Neonatal Therapeutic Hypothermia in Ireland

Annual Report | 2016-2017

National Neonatal Therapeutic Hypothermia Development Project

Prepared by the National Clinical Programme for Paediatrics and Neonatology and the National Perinatal Epidemiology Centre

HSE

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Person-centred, co-ordinated care

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List of Acronyms and Abbreviations

APGAR – Appearance, Pulse, Grimace, Activity, Respiration

ARM – Artificial Rupture of Membranes

BMI – Body Mass Index

CTG – Cardiotocograph Traces

EDD – Estimated Due Date

FGR – Fetal Growth Restriction

GROW – Gestation Related Optimal Weight

HIE – Hypoxic Ischaemic Encephalopathy

MDT – Multi-Disciplinary Team

MRI – Magnetic Resonance Imaging

NCPPN – National Clinical Programme for Paediatrics and Neonatology

NE – Neonatal Encephalopathy

NG – Nasogastric Tube

NICU/SCBU – Neonatal Intensive Care Unit/ Special Care Baby Unit

NNT – Number Needed to Treat

NNTP – National Neonatal Transport Programme

NPEC – National Perinatal Epidemiology Centre

NWIHP – National Women and Infants Health Programme

SHO – Senior House Officer

TH – Therapeutic Hypothermia

Foreword

This report is a collaborative initiative between the National Clinical Programme for Paediatrics and Neonatology (NCPPN) and the National Perinatal Epidemiology Centre (NPEC). The Therapeutic Hypothermia (TH) steering committee has overseen the governance for this project. A Multi-Disciplinary Team (MDT) approach has been adopted in order to best inform this process.

This report is based on the 19 maternity sites in Ireland. We would like to acknowledge with much appreciation each hospitals role in supporting the data collection process for this report. From the onset it was encouraging to observe the commitment from each hospital site towards the project. Their assistance and enthusiasm during the data collection phase and overall is greatly appreciated. Without their participation this report would not have come to fruition.

This report serves as a platform to continue the national review process in order to attain valuable data which can influence clinical practice in a constructive way.

We would like to thank the Clinical Strategy and Programme Division of the HSE and the National Women and Infants Health Programme (NWIHP) for their commitment to this project and the funding they contributed in order to progress this important piece of work. It is envisaged through the formation of a national electronic-register there will be a recording of all data around these cases. This data can then be analysed from a number of perspectives; antenatal, labour management, resuscitation of the neonate and the overall clinical management of this cohort. This will inform the development of best practice national guidelines, assurance of best practice, and evaluation of interventions. There is also the possibility that causative and maternal risk factors will be identified. This may facilitate the mitigation of these risk factors in the antenatal period. Identification of trends in the data will also encourage further enquiry which may impact on practices.

Further, we would like to acknowledge the staff in NPEC. Their professionalism, assistance and knowledge has been instrumental in getting this report published. We look forward to continuing our work with NPEC in order to establish the E-Register.

Lastly, we would like to extend our thanks to the steering committee for their involvement, dedication, expertise and support.

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Executive Summary

This report contains maternal and infant data pertaining to Neonatal Therapeutic Hypothermia (TH) in Ireland for the period of 2016/2017. Anonymised data was collected on maternal characteristics, history of antenatal care and delivery. Data were collected on infant characteristics, resuscitation, assessment, hospital transfers, their 72-hour clinical course, rewarming, feeding and outcomes.

There were 63 cases of TH in 2016 and 77 cases of TH in 2017; total of 140 in the two-year period. This suggests that one in 900 infants born in Ireland during 2016/2017 required TH. The survival rate for the TH cohort was 88%, as 17 of the 140 infants died.

Of the range of maternal characteristics examined, parity showed some evidence of being associated with increased risk of the infant requiring TH. Almost 40% of all infants born in Ireland are born to nulliparous women, whereas this was the case for 60% of the TH cohort. Based on available examinations, placental conditions were present for the vast majority of the infants indicating evidence of fetal compromise before delivery.

There was an overrepresentation of complications preceding and during the delivery of the infants. Many of these complications occur in the labour ward including uterine rupture, shoulder dystocia and maternal pyrexia during labour alongside an overrepresentation of complex modes of delivery. While these findings support the existing evidence that hypoxia requiring TH is caused by antepartum and intrapartum complications and events, disentangling the role of these complications and events requires more extensive data and analysis, in particular relating to labour. The fact that TH is rare in babies delivered by elective section (1.4%) it is likely that the events of labour play an important role in the aetiology of this condition.

In Ireland, TH is administered in four centres (National Maternity Hospital, Rotunda, Coombe Women and Infants University Hospital and Cork University Maternity Hospital). Infants born outside of these centres must be transferred. Forty percent of the TH cohort in 2016/2017 were born in a local or regional hospital and were subsequently transferred to a tertiary centre.

Practice guidelines state that TH should be started within six hours of birth. This report illustrates the logistical challenges faced with the delivery of a high acuity, uncommon treatment that has to be delivered on short notice.

The proportion of TH infants requiring intubation at delivery was 59%. Additionally, 66% of the TH infants had a cord pH of ≤7.0 which underlines the severity of the asphyxia for many cases. On Day 1 of TH therapy, 29% of TH infants experienced clinical seizures and 36% of TH infants experienced electrographic seizures. During this 24 hour period, 37% of infants given anticonvulsants.

Sarnat grade scores, which quantify the level of encephalopathy, were not uniformly recorded but the available data indicated that 20%, 55% and 25% of the TH cohort had mild, moderate and severe encephalopathy, respectively.

The effectiveness of TH in preventing brain damage to hypoxic neonates is a welcome development- though the number needed to treat (NNT) remains at 7 i.e. only 1 in 7 will benefit from the therapy. A future aspiration is the prevention/ reduction of the condition that necessitates cooling i.e. the avoidance of neonatal hypoxic ischemic encephalopathy (HIE).

The consequences of neonatal encephalopathy (NE) for the infant, their family and the wider society are considerable. Any information that signposts the way to avoid such outcomes is to be welcomed.

The next steps for this project include the development of the E-register in collaboration with NPEC. In the interim the process of data collection will recommence reviewing maternal and infant charts anonymously for the 2018 report.

Key Findings

- In 2016/2017, 140 infants were treated with TH, suggesting that TH is provided to one in 900 infants born in Ireland.
- Nulliparous mothers accounted for 60% of the TH cohort.
- 34% of the TH cohort had their labour induced, compared to 29% of all deliveries in Ireland for 2016. In this report nulliparous women were twice as likely to have their labour induced as compared with parous mothers in the TH cohort.
- Caesarean Section was the most common mode of delivery for all 140 infants accounting for 47% of deliveries. Of which:
  - 1.4% of mothers had an elective section.
  - 47% of mothers in the TH cohort had a Caesarean Section pre-labour.
  - 53% of Caesarean Sections occurred after the onset of labour.
- There were 18 (13%) documented cases of shoulder dystocia.
- 66% of the infants had a cord pH ≤7.0.
- 79% of the infants had an Apgar score of 0-3 at 1 minute of life.
- 59% of the TH infants required intubation at birth.
- 40% of the TH infants were born in a regional or local hospital of which 89% were transferred by the National Neonatal Transport Programme (NNTP).
- Data for Sarnat grading was incomplete in this report for both during TH and upon discharge.
- A specific placental pathology was present in 83% of cases where a placental examination was completed.
- There was an 88% survival rate amongst the infants who received TH in 2016/2017. Of the infants who passed away data were not collected on autopsy or post mortem results. As such, their cause of death is unknown.

Recommendations

1. **Ongoing national review of therapeutic hypothermia infant cases is required.**
   Ongoing national audit on the provision of care for these infants is warranted. The audit tool and dataset need to be continually assessed in order to ensure that it is capturing the appropriate indicators influencing outcomes of care.

2. **Development of a national E-Register of all infants treated with therapeutic hypothermia.**
   The development of the national E-register will facilitate benchmarking against international registries and databases. Such a register will also be well placed to evaluate new adjunctive therapies such as erythropoietin. Consequently, the establishment of the national E-register will contribute to a body of evidence which will inform standardised clinical practice, public health interventions, service planning and counselling of prospective parents.

3. **Regular training updates and drills are necessary to ensure optimum management of complex obstetric situations.**
   International evidence indicates that shoulder dystocia is associated with prolonged labour and thus is a risk factor for HIE. The current report reflects these findings, with 13% of deliveries complicated by a shoulder dystocia. Training on the management of shoulder dystocia and other complex obstetric situations is warranted.

4. **All therapeutic hypothermia infants require daily Sarnat grading assessment.**
   HIE classification is mild/moderate/severe. Assessment of the infant's encephalopathy determines the magnitude of injury and prognosis. The Sarnat grading scale (Grade 1 /Grade 2 /Grade 3) is an internationally recognised classification assessment tool for HIE in the newborn infant. The TH report for 2016/2017 cases yielded incomplete data for Sarnat scoring on TH day 1, 2 & 3.

5. **The start time of either active or passive cooling should be documented. However the 72 hour treatment clock begins when the infant reaches the targeted 33-34°C rectal temperature.**
   On 35/137 (26%) occasions the 72 hour period of cooling was instigated by staff despite the infant not being within the optimal rectal temperature range of 33-34°C.

6. **All therapeutic hypothermia infants require Cranial Ultrasounds to be carried out within the first four days of life.**
   Cranial ultrasounds are a standard of care for TH babies and should be carried out within the first 4 days of life.

7. **The development and implementation of a standardised review tool for perinatal events is advocated.**
   A standardised review tool for perinatal events which incorporates a comprehensive review of adverse outcomes using a multidisciplinary team approach will enable the identification of potential risk factors for pregnant women.

8. **Placental pathology examination is required in all therapeutic hypothermia infants.**
   Following the birth of an infant requiring TH the placenta should be sent to the pathology department and examined by a Perinatal Pathologist. In cases where an infant is not born in a tertiary hospital, the placenta should be stored appropriately and accompany the infant when transferred.

9. **All therapeutic hypothermia infants should have a formal neurodevelopmental assessment using the 3rd Ed. Bayley assessment at 2 years of age.**
   For this report the 2 year follow-up on 2016/2017 TH infants has not been reviewed. However, for the E-register there will be a dataset to review and document the formal follow up assessment. The optimal timing is 2 years of age. The TH centre where the infant was managed should coordinate this assessment.

Introduction

The NCPPN in collaboration with NPEC presents its first report on Neonatal Therapeutic Hypothermia in Ireland. To date, there had been no national overview of the current status and outcomes of Therapeutic Hypothermia (TH) in Ireland which represented a dearth in the knowledge available to clinicians, health managers and parents.

This is the first national investigation of TH and incorporates comprehensive data on every infant who underwent TH in the years 2016 and 2017 in Ireland. It aims to deliver a national overview of TH in Ireland by documenting the number of cases in 2016/2017 and collecting baseline data on the maternal, infant and clinical characteristics associated with TH.

Secondly, the current project aims to inform the development and implementation of a National Therapeutic Hypothermia E-Register for Ireland. A national E-register encompassing data on all cases of TH in Ireland will serve as a platform for identification of maternal, infant and clinical risk factors associated with the requirement for TH intervention; development of best practice guidelines; and identification of trends over time. Furthermore, a national E-register will facilitate benchmarking of TH in Ireland against international standards and thus ensure continual quality improvement.

Section 1 of this report contains the main maternal findings including;

- Maternal characteristics
- Maternal antenatal course
- Labour
- Delivery

Section 2 of this report contains the main infant findings including;

- Infant Characteristics
- Resuscitation
- Assessment for Therapeutic Hypothermia
- Transfer to tertiary unit
- Treatment days 1-3
- Rewarming
- Feeding
- Discharge diagnosis and neonatal death

Methods

Purpose of this report

The primary aim of this report is to present an overview and national statistics on Neonatal Therapeutic Hypothermia in the Republic of Ireland for the years 2016 and 2017. Therapeutic Hypothermia (TH) is administered in four centres only (National Maternity Hospital, Rotunda, Coombe Women and Infants University Hospital and Cork University Maternity Hospital). All infants born in other local and regional hospitals needing this treatment are transferred to one of these four centres.

The audit will examine the clinical details around each case of Neonatal Therapeutic Hypothermia. This will include the mothers' antenatal details, labour, delivery, resuscitation, neurological assessment, treatment of seizures, the supportive clinical care the examination of the placenta and post mortem, if applicable.

Data Collection

Retrospective reviews of inpatient medical records have been used as a gold standard approach when assessing multiple outcomes and rates of adverse events. Therefore, for the purposes of the National Neonatal Therapeutic Hypothermia Audit, medical records were considered the primary source of information. Data were collected on site in the 19 maternity units/hospitals and neonatal intensive care units or special care baby units (NICU/SCBU) in the Republic of Ireland. The NCPPN and NPEC collected data on all cases of neonatal therapeutic hypothermia in 2016 and 2017 by taking an active case ascertainment approach.

Processing of the data

Data on all infants who received therapeutic hypothermia were collected on site in the 19 maternity units/hospitals. The data were submitted by paper to the NPEC and were processed in a pseudonymised format. No hospital identifiers were included in the dataset, which means these data cannot be attributed a specific hospital or a specific individual.

Missing data

To ensure accuracy of information, missing or incomplete data were sought from the respective maternity hospitals/units by the Therapeutic Hypothermia Co-Ordinator. For analysis purposes, cases with missing data were excluded from calculations. However, the extent of missing data is reported in the results section.

Comparison to National Statistics

Comparisons are made with the most recent publications available, including the Central Statistics Office's Vital Statistics Fourth Quarter and Yearly Summary report as well as from the Healthcare Pricing Office.

Definitions & Terminology

Neonatal Encephalopathy (NE) is a clinical condition in the term infant defined by abnormal neurological behaviour, with the onset occurring at or shortly after birth.

NE is manifested by an abnormal level of consciousness, with or without the presence of seizures and is often accompanied by difficulty initiating and maintaining respirations, depressed tone and depressed reflexes, poor suck and swallow.

NE incidence is estimated as 3.0 per 1000 live births and for HIE is 1.5.[1] NE is graded as mild, moderate or severe using the Sarnat grading system.

A subgroup of infants with NE have been exposed to a hypoxic-ischaemic insult in-utero and therefore they are assigned a diagnosis of hypoxic-ischaemic encephalopathy. In a proportion of these cases, a sentinel event is identified i.e. placental abruption, uterine rupture etc.

Suggested criteria for an intrapartum hypoxic-ischaemic insult[2] include:

(i) Evidence of metabolic acidosis in fetal umbilical cord arterial blood obtained at delivery (pH < 7 and base deficit ≥ 12 mmol/L).
(ii) Early onset of severe or moderate NE in infants ≥ 34/40.
(iii) A sentinel hypoxic event occuring immediately before or during labour e.g. uterine rupture, placental abruption, cord prolapse etc.
(iv) A sudden and sustained fetal bradycardia or the absence of fetal heart rate variability in the presence of persistent late or persistent variable decelerations on cardiotocography, usually after a hypoxic sentinel event when the pattern was previously normal.
(v) Apgar scores of 0-3 beyond 5 minutes.
(vi) Onset of multisystem involvement within 72 hours of birth.
(vii) Early imaging study showing evidence of acute non-focal cerebral abnormality.
(viii) Exclusion of other identifiable aetiologies e.g. trauma, coagulation disorders, infection or genetic disorders.

TH has been found to be protective in those infants presenting with moderate or severe HIE by inhibiting various events in this cascade of HIE injury. Major randomized clinical trials[3-5] involving induced neonatal hypothermia have demonstrated a reduction in death and disability.[6-8] These trials have shown improved outcomes for babies with HIE if they are cooled within six hours of birth to a targeted core body temperature of between 33°C to 34°C for a duration of 72 hours. Rewarming to normothermic temperature occurs over a 6-12 hour period. TH is considered to be the standard of care for infants with moderate-to-severe HIE who meet inclusion criteria.

The inclusion criteria for TH are;

- >36 weeks completed gestation with a weight ≥ 1800grams.
- Acidosis (pH<7.0) present in the umbilical cord, or any blood sample taken within 60 minutes of birth.
- Base deficit ≥ -16.0 mmol/L in umbilical cord or any blood sample taken within 60 minutes of birth.
- History of acute perinatal event (such as but not limited to cord prolapse, placental abruption or uterine rupture).
- Apgar score ≤5 at 10 minutes or at least 10 minutes of positive-pressure ventilation.
- Evidence of moderate-to-severe encephalopathy, demonstrated by the presence of seizures OR at least one sign in three or more of the six categories shown In the Modified Sarnat Table (see Table 35).

Main Findings

The following analysis is based on 140 infants who underwent neonatal therapeutic hypothermia treatment in 2016-2017.

Maternal Characteristics

Age

The age of mothers whose infants underwent therapeutic hypothermia was known for all 140 mothers in the years, 2016 and 2017. The mothers whose infants underwent therapeutic hypothermia ranged in age from teenage years (the youngest 18 years of age) through to early-forties (43 years of age). Their age distribution broadly reflected that of the population of mothers who gave birth in Ireland in 2016 (Table 1). There was a higher proportion of mothers aged 20-24 years (11.4%) whose babies were cooled, than of mothers who gave birth in 2016 (7.9%). Over half of the population (52.3%) who gave birth in 2016 were aged 25-34 years, whereas a slightly lower proportion of mothers whose infants underwent therapeutic hypothermia were in this age group (50.7%).

Table 1: Age distribution of mothers whose infants underwent therapeutic hypothermia in 2016 or 2017 versus all births in 2016

Age group	TH cases N=140 2016/2017	All births[9] N=64,133 2016
<20yrs	1(0.7)	1.7%
20-24yrs	16(11.4)	7.9%
25-29yrs	24(17.1)	17.3%
30-34yrs	47(33.6)	35.0%
35-39yrs	43(30.7)	28.6%
≥40yrs	9(6.4)	6.7%

Note: Values are shown as N(%) unless otherwise stated.

Ethnicity

Assessment of risk associated with ethnic group is impeded by the absence of national data on ethnicity for the pregnant population in Ireland. The majority of mothers whose infants underwent therapeutic hypothermia were of white Irish ethnicity (76.1%) (Table 2). This is similar to the proportion of white Irish women in the female population aged 15-49 years enumerated by the National Census 2016. While the numbers involved were small, Irish Traveller and Asian ethnicities were overrepresented in the mothers whose infants underwent therapeutic hypothermia in 2016 or 2017 (6.5%) compared to 3.6% of the female 15-49-year-old population in 2016.

Table 2: Ethnicity of mothers whose infants underwent therapeutic hypothermia in 2016 or 2017 versus 15-49 year-old female population, 2016

Ethnicity	TH cases N=138* 2016/2017	15-49 year-old female population, 2016** (%)
White Irish	105(76.1)	79.2
Irish Traveller	2(1.4)	0.7
Other white background	20(14.5)	13.7
Asian/Asian Irish	7(5.1)	2.9
Black/Black Irish	4(2.9)	1.7
Other/mixed	0(0.0)	1.9

Note: Values are shown as N(%) unless otherwise stated.
*Ethnicity unknown for two mothers. **Population data from the National Census 2016.

Occupation

Table 3 provides a high-level overview of the data that were provided on mother's occupation, alongside data available for the most comparable occupation categories for mothers of all births in Ireland9 and for the 15-44 year-old female population from the National Census 2016. Employment status was specified for 84.3% of the mothers for whom data were recorded (Table 3). It can be seen that unemployed status was recorded for 9.3% of the mothers whose infants underwent therapeutic hypothermia compared to 4.5% of all mothers and 8.2% of the female population aged 15-44 years. The proportion of mothers engaged in home duties whose infants underwent therapeutic hypothermia (7.6%) was lower than the percentage of all women engaged in home duties who gave birth (20.5%) in 2016 but was similar to the proportion of females aged 15-49 years in the Irish population.

Table 3: Occupation at booking of mothers whose infants underwent therapeutic hypothermia in 2016 or 2017 versus all births in 2016 and 15-44 year-old female population in 2016

Occupation	TH cases N=118* 2016/2017	All births[9] 2016 (%)	15-44 year-old female population, 2016* (%)
Employed	91(77.1)	73.1	57.8
Unemployed	11(9.3)	4.5	8.2
Home duties	9(7.6)	20.5	10.4
Student	7(5.9)	n/a	21.1
Others not in labour force	0(0.0)	n/a	2.5

Note: *Data not known on employment for 22 mothers. **Population data from Census 2016.

Body Mass Index

Body mass index (BMI) was available for 134 of the 140 of women whose infants underwent therapeutic hypothermia in 2016 or 2017 (Table 4). The pattern of BMI in the mothers was similar to that in the women from the general population who participated in the 2015 Healthy Ireland Survey[10]. The BMI of 25.4% of these mothers was in the obese range (≥30.0kgm^{-2}) which is slightly higher compared to women from the general population.

Table 4: Body mass index of mothers whose infants underwent therapeutic hypothermia in 2016 or 2017 versus female participants in the Healthy Ireland Survey in 2015

BMI Category (kg/m²)	TH cases N=134* 2016/2017	Healthy Ireland Survey 2015[10]
Underweight (<18.5)	3(2.2)	3%
Healthy (18.5-24.9)	55(41.0)	44%
Overweight (25.0-29.9)	42(31.3)	31%
Obese (≥30.0)	34(25.4)	22%

Note: Values are shown as N(%) unless otherwise stated. *BMI value missing for six mothers.

Smoking and substance abuse

Smoking status of the mothers at their time of booking was recorded for 137 (97.9%) of the 140 women. Of these, 10 (7.3%) were smokers at the time of booking. Information on smoking was available for eight of the ten smokers (80.0%). Six women were smoking between 1 and 9 cigarettes per day (n=6 of 8, 75.0%) and two were smoking 10 or more cigarettes per day (n=2 of 8, 25%). Of the eight women who were smoking at booking, three (37.5%) stopped smoking during pregnancy. There were no pregnancies with a documented history of alcohol abuse but one woman had a documented history of drug abuse.

Previous pregnancy

In terms of parity of women who delivered infants requiring therapeutic hypothermia in 2016 and 2017, there was an overrepresentation of women who had not previously delivered (60.0%) compared to the general population of women who gave birth in 2016 (38.2%; Table 5).

Table 5: Distribution of parity, 2016-2017

Parity	TH cases N=140 2016/2017	All births[9] 2016 (%)
Nulliparous	84(60.0)	38.2
Para 1	34(24.3)	34.9
Para 2	13(9.3)	17.9
Para 3+	9(6.4)	9.0

Note: Values are shown as N(%) unless otherwise stated.

Over half of mothers whose infants underwent therapeutic hypothermia in 2016 or 2017 had at least one previous pregnancy (gravida > 0; 75 of 140, 53.6%). Table 6 specifies gravida/parity for 139 of the 140 women whose infants underwent neonatal therapeutic hypothermia in 2016 or 2017. Nearly half (n=65, 46.8%) had never been pregnant before (gravida = 0). Of the 74 women who had been pregnant (gravida > 0), 40.5% (n=30) had pregnancies exceeding 24 weeks or 500g birthweight (gravida = parity, indicated by green shading). Over one third of these 74 mothers (n=25, 33.8%) experienced at least one pregnancy exceeding 24 weeks or 500g birthweight and at least one pregnancy less than 24 weeks gestation and under 500g birthweight (gravida > parity > 0, indicated by yellow shading). Additionally, one quarter (25.7%, n=19) of these women's previous pregnancies never exceeded 24 weeks gestation or 500g birthweight (gravida > parity = 0, indicated by orange shading).

Table 6: Gravida/parity of mothers whose infants underwent therapeutic hypothermia in 2016 or 2017

GRAVIDA	PARITY										
	0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**Total**
0	65	0	0	0	0	0	0	0	0	0	**65**
1	14	19	0	0	0	0	0	0	0	0	**33**
2	2	11	8	0	0	0	0	0	0	0	**21**
3	3	2	3	0	0	0	0	0	0	0	**8**
4	0	0	2	0	1	0	0	0	0	0	**3**
5	0	0	0	1	2	0	0	0	0	0	**3**
6	0	1	0	1	1	0	1	0	0	0	**4**
7	0	0	0	0	0	0	0	0	0	0	**0**
8	0	0	0	0	0	0	0	0	0	0	**0**
9	0	0	0	0	0	0	0	1	0	1	**2**
10	0	0	0	0	0	0	0	0	0	0	**0**
11	0	0	0	0	0	0	0	0	0	0	**0**
Total	**84**	**33**	**13**	**2**	**4**	**0**	**1**	**1**	**0**	**1**	**139**

Note: We refer to gravida and parity prior to the pregnancy associated neonatal therapeutic hypothermia. Green represents women with previous pregnancies that were all ≥24 weeks or ≥500g; yellow represents women who had experienced pregnancy ≥24 weeks or ≥500g and also pregnancy <24 weeks and <500g; and orange represents women whose previous pregnancies were always <24 weeks gestation and <500g birthweight.

Of the 75 women who had a previous pregnancy, 37.3% (n=28) were reported to have had a previous pregnancy-related problem (undocumented for 7 women). Caesarean section delivery was the most common previous pregnancy-related problem with nearly twenty percent of mothers (n=14, 18.7%) having a previous caesarean section delivery (Table 7). Three or more miscarriages was the second most common, with 6.7% (n=5) of mothers experiencing this in a previous pregnancy. Infant requiring intensive care (n=3, 4.0%) was the third most common pregnancy-related problem in mothers who had a previous pregnancy. None of the mothers had an infant with HIE in a previous pregnancy.

Table 7: Previous pregnancy-related problems in mothers whose infants underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/2017 N=75
Previous caesarean delivery	14(18.7)
Three or more miscarriages	5(6.7)
Infant requiring intensive care	3(4.0)
Pre-term birth or mid-trimester loss	3(4.0)
Neonatal death	2(2.7)
Pre-eclampsia	2(2.7)
Stillbirth	2(2.7)
Other	1(1.3)
Infant with congenital anomaly	0(0)
Placenta praevia	0(0)
Post-partum haemorrhage requiring transfusion	0(0)
Previous infant with HIE	0(0)

Note: Percentage relates to total number of mothers who had a previous pregnancy (n=75). Categories are not mutually exclusive. Values are shown as N(%) unless otherwise stated.

Pre-existing medical problems

One in three of the women, whose infants underwent therapeutic hypothermia in 2016 or 2017, had a pre-existing medical problem (n=43, 30.7%). Thirty-two of the 140 women were taking prescribed medication during the pregnancy (22.9%). Four mothers had a documented family history of conditions which can affect newborn infants (2.9%, n=4). The most common type of pre-existing medical problems were the Endocrine disorders, with 7.1% of mothers (n=10) suffering from conditions of this type (Table 8). Psychiatric disorders had the second highest percentage of occurrence (5.0%, n=7). Asthma was also common among women (5.0%, n=7).

Table 8: Pre-existing medical problems in mothers whose infants underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/2017 N=140
Endocrine disorder	10(7.1)
Psychiatric disorder	7(5.0)
Asthma	7(5.0)
Hypertension	4(2.9)
Haematological disorder	3(2.1)
Diabetes	2(1.4)
Cardiac disease	1(0.7)
Inflammatory disorder	1(0.7)
Renal disease	0(0)
Epilepsy	0(0)
Other	18(12.9)

Note: Percentage relates to total number of mothers (n=140). Categories are not mutually exclusive.

Antenatal care

Fertility treatment

Currently in Ireland there is no national data on the number of births as a result of fertility treatment. Information was available for 137 of the 140 (97.9%) whose infants underwent therapeutic hypothermia in 2016 or 2017. In nine of these cases (6.6%) the pregnancy was reported to be the result of fertility treatment. In vitro fertilisation was the method of fertility treatment specified for all nine pregnancies.

During this pregnancy, the majority of the 140 women intended on delivering in an obstetric unit (99.3%; n=139) with obstetric-led care (96.4%; n=135). One-quarter of women had an antenatal ultrasound scan before 12 weeks gestation (27.1%; n=38) and two thirds of the women had a scan between 12 and 19 weeks gestation (67.1%; n=94). Gestation at booking was unknown for four women (Table 9). Estimated date of delivery (EDD) was documented for 139 of the 140 women. EDD was calculated using ultrasound scan in the majority of cases (91.4%; 127 of 139).

Table 9: Timing of antenatal hospital booking appointment for mothers whose infants underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/2017 N=140
Less than 12 weeks	38(27.1)
12-19 weeks	94(67.1)
20 weeks of later	4(2.9)
Unknown	4(2.9)

Note: Values are shown as N(%) unless otherwise stated.

Gestation at last antenatal hospital visit

Information on the last antenatal visit was available for 136 of the 140 women whose infants underwent therapeutic hypothermia in 2016 or 2017 (97.1%). These 136 women last attended the hospital clinic between 32 and 41 weeks. Almost 90% attended at 36 weeks or later (88.2%, n=120) with 11.8% (n=16) last attending the hospital before the last routine preterm antenatal clinic visit at 36 weeks gestation (Figure 1).

Of the 140 women, two (1.4%) were transferred from another maternity unit with the fetus in utero at 35 and 40 gestational weeks respectively.

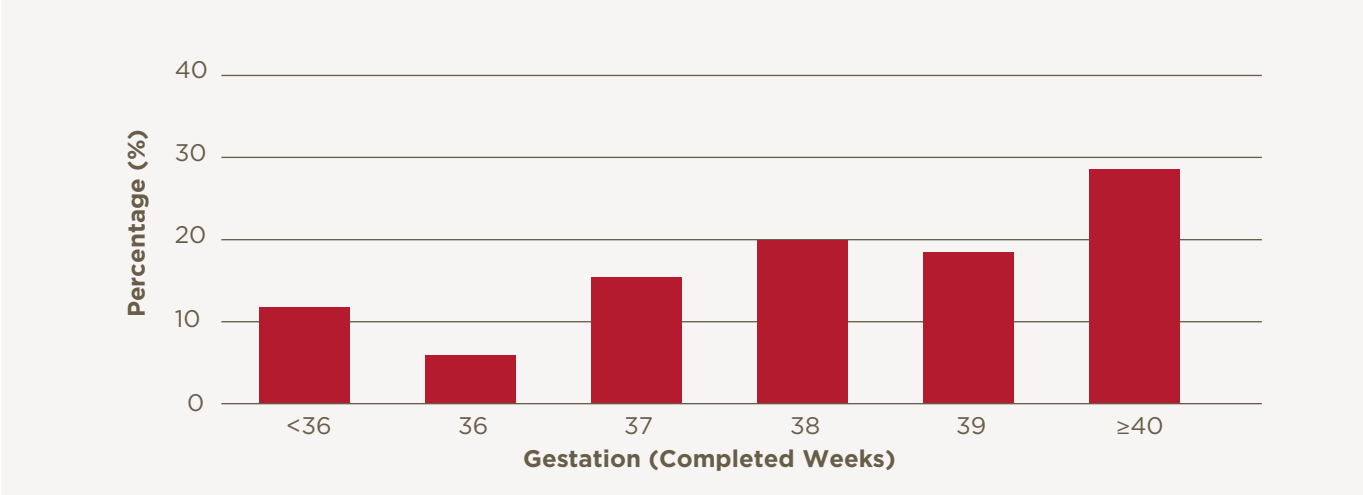

Figure 1: Weeks gestation at last antenatal visit, 2016/2017

Concern documented during pregnancy

Of the 140, there were concerns documented during the pregnancy for 53 of the mothers whose infants underwent therapeutic hypothermia in 2016 or 2017. The most common concern documented was women who developed hypertensive disorders during pregnancy with 9.3% of mothers (n=13) suffering from conditions of this type. This was followed by gestational diabetes mellitus which had second the highest percentage of occurrence (7.8%, n=11). Polyhydramnios was also common occurring in 6.4% (n=9) of these pregnancies.

Labour

Information on the onset of labour was available for all 140 women whose infants underwent therapeutic hypothermia (100%). Almost half of the women laboured spontaneously (49.3%; n=69), over a third of women were induced (34.3%; n=48) and 16.4% of women were never in labour (Table 10). Nulliparous women were twice as likely to be induced as parous women. Parous women were four times more likely never to labour than nulliparous women. Almost half of the women who laboured spontaneously had their labour accelerated (43.5%; n=30 of 69) either by artificial rupture of membranes (ARM; 56.7%, n=17 of 30) or syntocinin (43.3%; n=13 of 30). As indicated in Table 11, nulliparous women were much more likely to have their labour accelerated with syntocinin than parous women (66.7% versus 8.3%).

Table 10: Onset of labour for mothers whose infants underwent therapeutic hypothermia in 2016 or 2017

	Total N=140	Nulliparous N=65	Parous N=75
Spontaneous	69(49.3)	32(49.2)	37(49.3)
Induction	48(34.3)	29(44.6)	19(25.3)
Never in labour	23(16.4)	4(6.2)	19(25.3)

Note: Values are shown as N(%) unless otherwise stated.

Table 11: Method of acceleration for mothers who laboured spontaneously

	Total N=30	Nulliparous N=18	Parous N=12
ARM	17(56.7)	6(33.3)	11(91.7)
Syntocinin	13(43.3)	12(66.7)	1(8.3)

Note: Values are shown as N(%) unless otherwise stated.

As outlined in Table 12, liquor was clear in 68 of the 111 documented cases (61.3%). A quarter of women had meconium stained liquor (27.9%; n=31). The grade of meconium was specified for 24 of the 31 of these cases (77.4%) with 50% (n=12) of women having Grade 1, 41.7% (n=10) of women having Grade 2 and the remaining two women having Grade 3 (8.3%).

Table 12: Liquor colour

	TH cases 2016/2017 N=111
Clear	68(61.3)
Meconium	31(27.9)
Other	12(10.8)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive.

There was a documented reason for induction for 44 of the 48 women who were induced. As indicated in Table 13, the common reasons to induce labour were associated with post maturity (20.5%; n=9), reduced fetal movement (13.6%; n=6), hypertensive disorders (11.4%; n=5) and polyhydramnios (11.4%; n=5). Under the "Other" category a wide range of indications were captured including, but not limited to, fetal tachycardia, cardiotocograph traces (CTG) not meeting reassuring criteria, twins, antepartum bleeding and oligohydramnios.

Table 13: Reason for induction of mothers whose infants underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/2017 N=44
Post maturity	9(20.5)
Reduced Fetal Movements (RFM)	6(13.6)
Hypertensive disorders	5(11.4)
Polyhydramnios	5(11.4)
Large for dates	4(9.1)
IUGR/Small for dates	3(6.8)
Cholestasis	2(4.5)
Prolonged SROM	2(4.5)
Other	12(27.3)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive.

The method of induction was known for 47 of the 48 women who were induced (97.9%). The majority of women had their labour induced using multiple methods of induction (72.3%; 34 of 47). As illustrated in Table 14, the most common method of induction was the use of oxytocin (61.7%; n=29), followed by ARM (57.4%; n=27) and half of women had their labour induced with prostin (51.1%; n=24).

Table 14: Method of induction for mothers whose infants underwent therapeutic hypothermia in 2016 or 2017

	Total N=47	Nulliparous N=29	Parous N=18
Oxytocin	29(55.3)	18(62.1)	11(61.1)
Artificial rupture of membranes	27(57.4)	16(55.2)	11(61.1)
Prostin	24(51.1)	16(55.2)	8(44.4)
Propress	13(27.7)	9(31.0)	4(22.2)
Other	1(2.1)	1(3.4)	0(0)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive.

Fetal heart monitoring was undertaken for 110 of the 140 women whose infants underwent therapeutic hypothermia (78.6%). The method of fetal heart monitoring was documented for 108 of the 110 women (98.2%). As illustrated in Table 15, external continuous fetal heart monitoring was the most common method of monitoring used during labour (79.6%; n=86 of 108). Four women who had external continuous fetal heart monitoring also had internal continuous fetal heart monitoring undertaken (4.7%; n=4 of 86). A third of women were had external intermittent fetal heart monitoring (37.0%; n=40 of 108). Of these women, almost half also had external continuous fetal heart monitoring undertaken during labour (47.5%; n=19 of 40).

Table 15: Method of fetal heart monitoring for infants who underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/2017 N=108*
External continuous	86(79.6)
External intermittent	40(37.0)
Internal continuous	4(3.7)

Note: Values are shown as N(%) unless otherwise stated. *Data on fetal heart monitoring was missing for two women. Categories are not mutually exclusive.

Data on CTG were available for 104 of the 140 cases (74.3%). Of these 104, almost half were interpreted as suspicious (44.2%; n=46) and pathological in a quarter of cases (26.9%; n=28). A fetal blood sample was taken for 21 of the 140 infants underwent therapeutic hypothermia in 2016 or 2017 (15.0%). Fetal blood samples were more likely to be taken for infants with a suspicious CTG (21.7%; n=10 of 46) or a pathological CTG (28.6%; n=8 of 28) compared to those with a normal CTG (11.5%; n=3 of 26). All infants had a pH greater than 7.0 (Range: 7.1-7.5) from the initial fetal blood sample and the median base deficit was 2.7 (Range: 0.50-28.5).

Delivery

The type of care received at delivery was known for all mothers whose infants underwent therapeutic hypothermia (n=140). The vast majority of the infants (97.1%; n=136) were delivered under obstetric-led care which is the predominant model of care in Ireland. One baby was delivered at home under midwifery-led care, one baby was born in a general hospital and two babies were born before arrival at the maternity unit.

Presentation at delivery was known for 95.0% of mothers whose infants underwent therapeutic hypothermia (n=133 of 140). The majority of presentations at delivery were vertex presentations (n=123 of 133, 92.5%) and in ten cases, the presentation was breech (n=10 of 133, 7.5%). Mode of delivery was known for all mothers (n=140) whose infants underwent therapeutic hypothermia (Table 16). A third of the deliveries were instrumental (31.4%, n=43). Of the women who had an instrumental delivery, 14 mothers who had a ventouse delivery also had a forceps delivery. The interval time from decision to the instrumental delivery was known in 41 of the mothers. The median interval time to delivery was 16 minutes and ranged from two to 85 minutes.

Infants whose CTG was interpreted as suspicious or pathological were more likely to have an operative birth rather than a spontaneous vaginal delivery. Approximately twenty percent of infants had a spontaneous vaginal delivery (22.1%, n=31), which is considerably lower than the proportion of vaginal deliveries of all births occurring in 2016 (52.2%).

Caesarean section was the most common mode of delivery for all 140 of these infants (47.1%, n=66), with a small percentage more of caesarean sections happening after the onset of labour (53.0%, n=35 of 66) rather than pre-labour (47.0%, n=31 of 66). Two of mothers whose infants underwent therapeutic hypothermia in 2016 or 2017 had an elective caesarean section (1.4%). Three mothers had a caesarean section following a failed instrumental delivery. Emergency caesarean section delivery was the most common type of caesarean section delivery, accounting for 89.4% of cases where the infant was delivered by caesarean section (n=59 of 66).

Table 16: Mode of delivery for mothers whose infants underwent therapeutic hypothermia in 2016 or 2017

TH cases 2016/2017 N=140		All births 2016[1]	
Spontaneous Vaginal Cephalic Spontaneous Vaginal Breech	31(22.1) 0(0)	Vaginal birth[+]	52.2%
Pre-labour Caesarean Section Caesarean Section*	31(22.1) 35(25.0)	Caesarean section[++]	32.6%
Assisted breech	0(0)	Assisted breech	0.5%
Ventouse**	41(29.3)	Ventouse	11.1%
Forceps	19(13.6)	Forceps	3.6%

Note: Values are N(%) unless otherwise stated. Categories are not mutually exclusive.

[+]Vaginal births in this category include women who had both a Spontaneous Vaginal Cephalic and a Spontaneous Vaginal Breech delivery.

[++]Caesarean section in this category include women who had a pre-labour caesarean section as well as women who had a caesarean section after the onset of labour.

*Three mothers had a caesarean section following failed instrumental deliveries.

**14 mothers who had a ventouse delivery, also had a forceps delivery.

Other incidences at birth and following delivery

As outlined in Table 17, 18.6% of women whose infants underwent therapeutic hypothermia experienced maternal pyrexia during labour (n=26). One in ten women had a prolonged rupture of membranes (10%, n=14).

Table 17: Other incidences at the birth of infants who underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/2017 N=140
Maternal pyrexia in labour	26(18.6)
Shoulder dystocia	18(12.9)
Prolonged rupture of membranes	14(10.0)
Subgaleal haematoma	3(2.1)
Spontaneous premature labour	1(0.7)
Birth trauma	1(0.7)
Fracture	0(0)
Premature rupture of membranes	0(0)
Other	20(14.3)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive.

Uterine rupture

Over the two year period, there were five reported cases of uterine rupture which equates to a rate of 37.5 per 1,000 within this cohort. This rate is significantly higher than the incidence of uterine rupture in the Irish general population which has consistently been reported at 0.14 per 1,000 maternities since 2011[11]. All five women who experienced uterine rupture were parous. One woman was reported to have had a caesarean section in a previous pregnancy. Two of the women had an elective caesarean section in this pregnancy, with three women having a caesarean section after the onset of labour. The birth weight for these infants ranged from 2820 grams to 4260 grams.

Shoulder dystocia infants

During delivery of the 140 infants, there were 18 reported incidents of shoulder dystocia (12.9%). This rate is 9 times higher than that which is reported for all deliveries (1.4%) in high-income countries[12]. Of 18 reported incidents of shoulder dystocia, three-quarters of the women were nulliparous (77.8%; n=14 of 18). Eight of these 18 women had an induction of labour (Table 18) and seven of the women who laboured spontaneously had their labour accelerated.

Of the 18 women, 14 of the women had an instrumental delivery (77.8%; n=14 of 18). The median interval time between decision and delivery was 21.5 minutes, ranging from 13 to 35 minutes. Of the 14 women who had an instrumental delivery, nine women (64.3%; n=9 of 14) had their birth assisted with ventouse, with three women (21.4%; n=3 of 14) having a combination of ventouse and forceps.

The most common manoeuvre utilised for all deliveries was a combination of McRoberts and Suprapubric pressure (55.6%; n=10 of 18). The birth weight for these infants ranged from 3,040 grams to 5,340 grams, with a third of these infants (38.9%; n=7 of 18) weighing 4,000-4,499 grams.

Table 18: Maternal and Infants characteristics for deliveries with a reported shoulder dystocia

	Shoulder dystocia cases N=18 2016/2017
Age Group	
<30yrs	5(27.8)
30-34yrs	7(38.9)
35-39yrs	6(33.3)
BMI Category (kg/m²)	
Underweight (<18.5)	0(0)
Healthy (18.5-24.9)	5(27.8)
Overweight (25.0-29.9)	9(50.0)
Obese (>30.0)	4(22.2)
Parity	
Nulliparous	14(77.8)
Parous	4(22.2)
Induction of labour	8(44.4)
Mode of delivery	
Spontaneous Vaginal Cephalic	4(22.2)
Instrumental	14(77.8)
Manoeuvres	
McRoberts	3(16.7)
McRoberts and Suprapubic pressure	10(55.6)
Other	5(27.8)
Birthweight (grams)	
3000-3499	4(22.2)
3500-3999	5(27.8)
4000-4499	7(38.9)
>4500	2(11.1)

Note: Values are shown as N(%) unless otherwise stated.

Infant characteristics

Over half of the infants who received therapeutic hypothermia were male (57.1%; n=80). In the overall population of births in 2016, 51.3% were male and 48.7% female (Table 19). There were six infants who underwent therapeutic hypothermia from multiple births (4.3%). This is similar to the proportion of multiples among all births in 2016 (3.8%).[9]

Table 19: Sex of infants who underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/2017 N=140	All births[9]
Male	80(57.1)	51.3%
Female	60(42.9)	48.7%

Note: Values are shown as N(%) unless otherwise stated.

Gestation at delivery

Figure 2 outlines the gestational age at delivery for infants who underwent therapeutic hypothermia in 2016 or 2017 versus all infants born in 2016. The majority of infants were born between 36 and 41 completed weeks gestation (88.6%; n=124). Seven infants were born between 32 and 35 completed weeks (5.0%), these seven infants had a birthweight greater than 1,800 grams.

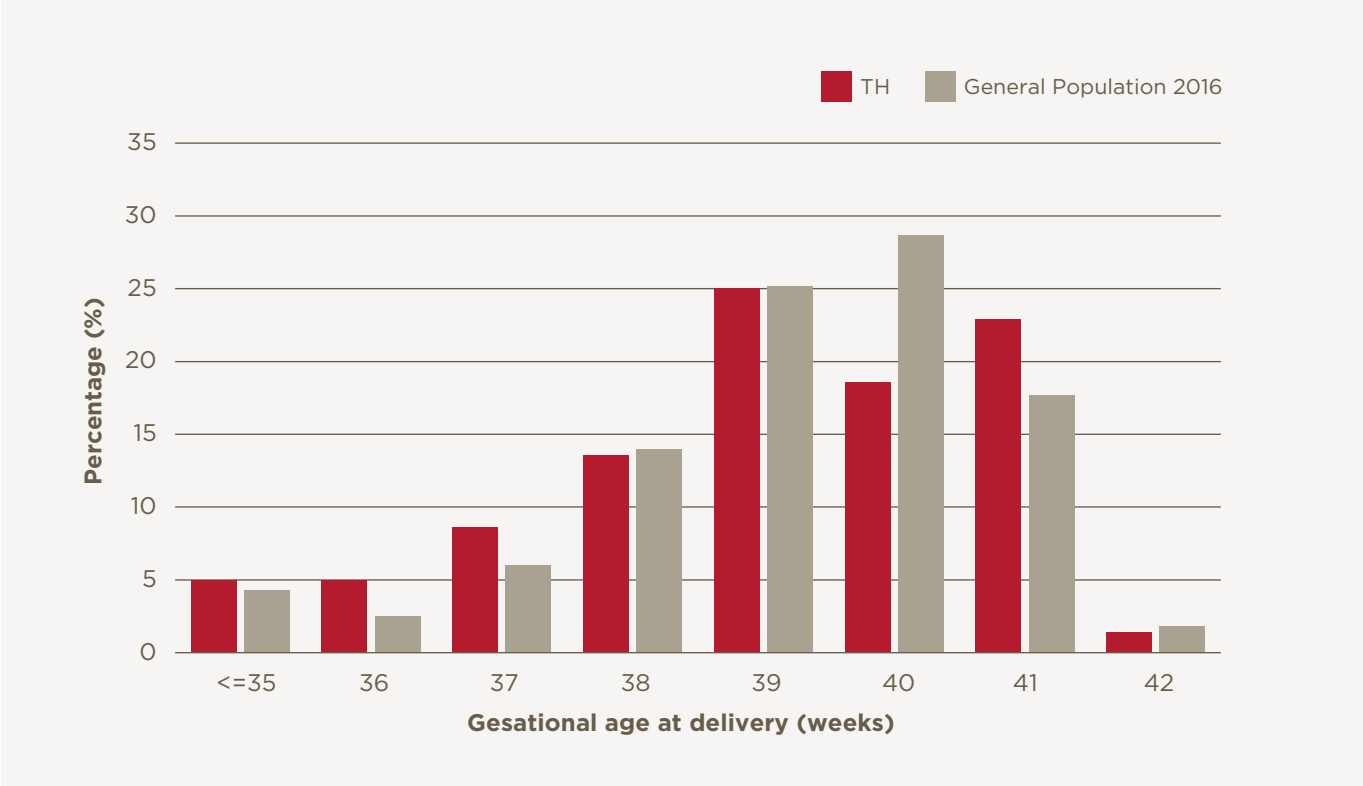

Figure 2: Gestational age at delivery (weeks) for infants who underwent therapeutic hypothermia in 2016 or 2017 versus all infants born in 2016

Birthweight at delivery

The mean birthweight for infants who underwent neonatal therapeutic hypothermia in 2016 or 2017 was 3,396 grams (Standard Deviation: 637). The birth weight ranged from 1,810 grams to 5,340 grams. As outlined in Figure 3, almost a third of infants weighed 3,000-3,499 grams (29.3%, n=41). Almost half of infants weighed 3,500 grams or more (45.0%, n=63). A small proportion of infants weighed between 1,800 and 2,499 grams (7.9%, n=11).

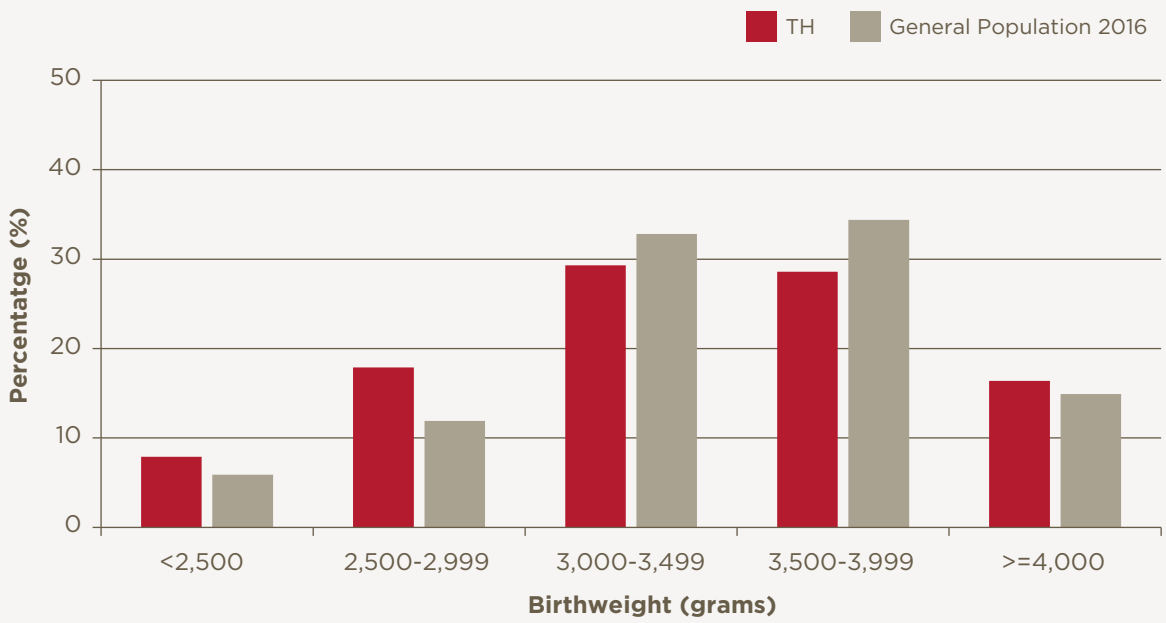

Figure 3: Distribution of birthweight for infants who underwent therapeutic hypothermia in 2016 or 2017 versus all infants born in 2016

Birthweight Centiles

Gestation Related Optimal Weight (GROW) software and coefficients derived from the multiple regression analysis of data on 11,072 births in six maternity units in Dublin, Galway, Limerick and Belfast in 2008-2009[13], was used to produce Figure 4, which illustrates the fetal growth in utero of the infants who underwent neonatal therapeutic hypothermia in 2016 or 2017.

The optimal weight and normal range for all gestations are plotted with the actual birthweights of the infants in Figure 5. For these infants, it can also be seen in Table 20, almost one in five infants were below the lower limit of the normal range (10th centile).

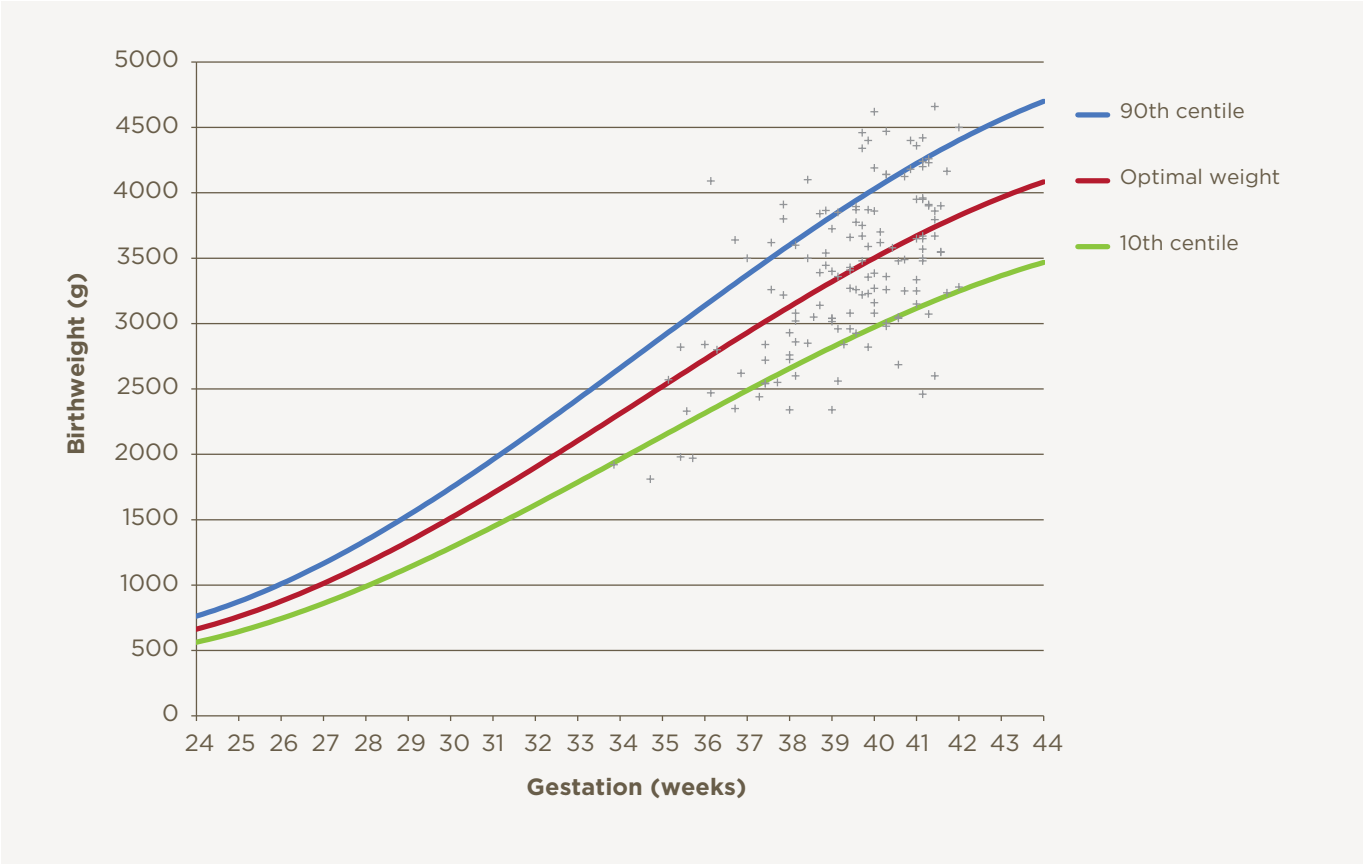

Figure 4: Optimal birthweight and normal range compared to actual birthweights for infants who underwent therapeutic hypothermia in 2016 or 2017

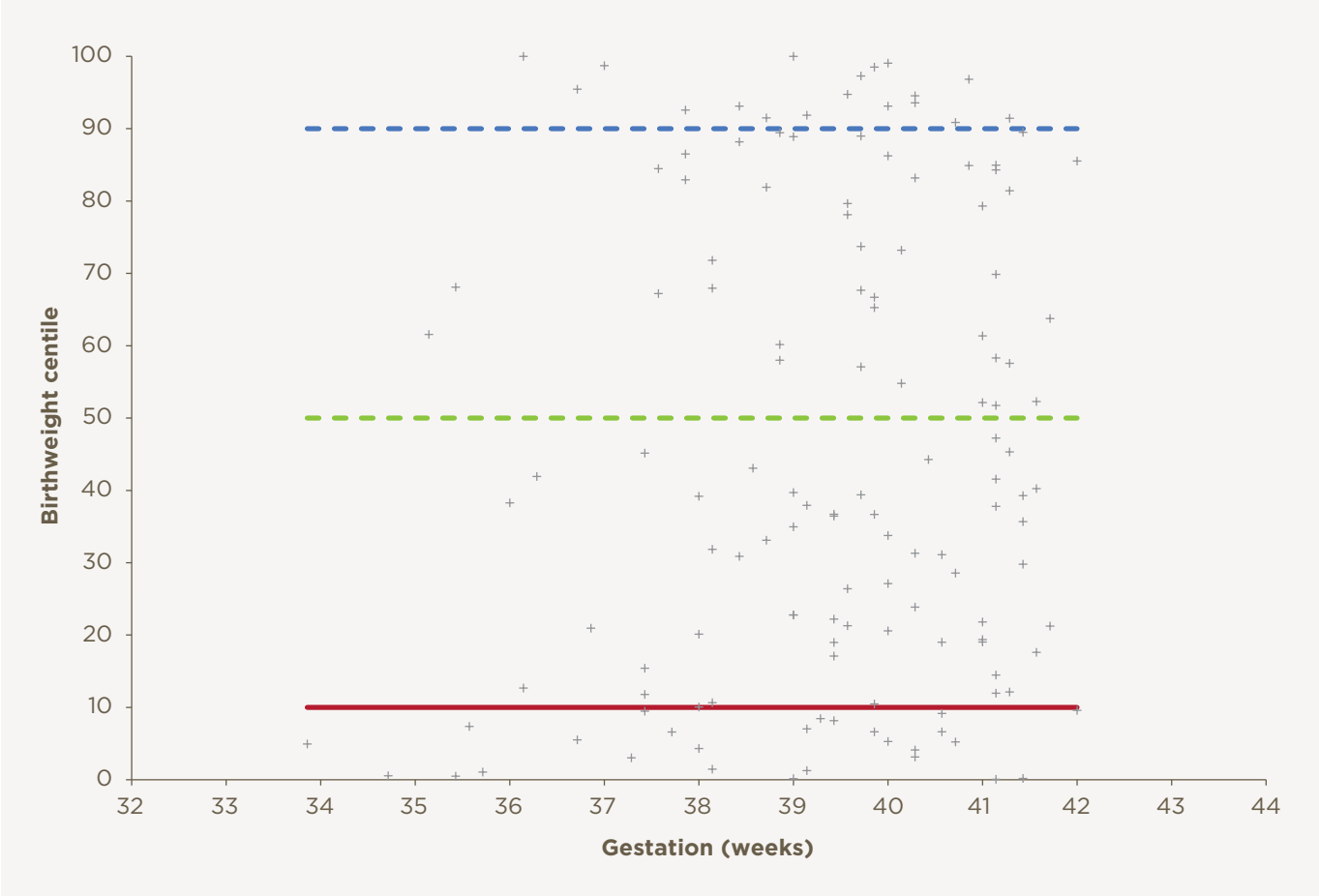

Figure 5: Distribution of customised birthweight centiles for infants who underwent therapeutic hypothermia in 2016 or 2017

When examined by birth weight centile category the distribution of the TH cohort was broadly similar to that expected but there was some evidence of poor fetal growth. Almost 20% of the infants (n=26, 18.6%) were below the 10th centile.

Table 20: Birth weight centiles for infants who underwent therapeutic hypothermia in 2016 or 2017

Centiles	TH cases 2016/2017 N=140
<3rd	8(5.7)
3rd to 9th	18(12.9)
10-49th	55(39.3)
50-89th	41(29.3)
≥90th	18(12.9)

Note: Values are shown as N(%) unless otherwise stated.

Diagnosis of fetal growth restriction (FGR)

Data on diagnosis of FGR were recorded for 137 of the 140 infants that underwent therapeutic hypothermia (97.9%). A diagnosis of FGR was reported for 11 (8.0%) of the 137 infants (Table 21). An antenatal diagnosis of FGR (as opposed to diagnosis based on observation at delivery or post-mortem) was reported for 6 of the 11 infants (54.5%).

Table 21: Diagnosis of fetal growth restriction for infants who underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/2017 N=137
No diagnosis documented	126(92.0)
Diagnosis of fetal growth restriction	11(8.0)
Fetal growth restriction suspected antenatally	6 of 11(54.5)

Note: Values are shown as N(%) unless otherwise stated.

Resuscitation

Neonatal or paediatric support was called prior to the delivery of the majority of cases (80.7%; n=113 of 140). As outlined in Table 22, a Registrar was present at the vast majority of births (93.5%; n=129 of 138; data missing for two infants). A Senior House Officer (SHO) was also present at the majority of births (84.1%); n=116. A Neonatal Nurse was present at almost half of births (42.8%; n=59) with a Midwife present for one in four births (23.9%; n=33). A Consultant was present for a third of births (34.8%; n=48).

Table 22: Who was present at the birth of infants who underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/17 N=138*
Consultant(Neonatology/Paediatrics)	48(34.8)
Registrar	129(93.5)
Senior House Officer	116(84.1)
Neonatal Nurse	59(42.8)
Midwife	33(23.9)

Note: Values are shown as N(%) unless otherwise stated. *Data missing for two infants.

As indicated in Table 23, at one minute after birth over three quarters of infants (79.7%; n=110 of 138) had an Apgar score between zero and three. At ten minutes infants with an Apgar score between zero and three had reduced to (19.7%; n=25 of 127). At twenty minutes one fifth of infants had an Apgar score of eight or greater (19.0%; n=8 of 42).

Table 23: Apgar Scores at 1, 5, 10 and 20 minutes for infants who underwent therapeutic hypothermia in 2016 or 2017

	1 minute N=138	5 minutes N=139	10 minutes N=127	20 minutes N=42
0-3	110(79.7)	57(41.0)	25(19.7)	9(21.4)
4-7	26(18.8)	73(52.5)	76(59.8)	25(59.5)
8-10	2(1.4)	9(6.5)	26(20.5)	8(19.0)

Note: Values are shown as N(%) unless otherwise stated.

Spontaneous breath was sustained by half of infants (52.9%; n=74 of 140). The age at which spontaneous breath was sustained was recorded for 58 of the 140 infants (41.4%) and began between 1 and 25 minutes (median 5 minutes).

As illustrated in Table 24, almost all infants required resuscitation (95%; n=133 of 140). Over half of the 140 infants needed intubation (59.3%; n=83) which occurred between 1 and 40 minutes (median 6 minutes). One third of infants required chest compressions (33.6%, n=47), which lasted between 1 and 25 minutes (data missing for one infant). FIO2 was required for the majority of infants (95.6%, n=129 of 135; data missing for five infants).

Table 24: Resuscitation for infants who underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/2017 N=140
Spontaneous breath taken	74(52.9)
Resuscitation required	133(95.0)
Intubation required	83(59.3)
Chest compression required	47(33.6)
FIO_2 required	129(95.6)*

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive.
*Data missing for five infants.

Table 25: Drugs or fluid treatment administered at birth for infants who underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/2017 N=140
Adrenaline	18(12.9)
Dextrose	6(4.3)
Saline	42(30.0)
O neg blood	13(9.3)
Sodium Bicarbonate	3(2.1)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive.

One of the key indicators for intrapartum asphyxia is severe metabolic acidosis evident in umbilical cord blood at delivery.[14] As outlined in Table 26, at delivery, half of infants (65.6%, n=84 of 128; data missing for 12 infants) had a pH of 7.0 or lower. The median base deficit was 11.6 (Range: 2.90-31.4) from cord blood gases and 14.5 (Range: 1.9-33.5) from initial infant blood gases.

Table 26: pH level from cord and initial infant blood gases for infants who underwent therapeutic hypothermia in 2016 or 2017

	Cord blood Gas	Initial Infant Blood Gas			
	N=128	Venous N=63	Capillary N=37	Arterial N=31	Unspecified N=9
pH level					
6.6-6.7	16(12.5)	3(4.8)	4(10.8)	3(9.7)	1(11.1)
6.71-6.8	24(18.8)	5(7.9)	3(8.1)	4(12.9)	1(11.1)
6.81-6.9	25(19.5)	10(15.9)	7(18.9)	2(6.5)	-
6.91-7.0	19(14.8)	9(14.3)	5(13.5)	3(9.7)	-
7.01-7.1	17(13.3)	13(20.6)	6(16.2)	5(16.1)	3(33.3)
7.11-7.2	15(11.7)	12(19.0)	6(16.2)	8(25.8)	1(11.1)
7.21-7.3	10(7.8)	7(11.1)	4(10.8)	5(16.1)	2(22.2)
7.31-7.4	2(1.6)	4(6.3)	2(5.4)	1(3.2)	1(11.1)

Note: Values are shown as N(%) unless otherwise stated.

Assessment for Therapeutic Hypothermia

All 140 infants met one or more criteria for therapeutic hypothermia (Table 27). Three quarters of the women (76.4%), whose infants underwent therapeutic hypothermia, experienced an acute perinatal event. Almost half of infants experienced variable and/or late foetal heart rate decelerations during labour (45.7%; n=64).

Table 27: Assessment for therapeutic hypothermia

	TH cases 2016/17 N=140
>36 completed weeks gestational age	**133(95.0)**
Apgar score ≤ 5 at 10 minutes	59(42.1)
Weight ≥ 1800 grams	140(100)
Continued need for PPV or Intubation at 10 mins	87(62.1)
Did an acute perinatal event occur?	**107(76.4)**
Variable / late foetal heart rate decelerations	64(45.7)
Prolapsed / ruptured / tight nuchal cord	18(12.9)
Uterine Rupture	5(3.6)
Maternal haemorrhage / placental abruption	22(15.7)
Maternal trauma	0(0.0)
Other	16(11.4)
Acidosis present in umbilical cord, or any blood sample within 60 minutes of birth	**101(72.1)**
Base Deficit >16.0 mmol/L in umbilical cord, or any blood sample, within 60 minutes of birth	**73(52.1)**

Note: Values are shown as N(%) unless otherwise stated.

The majority of the infants (83.3%, n=115 of 138; data missing for two infants) had a diagnosis of encephalopathy consisting of altered state of consciousness, (lethargy, stupor or coma). A grade of encephalopathy was assigned to 69 of the 115 infants (60.0%). Table 28 illustrates that over half of infants were graded as moderately encephalopathic during assessment for therapeutic hypothermia (56.5%; n=39).

Table 28: Grade of encephalopathy during assessment for therapeutic hypothermia

	TH cases 2016/17 N=69
Mild	11(15.9)
Moderate	39(56.5)
Severe	19(27.5)

Note: Values are shown as N(%) unless otherwise stated.

Transfer to Tertiary Unit

Half of all infants who were delivered in Ireland in 2016 were born in a tertiary unit (52%).[1] Eighty-four of the 140 infants who underwent neonatal therapeutic hypothermia in 2016 or 2017 were born in a tertiary hospital (60.0%; Table 29). Fifty-six infants required transfer to a tertiary unit for therapeutic hypothermia treatment (40.0%). The majority of infants were transferred with the National Neonatal Transport Programme (87.5%; n=49 of 56) with the remaining seven infants transferred by the Health Service Executive.

Table 29: Transfer of infants to a tertiary unit for therapeutic hypothermia treatment

	TH cases 2016/17 N=140
Inborn at tertiary unit	84(60.0)
Out-born requiring transfer	56(40.0)
Transferred by the National Neonatal Transport Programme	49 of 56(87.5)
Transferred by the Health Service Executive	7 of 56(12.5)

Note: Values are shown as N(%) unless otherwise stated.

For almost two-thirds of infants who required transfer, a call was made to the transfer team within two hours of birth (60%, n=27 of 45; missing data for 11 infants). A call was made between two and three hours for one-quarter of infants requiring transport (24.5%; n=11). Half of infants requiring transfer (44.6%; n=25 of 54; missing data for two infants) departed the referral hospital within six hours of birth (Table 30).

Table 30: Timing of departure and admission to a tertiary unit from birth to a referring hospital

	National Neonatal Transport Programme N=49	Health Service Executive N=7
Call for transport within 2 hours	27(56.3%)*	0(0)**
Departed referring unit within 6 hours	19(39.6)*	6(100)*
Admitted to tertiary unit within 6 hours	2(4.1)	5(71.4)

Note: Values are shown as N(%) unless otherwise stated.
*Missing data for one infant. **Data missing for six infants.

As illustrated in Figure 6, two-thirds of the infants transferred had a core temperature between 33°C and 34°C on departure from the referring hospital (70.5%, n=31 of 44; data missing for twelve infants) with one-quarter of infants (25.0%; n=11 of 44; data missing for twelve infants) having a core temperature ranging from 34.1°C to 36.8°C.

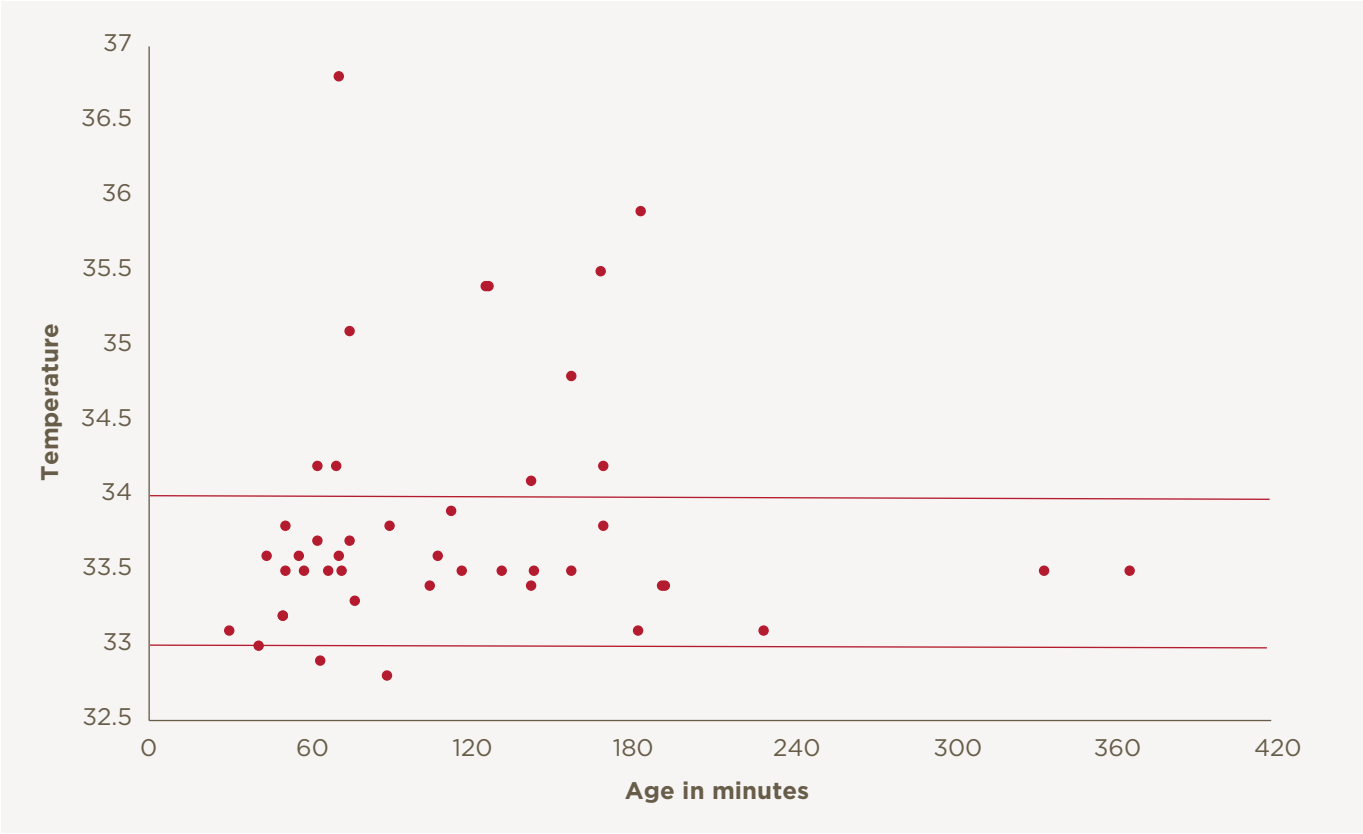

Figure 6: Temperature (°C) of infant by age (mins) on departure from referring hospital

Over two-thirds of the 56 infants transferred for neonatal therapeutic hypothermia treatment required respiratory support (71.4%; n=40) and sedation (67.9%; n=38) en-route to a tertiary unit (Table 31).

Table 31: Management during transfer of infants for therapeutic hypothermia

	NNTP N=49	HSE N=7
Respiratory support	**38(77.6)**	**2(28.6)**
Ventilation*	31 of 36(86.1)	2of 2 (100)
CPAP*	3 of 36(8.3)	-
Nasal prong O_2*	2 of 36(5.6)	-
Sedation	**36(73.5)**	**2(28.6)**
IV access	**46(93.9)**	**7(100)**
Peripheral	42 of 46(91.3)	7(100)
UVC	36 of 46(78.3)	3(42.9)
UAC	22 of 46(47.8)	2(28.6)

Note: Values are shown as N(%) unless otherwise stated. *Data missing for two infants

Eighty-seven percent of the infants requiring transfer to a tertiary unit for therapeutic hypothermia treatment were admitted more than six hours after birth (87.0%; 47 of 54; missing data for 2 infants). One third (32.1%; n=18 of 56) of the infants requiring transfer to a tertiary unit for neonatal therapeutic hypothermia treatment were admitted nine or more hours after birth.

As illustrated in Figure 7, three-quarters of infants had a core temperature between 33°C and 34°C (77.4%, n=41 of 53; data missing for three infants) on admission to a tertiary unit. While 15.1% had a core temperature ranging from 34.1°C to 36.6°C.

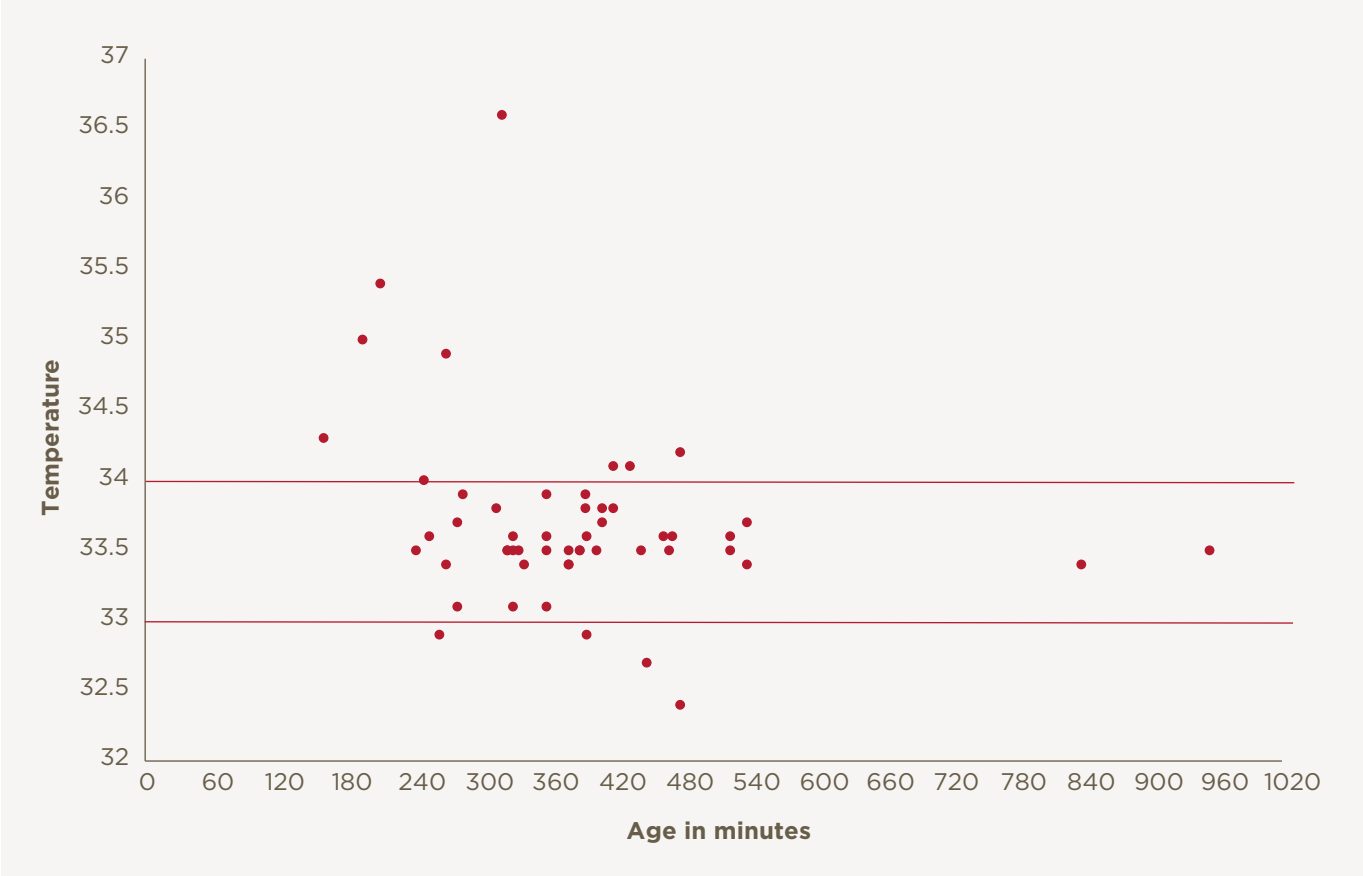

Figure 7: Temperature (°C) of infant by age (mins) on admission to a tertiary unit from a referring hospital

Treatment Days 1-3

In line with practice guidelines, therapeutic hypothermia should be started within 6 hours of birth and should be continued for 72 hours. The optimum core temperature of 33°C to 34°C is targeted over this 72 hour period. The time that the optimum core temperature was reached was recorded for 126 of the 140 infants (90.0%). Of these 78.9% of infants were reported to have achieved optimum core temperature within 6 hours of birth.

As illustrated in Figure 8, three-quarters of infants (74.5%; n=102 of 137: data missing for three infants) began therapeutic hypothermia at the optimum core temperature of 33°C to 34°C. Seven infants (5.1%, n=7 of 137) had a temperature which was below optimum as therapeutic hypothermia began, these infants had temperatures ranging from 32.4°C to 32.9°C.

Twenty eight infants (20.4%; n=28 of 137) began therapeutic hypothermia with core temperature ranging from 34.1 °C to 36.8°C. Within two hours of therapeutic hypothermia those who were above optimum temperature had reduced from 20.4% to 3.0%. No infants were above optimum temperature after 54 hours of cooling (Figure 8).

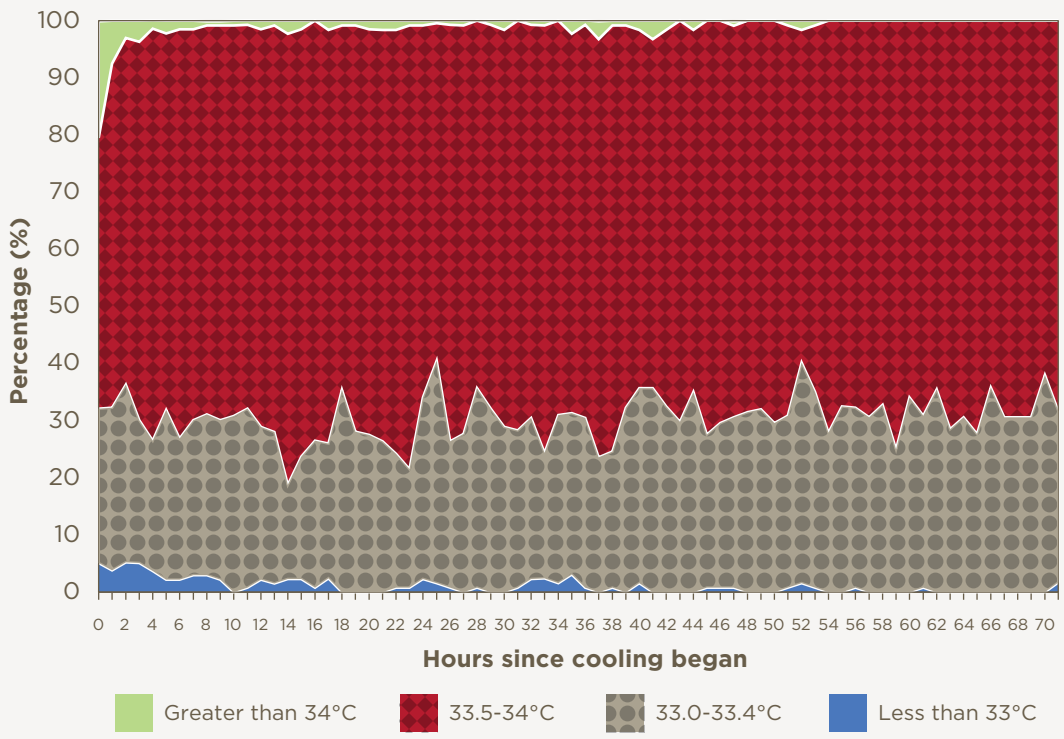

Figure 8: Percentage of infants at optimum temperature (33-34°C) over 72 hours of therapeutic hypothermia

As outlined in Table 32, almost all infants who were admitted for neonatal therapeutic hypothermia received sedation on Day 1 (98.6%; n=138 of 140), Day 2 (96.4%; n=135 of 140) and Day 3 (90.0%; n=126 of 140) of treatment. The vast majority of infants were administered antibiotics on Day 1 and Day 2 of treatment with almost half receiving antibiotics on Day 3 (47.1%; n=66).

Table 32: Drugs and Volume Replacement Day 1, 2 & 3

	Day 1 N=140	Day 2 N=140	Day 3 N=140
Sedation	138(98.6)	135(96.4)	126(90.0)
Antibiotics	134(95.7)	122(87.1)	66(47.1)
Anticonvulsants	52(37.1)	38(27.1)	25(17.9)
Inotropes	34(24.3)	25(17.9)	18(12.9)
Blood products	27(19.3)	12(8.6)	4(2.9)
Volume replacement	18(12.9)	12(8.6)	5(3.6)
Other	36(25.7)	29(20.7)	23(16.4)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive.

As outlined in Tables 33 and 34 a number of diagnostic investigations were undertaken during the 72 hours of therapeutic hypothermia treatment.

Table 33: Laboratory Parameters Day 1, 2 & 3*

	Day 1 N=140	Day 2 N=140	Day 3 N=140
Haematology	23(16.4)	5(3.5)	3(2.1)
Coagulation	12(8.6)	6(4.3)	0(0)
Biochemistry	22(15.7)	14(10.0)	9(6.4)
LP	6(4.3)	3(2.1)	1(0.7)
Metabolic Screen	8(5.7)	2(1.4)	1(0.7)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive.
*Data for laboratory tests which may have been undertaken during assessment for therapeutic hypothermia were not recorded and therefore are not presented here.

In relation to neuro imaging, 71.4% (n=100) of infants had a cranial ultrasound in the first three days of life. Eleven of these 100 infants had more than one cranial ultrasound undertaken. During the three day period, 2.1% of infants (n=3) had magnetic resonance imaging (MRI) of the brain undertaken in Day 1 (Table 34).

Table 34: Investigations Day 1, 2 & 3

	Day 1 N=140	Day 2 N=140	Day 3 N=140
Cranial ultrasound	56(40.0)	32(22.9)	24(17.1)
MRI of the brain	3(2.1)	0(0)	0(0)
Cardiac echo	21(15.0)	13(9.3)	1(0.7)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive.

SARNAT Scoring

Infants were assigned a SARNAT[15] score based on clinical behaviour on Day 1, Day 2 and Day 3 of treatment (Table 35). A diagnosis of encephalopathy, consisting of an altered state of consciousness (lethargy, stupor or coma) was only assigned to half of infants who had the SARNAT completed over the 72 hour period of therapeutic hypothermia. As outlined in Table 36, half of infants were graded as moderately encephalopathic on Day 1 (55.4%; 41 of 74), Day 2 (44.9%; 22 of 49) and Day 3 (47.7%; 21 of 44) of treatment.

Electrical seizures were identified in 50 of the 140 infants (35.7%) on Day 1, 32 of the infants (22.9%) on Day 2 and 14 of all the infants (10.0%) on Day 3.

Table 35: SARNAT Scoring on Treatment Day 1, 2 & 3

		Day 1	Day 2	Day 3
Level of consciousness				
	Hyper alert	22(15.7)	11(7.9)	5(3.6)
	Lethargic or obtunded	53(37.9)	37(26.4)	33(23.6)
	Stupor or Coma	13(9.3)	7(5.0)	7(5.0)
	Normal	30(21.4)	26(18.6)	39(27.9)
	Undocumented	22(15.7)	59(42.1)	56(40.0)
Activity				
	Normal	59(42.1)	43(30.7)	46(32.9)
	Decreased	49(35.0)	36(25.7)	30(21.4)
	Absent	14(10.0)	8(5.7)	8(5.7)
	Undocumented	18(12.9)	53(37.9)	56(40.0)

Neuromuscular Control				
Muscle tone	Normal	35(25.0)	37(26.4)	41(29.3)
	Mild hypotonia	63(45.0)	24(17.1)	18(12.9)
	Flaccid	22(15.7)	13(9.3)	9(6.4)
	Undocumented	20(14.3)	66(48.2)	72(51.4)
Posture	Mild distal flexion	13(9.3)	10(7.1)	12(8.6)
	Strong distal flexion	10(7.1)	5(3.6)	7(5.0)
	Intermittent decerebration	4(2.9)	3(2.1)	1(0.7)
	Normal	9(6.4)	3(2.1)	4(2.9)
	Undocumented	104(74.3)	119(85.0)	116(82.8)
Stretch reflexes	Overactive	7(5.0)	2(1.4)	2(1.4)
	Decreased or absent	12(8.6)	6(4.3)	5(3.6)
	Normal	24(17.1)	20(14.3)	20(14.3)
	Undocumented	97(69.3)	112(80.7)	113(80.7)
Complex Reflexes				
Suck	Weak	49(35.0)	37(26.4)	25(17.9)
	Weak or absent	10(7.1)	7(5.0)	4(2.9)
	Absent	30(21.4)	13(9.3)	14(10.0)
	Normal	24(17.1)	18(12.9)	25(17.9)
	Undocumented	27(19.3)	65(46.4)	72(51.4)
Moro	Strong; low threshold	5(3.6)	4(2.9)	3(2.1)
	Weak; incomplete high threshold	19(13.6)	4(2.9)	5(3.6)
	Absent	12(8.6)	2(1.4)	2(1.4)
	Normal	15(10.7)	11(7.9)	10(7.1)
	Undocumented	89(63.6)	119(85.0)	120(85.7)
Tonic Neck	Slight	5(3.6)	0(0)	1(0.7)
	Strong	1(0.7)	0(0)	0(0)
	Absent	5(3.6)	1(0.7)	0(0)
	Normal	1(0.7)	1(0.7)	2(1.4)
	Undocumented	128(91.4)	138(98.6)	137(97.9)
Autonomic Function				
Pupils	Mydriasis	3(2.1)	2(1.4)	0(0)
	Miosis	19(13.6)	5(3.6)	4(2.9)
	Variable; often unequal, poor light reflex, fixed, dilated	20(14.3)	13(9.3)	7(5.0)
	Normal	44(31.4)	28(20.0)	30(21.4)
	Undocumented	54(38.6)	92(65.7)	99(70.7)
Heart rate	Tachycardia	2(1.4)	1(0.7)	0(0)
	Bradycardia	105(75.0)	110(78.6)	108(77.1)
	Variable	23(16.4)	12(8.6)	15(10.7)
	Normal	7(5.0)	6(4.3)	4(2.9)
	Undocumented	3(2.1)	11(7.9)	13(9.3)
Seizures	None	96(68.6)	99(70.7)	113(80.7)
	Common; focal or multifocal	41(29.3)	32(22.9)	17(12.1)
	Uncommon (excluding decerebration)	0(0)	0(0)	0(0)
	Normal	0(0)	0(0)	0(0)
	Undocumented	3(2.1)	9(6.4)	10(7.1)

Note: Values are shown as N(%) unless otherwise stated.

Table 36: Grade of Encephalopathy on Treatment Day 1, 2 & 3

	Day 1 n=74	Day 2 n=49	Day 3 n=44
Mild HIE	7(9.5)	5(10.2)	6(13.6)
Mild-Moderate HIE	8(10.8)	7(14.3)	3(6.8)
Moderate HIE	41(55.4)	22(44.9)	21(47.7)
Moderate to Severe HIE	1(1.4)	3(6.1)	1(2.3)
Severe HIE	17(22.9)	12(24.5)	13(29.5)

Note: Values are shown as N(%) unless otherwise stated.

Rewarming

Of the 140 infants who underwent therapeutic hypothermia treatment, 13 infants (9.3%) did not complete 72 hours of therapeutic hypothermia. As outlined in Table 37, three-quarters of these infants had care redirect (76.9%; n=10 of 13).

Table 37: Indication to cease rewarming of infants who underwent therapeutic hypothermia in 2016 or 2017 before 72 hours of therapy were complete

	TH cases 2016/17 N=13
Redirection of care	10(76.9)
PPHN	2(15.4)
Sepsis	1(7.7)

Note: Values are shown as N(%) unless otherwise stated.

Excluding the 13 infants whose treatment was ceased, data on rewarming was available for 125 of the 127 infants (98.4%). As outlined in Table 38, most infants were rewarmed within 12 hours (78.4%; n=98 of 125). During the rewarming period eight of the 125 infants (6.4%) had seizures. Infants were rewarmed over periods between 12 and 72 hours.

Table 38: Duration of rewarming for infants who underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/17 N=125
12 hours	98(78.4)
13 – 15 hours	4(3.2)
16 - 18	21(16.8)
Greater than 19 hours	2(1.6)

Note: Values are shown as N(%) unless otherwise stated.

Feeding

Data on the introduction of feeding was recorded for 126 of the 140 infants who underwent therapeutic hypothermia treatment (90.0%). Nine of the 126 mothers' breastfed (7.1%), three-quarters of infants were fed with expressed breastmilk (65.1%; n=82) and over one quarter were fed with formulae (28.6%; n=36). As outlined in Table 39, the majority of infants had feed introduced on Day 4 (30.2%; n=38) or Day 5 (42.1%; n=53). The majority of infants reached full oral requirement (96.8%; n=122 of 126).

Table 39: Age that infants who underwent therapeutic hypothermia in 2016 or 2017 had feed introduced

	TH cases 2016/17 N=126
Up to Day 3	8(6.3)
Day 4	38(30.2)
Day 5	53(42.1)
Day 6	19(15.1)
Day 7+	8(6.3)

Note: Values are shown as N(%) unless otherwise stated.

Of these 126, over half of infants were initially fed with a nasogastric tube (57.9%; n=73). Of these, one quarter of infants were fed with a nasogastric tube for less than 24 hours (24.2%: n=16 of 66; missing data for 7 infants). As indicated in Table 40, 11 infants were discharged home with a nasogastric tube (16.7%).

Table 40: Duration of feeding with a nasogastric tube for infants who underwent therapeutic hypothermia in 2016 or 2017

	TH cases 2016/17 N=66
Less than 24 hours	16(24.2)
24-47 hours	13(19.7)
48-71 hours	12(18.2)
Greater than 72 hours	14(21.2)
Discharged home with a nasogastric tube	11(16.7)

Note: Values are shown as N(%) unless otherwise stated.

Specific placental conditions

Of the 136 infants who were born in a maternity unit/hospital, the placenta was retained for 104 (76.5%) and histological analysis was performed on all 104 placentas (100%). Of these, 72 (69.2%, n=72 of 104) placental examinations were complete, with 59.5% (n=50 of 84) of infants born in tertiary hospital having their report completed compared to 39.3% (n=22 of 34) of infants who were not born in a tertiary hospital. All 72 completed reports were made available to the NPEC for inclusion in this report.

Specific placental pathology was present in 60 (83.3%, n=60 of 72) of these infants, with more than one placental condition was present for some cases. As outlined in Table 41, the presence of a specific condition in these infants was higher than the 66% of placental conditions which were present in stillbirths occurring in 2016.[16]

Abnormal placental findings have been classified in line with recommendations from the publication from the international consensus meeting of pathology.[17] These are presented under the following broad categories: maternal vascular malperfusion, fetal vascular malperfusion, cord pathology, cord pathology with distal disease, chorioamnionitis, villitis and other.

Chorioamnionitis was present in a quarter of cases (27.8%, n=20). Five of these 20 cases were reported as having severe chorioamnionitis present (25%; n=5 of 20). Conditions within the categories of maternal vascular malperfusion (26.4%, n=19) and fetal vascular malperfusion (22.2%, n=16) were most commonly reported. The prevalence of these major categories, including cord pathology, were similar to those reported for stillbirths occurring in 2016 (see Table 41).

Table 41: Placental histology findings for infants who underwent therapeutic hypothermia in 2016 or 2017 versus Stillbirths in 2016

	TH cases N=72 2016/17	Stillbirth[16] N=242 2016
Maternal vascular malperfusion	19(26.4)	73(30.2)
Fetal vascular malperfusion	16(22.2)	64(26.4)
Cord pathology	14(19.4)	44(18.2)
Cord pathology with distal disease	N/A	6(2.5)
Chorioamnionitis	20(27.8)	20(8.3)
Villitis	3(4.2)	2(0.8)
Other placental condition	28(38.9)	28(11.6)
Any placental condition	60(83.3)	160(66.1)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive.

Discharge diagnosis and neonatal death

Of the 140 infants who underwent therapeutic hypothermia treatment, 96 infants (68.6%) had magnetic resonance imaging (MRI) of the brain undertaken. The MRI reports were assessed by adopting the Barkovich HIE scoring system18. Two-thirds of infants (64.8%; n=61) had a normal MRI and one third of infants (35.0; n=34) were reported to have had an abnormal MRI. Of the 34 infants were an abnormal MRI, one infant was reported to have had a large focal infarct. Of the 96 MRI reports, two reports (2.1%) were unclear and no result was assigned to these two cases. The full set of Barkovich HIE scores are outlined in Appendix A.

A discharge diagnosis was recorded for 128 of the 140 infants. In 7 of the cases no reference was made to HIE on discharge (Table 42). When HIE was referenced at discharge, there was no grade of encephalopathy assigned to the infant in almost half of cases (43.8%; n=56).

Table 42: Grade of encephalopathy on discharge

	TH cases 2016/17 N=128
HIE – no grade assigned	56(43.8)
Mild HIE	5(3.9)
Mild-Moderate HIE	7(5.5)
Moderate HIE	41(32.0)
Moderate to Severe HIE	1(0.8)
Severe HIE	11(8.6)
HIE not documented	7(5.5)

Note: Values are shown as N(%) unless otherwise stated.

The survival rate for the infants who underwent therapeutic hypothermia in 2016 or 2017 was 88%, as 17 of the 140 infants died. Almost one third of deaths occurred within 7 completed days of birth and were classified as early neonatal deaths (29.4%; n=5). As outlined in Table 43, a third of deaths occurred after the 7th day and within 28 completed days of birth and were classified as late neonatal deaths (29.4%; n=5 of 17). Twelve infants had an autopsy performed (75.0%; n=12 of 16 infants; missing data for one infant). It is important to note that data on the findings of these reports and infants cause of death were not collected for this report.

Table 43: Perinatal and infant mortality for infants who underwent therapeutic hypothermia in 2016 or 2017

	TH cases N=17 2016/17
Early neonatal death	5(29.4)
Late neonatal death	6(35.3)
Infant death	6(35.3)

Note: Values are shown as N(%) unless otherwise stated.

Appendix A

Barkovich HIE Scores

Basal Ganglia (BG)	Watershed (W)	Basal Ganglia/Watershed (BG/W)	Result
1	0	1	Abnormal
1	0	1	Abnormal
0	2	2	Abnormal
0	2	2	Abnormal
4	5	4	Abnormal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
4	4	3	Abnormal
0	0	0	Normal
0	2	2	Abnormal
0	0	0	Normal
0	0	0	Normal
1	3	3	Abnormal
1	4	3	Abnormal
0	0	0	Normal
0	2	2	Abnormal
0	0	0	Normal
2	2	3	Abnormal
0	0	0	Normal
0	0	0	Normal
0	2	2	Abnormal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	1	2	Abnormal
1	2	3	Abnormal
0	0	0	Normal
0	2	2	Abnormal
0	0	0	Normal
0	0	0	Normal

0	0	0	Normal
0	0	0	Normal
1	0	1	Abnormal
0	0	0	Normal
2	0	1	Abnormal
0	0	0	Normal
0	Unclear 2	Unclear 2	Unclear
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	2	2	Abnormal
2	5	3	Abnormal
0	0	0	Normal
0	2	2	Abnormal
0	4	2	Abnormal
1	2	2	Abnormal
1	5	4	Abnormal
0	3	2	Abnormal
1	4	4	Abnormal
Unclear 0	Unclear 0	Unclear 0	Unclear
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
4	4	3	Abnormal
4	0	3	Abnormal
4	4	4	Abnormal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
0	4	2	Abnormal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
4	2	3	Abnormal
0	0	0	Normal
0	4	2	Abnormal
0	1	3	Abnormal
4	5	4	Abnormal
0	0	0	Normal
0	0	0	Normal
0	0	0	Normal
4	0	1	Abnormal
0	0	0	Normal

Appendix B

Neonatal Therapeutic Hypothermia Working Group Members

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Appendix C

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Midland Regional Hospital, Mullingar; Ms Geraldine Kavanagh

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References

1. Kurinczuk JJ, White-Koning M, Badawi N. Epidemiology of neonatal encephalopathy and hypoxic–ischaemic encephalopathy. Early human development. 2010 Jun 1;86(6):329-38.
2. Hankins GD, Speer M. Defining the pathogenesis and pathophysiology of neonatal encephalopathy and cerebral palsy. Obstetrics & Gynecology. 2003 Sep 1;102(3):628-36.
3. Azzopardi DV, Strohm B, Edwards AD, Dyet L, Halliday HL, Juszczak E, Kapellou O, Levene M, Marlow N, Porter E, Thoresen M. Moderate hypothermia to treat perinatal asphyxial encephalopathy. New England Journal of Medicine. 2009 Oct 1;361(14):1349-58.
4. Jacobs SE, Stewart M, Inder T, Doyle LW, Morley CJ, ICE Collaboration. ICE: the Australian cooling trial for hypoxic-ischemic encephalopathy—in hospital outcomes. In Proceedings of the Hot Topics in Neonatology Conference, Washington, DC 2008 Dec 7.
5. Shankaran S, Laptook AR, Ehrenkranz RA, Tyson JE, McDonald SA, Donovan EF, Fanaroff AA, Poole WK, Wright LL, Higgins RD, Finer NN. Whole-body hypothermia for neonates with hypoxic–ischemic encephalopathy. New England Journal of Medicine. 2005 Oct 13;353(15):1574-84.Healthcare Pricing Office. (2017) Perinatal Statistics Report 2015. Dublin: Health Service Executive. [in press]
6. Ferriero DM. Neonatal brain injury. New England Journal of Medicine. 2004 Nov 4;351(19):1985-95.
7. Perlman JM. Brain injury in the term infant. InSeminars in perinatology 2004 Dec 1 (Vol. 28, No. 6, pp. 415-424). WB Saunders.
8. Grow J, Barks JD. Pathogenesis of hypoxic-ischemic cerebral injury in the term infant: current concepts. Clinics in perinatology. 2002 Dec;29(4):585-602.
9. Healthcare Pricing Office. (2017) Perinatal Statistics Report 2015. Dublin: Health Service Executive. [in press]
10. Ipsos MRBI (2015).Healthy Ireland Survey 2015. Dublin: The Stationery Office.
11. Manning E, Leitao S, Corcoran P, McKernan J, de Foubert P, Greene RA, on behalf of the Severe Maternal Morbidity Group. Severe Maternal Morbidity in Ireland Annual Report 2016. Cork: National Perinatal Epidemiology Centre, 2018.
12. Hansen A, Chauhan SP. Shoulder dystocia: definitions and incidence. InSeminars in perinatology 2014 Jun 1 (Vol. 38, No. 4, pp. 184-188). WB Saunders.
13. Gardosi J, Francis A. Customised Weight Centile Calculator. GROW version 6.7.6.5(IE), 2015 Gestation Network, www.gestation.net
14. Massaro AN, Chang T, Kadom N, Tsuchida T, Scafi di J, Glass P, et al. Biomarkers of brain injury in neonatal encephalopathy treated with hypothermia. J Pediatr 2012;161:434-40.
15. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress: a clinical and electroencephalographic study. Arch Neurol.1976;33 :695– 706
16. Manning E, Leitao S, Corcoran P, McKernan J, de Foubert P, Greene RA, on behalf of the Perinatal Mortality Group. Perinatal Mortality in Ireland Annual Report 2016. Cork: National Perinatal Epidemiology Centre, 2018
17. Khong TY, Mooney EE et al (2016). Sampling and definition of placental lesions. Arch Pathol Lab Med 2016 Jul;140 (7):698-713
18. Barkovich AJ, Hajnal BL, Vigneron D, Sola A, Partridge JC, Allen F, Ferriero DM. Prediction of neuromotor outcome in perinatal asphyxia: evaluation of MR scoring systems. American Journal of Neuroradiology. 1998 Jan 1;19(1):143-9.

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