≥36 | ≥ 2 of the following: i) Apgar <6 at 6 min, ii) ventilation 10 min or iii) pH <7.1 or BE > -12 (SIC, unclear timing) | Modified Sarnat (unspecific) | genetical syndromes or congenital malformations not compatible with life | UM | Mid | TER | Private |
| Yang & Li 2020 | Effect of TH on oxidative factors | 7 days | Unclear | ≥37 | Any 1 of: i) Apgar <4 at 1 min and <6 at 5-min, ii) pH <7.0 or BE ≤-16 in umbilical artery, iii) resuscitation or mechanical ventilation was for 5 min | Chinese medical association society of pediatrics definition | Birth weight < 2500g, i) convulsions caused by electrolyte disorder, intracranial hemorrhage and birth injury, as well as brain injury caused by intrauterine infection, genetic and metabolic diseases, and other congenital diseases; ii) neonates with congenital malformation or congenital metabolic abnormality; and iii) intrauterine, prenatal or intrapartum infection. | UM | Low | TER | Public |

NEONATAL MORTALITY AND DEVELOPMENTAL OUTCOME:

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| Aker 2021 | MRI at 5d to predict GMA at 3m and BSID-III score at 18m | NMR = Neonatal period, Develop. = 18 m | NMR = 0/50, Develop. = 3/50 | >35 | For inborn any of: pH <7 or BD ≥12 within 1 hr, Apgar ≤5 at 5 min, or PPV for ≥ 10min. For outborn no cry at birth | NICHD Sarnat Grade II-III < 6 hrs | Major congenital anomalies or imminent death | LM | High | TER | Private |
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| Catherine 2021 | To assess the effect of therapeutic hypothermia on the outcome | NMR = Until discharge , Develop. = 18 m | NMR = 0/162, Develop . = 7/158 | Term | pH<7 or BE < 12 within 1 hr and ≥2 of: (i) Apgar <6 at 10 min; (ii) foetal distress; (iii) assisted ventilation ≥ 10 min; (iv) organ dysfunction | Sarnat&Sarnat <6hrs | Serious congenital anomalies, outborn, no spontaneous respiration by 20 min | LM | Mid | TER | Public |
| Catherine 2020 | Effect of TH on the levels of S100B and NSE and their usefulness in predicting NDD | NMR = Until discharge , Develop. = 18 m | NMR = 0/162, Develop . = 7/158 | Term | pH<7 or BE < 12 within 1 hr and ≥2 of: (i) Apgar <6 at 10 min; (ii) foetal distress; (iii) assisted ventilation ≥ 10 min; (iv) organ dysfunction | Sarnat&Sarnat <6hrs | Serious congenital anomalies, outborn, no spontaneous respiration by 20 min | LM | Mid | TER | Public |
| Celik 2015 | Effects of TH on neuronal biomarkers | NMR = Until discharge , Develop. = 12 m | 0/7 | > 36 | Any of: (i) Apgar score <5 at 10 min of age, (ii) Continued need for ventilation 10 min after birth (iii) pH <7 or BE < -16 within 1 hr | aEEG and Levene staging <6hrs | >6 h of age, severe congenital, anomalies or severe intrauterine growth retardation | UM | Mid | TER | Public |
| Celik 2016 | Differences in outcome of whole body hypothermia and selective head cooling | NMR = Until discharge , Develop. = 12 m | 1/30 (1 cessatio n of cooling) | ≥ 36 | Apgar ≤5 at 10 min, PPV 10 min after delivery, or pH <7.0 or base excess ≤ -16 within 1 h after birth | aEEG and Levene staging <6hrs | >6 h of age, severe congenital, anomalies or severe intrauterine growth retardation | UM | Mid | TER | Public |

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| Das 2021 | Safety and effectiveness of TH | NMR = Until discharge , Develop. = 30 m | Both 0/60 | ≥ 37 | pH < 7 or BE < -12 and ≥ 2 of: i) Apgar < 6 at 10 min ii) PPV > 1 min, or first cry delayed > 5 min iii) Perinatal predisposition for asphyxia | Sarnat (own modification) <6 hrs | SGA, chromosomal or major congenital anomalies, refusal of consent, major intracranial hemorrhage, birth weight < 2000g, no spontaneous respiration ≥ 20 min | LM | High | TER | Public |
| Gucuyener 2012 | Association between aEEG and NIRS during TH and short and long-term outcome | NMR = neonatal, Develop. = 18 m (incl. 4 additional cases with <12m follow-up) | NMR = 0/10, Develop. = 0/5 | Term | Unclear if both or either: Apgar <5 at 5 min and/or cord blood pH <7.0 | Sarnat & Sarnat Grade II-III and aEEG or seizures | Not reported | UM | Mid | TER | Public |
| Jia 2018 | Effect of timing of TH on aEEG and NSE after 3d and neonatal death or severe disability at 18m (lacks information on death beyond neonatal period) | NMR = neonatal, Develop. = 18 m | Both 0/152 | ≥36 | Any of: i) Apgar ≤ 5 at 5 min; ii) ventilation for 10 min; iii) pH ≤ 7 (unclear timing) | Sarnat&Sarnat within 12 hrs | 1) major congenital abnormalities; 2) known or suspected chromosomal abnormalities; 3) major brain malformations; or 4) aEEG abnormalities from causes other than HIE | UM | Mid | TER | Public |

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| Khuwuthy akorn 2021 | Long-term outcomes after TH | NMR = Until discharge , Develop. = ≥ 24 m | NMR = 0/23, Develop . = 3/23 (3 addition ≥35 al with incompl ete follow-up) | ≥ 2 of: i)Apgar ≤5 at 10 min, ii)PPV or continued resuscitation 10 min, iii) pH < 7 or BD >16 within 1 hr | Modified Sarnat (unspecified) within 6 hrs | Birth weight <1800g | UM | Mid | TER | Public |
| Malla 2017 | Efficacy and safety of EPO | NMR = Neonatal period, Develop. = 19 m | Both 0/50 ≥37 | Apgar <5 at 10 min and ≥2 of: i) fetal distress ii) ventilation ≥10 min iii) pH <7 or BD ≥ 16 or | NICHD Sarnat Grade II-III < 6 hrs | Congenital or chromosomal anomalies, congenital infections, severe IUGR, inborn errors of metabolism | LM | High | TER | Public |
| Maoulaini ne 2017 | Feasibility of TH | NMR = Until discharge , Develop. = 18 m | NMR = unclear, Develop = 19 % ≥36 in TH and 42 % NT | Not specified (95 % had Apgar <6 at 5 min) | Sarnat&Sarnat within 6 hrs for cooled, unspecified for non-cooled | Birth weight < 1800g, imperforate anus, major intracranial hemorrhage, and severe chromosomal or congenital anomalies | LM | High | TER | Public |
| Perez 2018 | Efficacy of a new cooling method | NMR = Unclear, Develop. = 18-24m | Both = 0/53 ≥35 | pH < 7.1 (timing and source unspecified) or requiring ventilatory support (timing unspecified) | Sarnat&Sarnat (without EEG) or SIBEN Grade II-III within 6 hrs | Not reported | UM | Mid | 3 TERs | Private |

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| Procianoy 2019 | Describe the experience of TH | NMR = Until discharge Develop. = 12 m | NMR = unclear, Develop ≥36 . = 13/72 | pH <7 or BD <15 (SIC) within 1 hr, or acute perinatal event, or Apgar <6 at 10 min, or ventilation ≥10 min | Sarnat&Sarnat Grade II-III < 6 hrs | birth weight < 1800g, major congenital malformations | UM | Mid | TER | Public |
| Sun 2012 | Effect of TH on levels of NSE and S-100 protein in CSF | NMR = Neonatal period, Develop. = 12 m | Both 0/51 ≥37 | Any of following: i) Apgar score <4 at 1 min and <6 at 5 min, ii) pH <7 or ≤ BD 16 (SIC) iii) resuscitation or ventilation at 5 min | Sarnat&Sarnat in < 6 hrs | <2500g, major congenital abnormalities, infection on admission (rupture of membranes >18 h, maternal fever >38C or foul-smelling amniotic fluid), other encephalopathy | LM | High | TER | Public |
| Thayyil 2021 | Efficacy of TH on death and moderate to severe developmental disability | NMR = Until discharge , Develop. = 20 m | NMR = unclear, Develop ≥36 . = 14/408 | Hospital born: resuscitation at 5 min and/or Apgar <6 at 5 min. Home born: no cry by 5 min | NICHD Sarnat Grade II-III 1-6hrs age | Birth weight <1800g, no heart rate at 10 min despite adequate resuscitation, life threatening congenital malformations, parents unable to attend follow-up | All LM | Low & High | 7 TER | Public |

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| Valera 2015 | Describe the implementation of TH | NMR = Neonatal period, Develop. = > 12 m | NMR = 0/27, Develop . = 3/27 ≥36 lost and 5/27 were < 12m | Inborn: all of i) Apgar < 6 at 10 min, ii) pH ≤ 7 or BD ≥-16 (SIC), iii) sentinel event and iv) assisted ventilation ≥ 10 min | Sarnat&Sarnat in < 6 hrs | Moridbund patient not fit for transfer or arrival > 6hrs of life | UM | Mid | TER | Public |
| Zhou 2010 | Randomized controlled trial of selective head cooling to treat infants with NE | NMR = Unclear, Develop. = 18 m | NMR = unclear, Develop ≥ 37 . = 41/194 | All of (?): i) Apgar <4 at 1 min and <6 at 5 min, ii) pH <7 or BD ≤ 16 (SIC) in cord blood iii) resuscitation or ventilation at 5 min | Sarnat&Sarnat in < 6 hrs | Birth weight < 2500g, major congenital abnormalities, Infection (rupture of membranes >18 hours or maternal fever >38C or amniotic fluid foul smell), other encephalopathy (neonatal stroke, central nervous system) | UM | High | 12 hospit als | Public |

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| Zhu 2009 | Efficacy and safety of EPO | NMR = neonatal, Develop. = 18 m | NMR = unclear, but 118/285 potential cases were excluded, Develop. = 14/167 | >37 | Apgar scores of <6 at 5 min or resuscitation at 10 min | Sarnat & Sarnat Grade II-III | Birth weight < 2500g, major congenital abnormalities, head trauma or skull fracture causing intracranial hemorrhage, body temperature of 34°C, financial problems of the parents, lack of permanent address, and postnatal age of > 48 hrs | UM | Mid | 2 TER | Public |
| Zou 2019 | Hyperbilirubinemia as a risk factor for HIE and whether TH affected bilirubin levels | NMR = Until discharge, Develop. = 18-24 m | NMR = 0/89, Develop. = 3/89 | ≥ 37 | All of (?): i) Apgar <4 at 1 min and <6 at 5 min, ii) pH <7 or BD ≤ 16 (SIC) in cord blood iii) resuscitation or ventilation at 5 min | Sarnat&Sarnat in < 6 hrs | Birth weight < 2500g, major congenital abnormalities, Infection (rupture of membranes >18 hours or maternal fever >38C or amniotic fluid foul smell), other encephalopathy | UM | Mid | TER | Public |

DEVELOPMENTAL OUTCOME:

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| Ballot 2020 | To compare developmental outcomes in survivors of NE with those in healthy children born at full term | 9-18 m (mean 14.31 m (95% CI 13.3 - 15.3)) | 15/99 | > 36 | Any one: Resuscitation >10 min, BE ≤16 (SIC) within 1 hr, Apgar <5 at 10 min | Sarnat&Sarnat <6hrs for TH, undefined for others | Birth weight < 2000g | UM | Mid | TER | Public |
| Charki 2020 | Outcomes of TH | 18 m | 54/210 (87 %, based on 32 cases death or DAMA + 22 lost) | > 36 | Arterial blood gas pH <7.1 and BD >16, timing not specified | Sarnat & Sarnat Grade II-III, EEG not mentioned | Birth weight <1800 g, severe chromosomal or congenital anomalies, major intracranial hemorrhage, refusal from parents | LM | High | TER | Public |

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| Koshy 2011 | Evaluate NDD after TH | 18-24 | 5/20 | ≥35 | Inborn: pH < 7.0 or BD ≥ 12 and ≥2 of: i) Apgar ≤5 at 5 min; ii) ventilation for ≥ 10 min; iii) Perinatal predisposition to perinatal asphyxia. Outborn: not having cried/breathed immediately after birth with evidence of any of: i) not breathing normally at 5min; ii) given assistance for breathing soon after birth; iii) flaccid since birth; iv) poor feeding; v) Apgar ≤5 at 5 min encephalopathy at admission | NICHD Sarnat Grade II-III <5 hrs age | Small for gestational age, chromosomal or major congenital anomaly, refusal of consent, or inability to start cooling by 5 hrs' age | LM | High | TER | Private |
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| Mbatha 2021 | To determine the long-term outcome of neonates managed with TH outside of NICU | 12-24m | 56/113 | >36 | Apgar ≤ 5 at 10 min or need for resuscitation for ≥ 10 min or pH <7.00 or BD ≥ 16 in cord blood or within 1 hr of birth | Lethargy, stupor, or coma and either hypotonia, abnormal reflexes, an absent or weak suck, or clinical seizures, and abnormal background activity in aEEG | Major congenital abnormalities | UM | Mid | TER | Public |
| Weng 2021 | Effect of TH on aEEG after 3d, NBNA at 28d and BSID-II at 18m | 18 m | 0/61 | ≥ 35 | Both i) Apgar score ≤ 3 1 min or ≤ 5 at 5 min; and ii) pH ≤ 7.0 or BD ≥ 16 in the umbilical cord or arterial blood < 1 hr | Clinical Sarnat&Sarnat or aEEG | Birth weight < 1800 g, normal aEEG monitoring; serious congenital malformations; traumatic brain injury or moderate to severe intracranial hemorrhage; systemic congenital viral or bacterial infection; spontaneous bleeding tendency or platelets less than $50 \times 10^9/L$ 12 hrs after birth | UM | Mid | TER | Public |

aEEG = amplitude-integrated electroencephalography

BD = Base Deficit

BE = Base Excess

BSID = Bayley Scales of Infant Development

CNS = central nervous system

CSF = cerebrospinal fluid

DAMA = discharge against medical advice

EEG = electroencephalography

EPO = erythropoietin

GMA = general movements assessment

IUGR = intrauterine growth restriction

LM = Lower middle-income country

MRI = magnetic resonance imaging

NBNA = neonatal behavioural neurological assessment

NDD = neurodevelopmental disability

NICHD = National Institute of Child Health and Development

NICU = Neonatal Intensive Care Unit

NMR = Neonatal Mortality Rate

NSE = neuronal specific endolase

NT = normothermia

PPV = positive pressure ventilation

SD = Standard Deviation

SEC = Secondary Hospital

TER = Tertiary Hospital

TH = Therapeutic hypothermia

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|------------------------------|------|------|
| Low | <5 | per |
| Neonatal Mortality Rate, Mid | 5-15 | 1000 |
| High | >15 | live |