Neonatal Therapeutic Hypothermia in Ireland

Annual Report | 2020

Aggregate Report 2016-2020

Contents >

National Neonatal Therapeutic Hypothermia Development Project

Prepared by the National Clinical Programme for Paediatrics and Neonatology, the National Women and Infants Health Programme and the National Perinatal Epidemiology Centre

HSE
NATIONAL PERINATAL EPIDEMIOLOGY CENTRE
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National Clinical & Integrated Care Programmes
Person-centred, co-ordinated care

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List of Acronyms and Abbreviations

aEEG – Amplitude Integrated Electroencephalogram

APGAR – Appearance, Pulse, Grimace, Activity, Respiration

APH – Antepartum haemorrhage

ARM – Artificial Rupture of Membranes

BAPM – British Association of Perinatal Medicine

BMI – Body Mass Index

BSID – Bayley Scales of Infant Development

CI – Confidence Interval

CTG – Cardiotocograph

EDD – Estimated Due Date

FGR – Fetal Growth Restriction

FiO2 – Fraction of Inspired Oxygen

FVM – Fetal Vascular Malperfusion

GROW – Gestation Related Optimal Weight

HIE – Hypoxic Ischaemic Encephalopathy

HIPE – Hospital Inpatient Enquiry

IUGR – Intrauterine Growth Restriction

MAVN – meconium-associated vascular necrosis

MDT – Multi-Disciplinary Team

MRI – Magnetic Resonance Imaging

MVM – Maternal Vascular Malperfusion

NCHD – Non Consultant Hospital Doctor

NCPPN – National Clinical Programme for Paediatrics and Neonatology

NDTP – National Doctors Training Programme

NE – Neonatal Encephalopathy

NG – Nasogastric Tube

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

NNEAG – National Neonatal Encephalopathy Action Group

NNT – Number Needed to Treat

NNTP – National Neonatal Transport Programme

NPEC – National Perinatal Epidemiology Centre

NRP – Neonatal Resuscitation Programme

NWIHP – National Women and Infants Health Programme

OEST – the Obstetric Event Support Team

OT – occupational therapist

PPV – Persistent Pulmonary Ventilation

QI – Quality Initiative

RCPI – Royal College of Physicians of Ireland

RCTs – Randomised Control Trials

SHO – Senior House Officer

SOL – Spontaneous onset of Labour

SIMF – Serious Incidence Management Forum

SRE – Serious Reportable Event

TH – Therapeutic Hypothermia

UPI – Uteroplacental ischaemia

Foreword

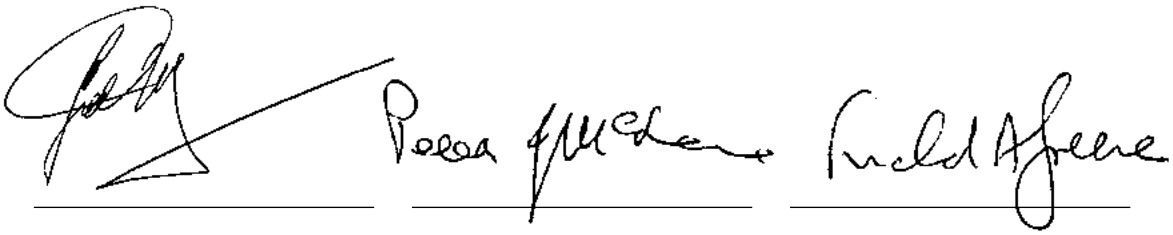
This is the National Neonatal Therapeutic Hypothermia report for cases occurring in 2020. The working partnership between the National Perinatal Epidemiology Centre, the National Women and Infants' Health Programme and the Clinical Programme for Paediatrics and Neonatology continues to be productive as we welcome this the fourth neonatal therapeutic hypothermia report covering the five consecutive years of data 2016-2020.

The purpose of the National Neonatal Therapeutic Hypothermia report is twofold. Firstly, it is a description of the epidemiology, antecedent obstetric, and intrapartum factors leading to neonatal encephalopathy. Secondly, it is a documentation of the immediate and subsequent neonatal management and outcomes of the infants diagnosed with neonatal encephalopathy.

As the repository of national anonymised data builds it provides us with the opportunity to carry out research in both specialities of Obstetric and Paediatric medicine. Using the Therapeutic Hypothermia data for this purpose will inform clinical practice and enhance the quality of services we offer to mothers and their infants both in Ireland and internationally.

Data for this report was collected in 2021 which was another difficult year for staff working in healthcare settings as COVID-19 yet again impacted on the way maternity services are delivered in Ireland. Staff demonstrated their ability to adapt and were unwavering in their commitment to ensure quality services continued to be delivered to mothers and their babies despite the adversities and challenges that COVID-19 presented.

With much appreciation, we would like to thank all stakeholders and the 19 maternity sites for their continued support with this project and we look forward to working with you all into the future.



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Executive Summary

This report provides details on 76 cases of mothers and their infants who required Therapeutic Hypothermia (TH) following a diagnosis of Neonatal Encephalopathy (NE) in Ireland for the year 2020. To date five years of data has been collected contributing to important knowledge in the area of NE. Aggregate data 2016-2019 is documented and is used for comparative analysis throughout this report. The aggregate data plus the 2020 data represents 357 cases over a five-year period where there were 301,940 infants born in Ireland equating to an incidence rate of TH of 1.2 per 1,000 births overall with an incidence of TH in 2020 of 1.4. It is worth repeating that the incidence rate of TH has remained consistent over the five-year period of data collection with minor fluctuations (2016 n=63, 2017 n=77, 2018 n=69, 2019=72).

TH is an important intervention and while it is an advance it is not without risk. It does have complications and infants with TH do have increased morbidity and mortality. In 2020, 12 deaths occurred within this cohort of infants. Over the five-year period of data collection, the mortality rate for infants with NE treated with TH stands at 14%. There is strong evidence to suggest improved long-term outcomes for infants with moderate NE, however there is limited evidence in terms of improved mortality rates for infants receiving a diagnosis of severe NE.

Obstetric Observations

Again, as with previous years it is noted that the need for TH is strongly associated with nulliparous mothers. Infants of nulliparous mothers accounted for 58% requiring TH treatment in 2020. Considering all infants born to multiparous mothers as one group, there were 147 cases of TH in 2016-2020 and their risk of TH was 0.80 (95% Confidence Interval, CI=0.67-0.93) per 1,000 births. Compared to these infants, the rate of TH for infants born to nulliparous mothers is 1.78 per 1,000 births with the risk of TH 2.78 times higher (Risk ratio=2.25, 95% CI=1.94-4.0, p-value<0.001).

Within our data, age does not appear to have an association with the need for TH, which is reassuring given the increase in age for women who are giving birth for the first time. The role of ethnicity in terms of TH remains difficult to interpret given the paucity in national data; however, minority groups do appear over-represented when compared to the overall female population aged 15-49 years old.

Of the 76 mothers whose infants underwent TH in 2020 the BMI of 29% of the mothers was in the obese range (>30.0kgm-2), which is higher than those from the general population in 2020 (21.1%).

Poor fetal growth may be linked to both short and long term adverse outcomes. Consistently since the onset of data collection, small for date's infants have been associated with the need for TH. The risk is doubled for infants with a birthweight under the 10th centile (n=14 infants in 2020). In 2020, 57% (n=8) of infants who were small for dates were diagnosed in the antenatal period and 50% (n=4) of these cases were induced for this reason. Detection of small for date's infants facilitates early risk mitigation in terms of delivery and a standardised approach to the detection of small for dates is advocated.

Of the 76 mothers whose infant required TH in 2020, 34 mothers had their labour induced. A Bishop score was documented for 56% of cases, of which the median Bishop score was 3. The Bishop score is an assessment used by medical professionals to decide how likely it is that the delivery will end in a vaginal birth. A score of 6 or less is considered to be unfavourable for an induction. Assessment, accurate documentation of care episodes and continual risk assessment for this cohort of women is encouraged to prevent adverse outcomes for infants.

In 2020 there were no elective caesarean sections amongst the TH cohort. Since the onset of data collection for the TH project four infants have been delivered by elective section. It would be remiss not to comment on this finding which suggests that labour and its management play an important role in the determinants of an outcome that result in NE requiring TH treatment. Delivery of infants requiring TH by means of Caesarean section is over-represented at 44% (n=33) when compared to the national figure of 34%. Of the pre-labour caesarean sections (n=17, 22% of all babies requiring TH in 2020) the most common reason for presentation to hospital of birth was a maternal complaint of reduced fetal movement (n=7). Access to correct, evidence based antenatal education is warranted to ensure mothers are informed and educated on the importance of seeking advice about reduced fetal movements. Currently, work is underway to implement antenatal education standards nationally. The second most common reason was an Antepartum Haemorrhage (APH) (n=2).

Since the onset of this project, cardiotocograph (CTG) data has been collected adopting two approaches. Initially, data was collected by examining the full CTG. Thereafter, CTG data was collected by clipping the final hour of CTG trace where available pre delivery. With both approaches an expert panel reviewed the data anonymously to determine if the CTGs were normal, suspicious or pathological. This year 30 CTGs were reviewed anonymously and five CTGs cases were repeated during a workshop to determine whether the expert panel would categorise the same CTG twice with the same result. Of them, 25 were TH cases and 5 were controls. Of the 25 TH cases 75% were interpreted as pathological (n=20), 15% were undetermined (n=3), 5%

were interpreted as suspicious (n=1) and another 5% as non-pathological (n=1). Of the 5 controls, 60% were interpreted as pathological, and 20% were interpreted as suspicious and 20% as non-pathological (n=20, respectively). The CTG is only one element of a labour and fails to address the full context in which the labour is occurring. It is suggested that a normal CTG is strongly predictive of a normal outcome but an abnormal CTG in isolation is a poor predictor of an abnormal outcome. This implies that the primary function of CTG training should be the ability to distinguish between normal and abnormal CTG traces.

Looking at sentinel events, the aggregated 2016-2020 data yielded that shoulder dystocia was associated with 11.8% (n=42 of 357) of births whose infants required TH intervention. The figure is overrepresented when compared to 2016-2020 Hospital Inpatient Enquiry (HIPE) data of which 0.8% of 295,753 mothers who delivered with a shoulder dystocia. Based on these data, the risk of an infant receiving TH was 18.4 (95% CI=13.3-24.9) per 1,000 women if the birth was complicated by shoulder dystocia compared to 1.1 (95% CI=1.0-1.2) per 1,000 women if there was no reported should dystocia, a 17-fold difference (Risk ratio=17.18, 95% CI=12.45-23.70, p-value<0.001).

It is observed that 59% (n=43) of births requiring TH occurred after 8pm and before 8am, and 22% (n=17) on weekends (i.e. Saturday or Sunday) in 2020. This data is consistent with the years 2018 and 2019 for which 60% of infants requiring TH were born 'out of hours'. The findings underline the need for senior input into antenatal and labour ward management at all times.

It is noted within the report that 'high risk mothers' are not over represented amongst the mothers who deliver an infant requiring TH intervention. This suggests that the obstetric management in high-risk cases is satisfactory.

As alluded to previously, the incidence of TH has remained relatively consistent over the five-year period. This therefore prompts the question whether the problem is intractable. By general consensus, a certain amount of TH cases are preventable. In all cases of NE an internal review is advocated. Included in appendix A is a suggested obstetric case review tool template for use by sites when reviewing cases of NE requiring TH. The template has been updated from the 2019 TH report and has been designed to reflect sentinel events and recurring themes which have emerged in the aggregated data since the onset of TH data collection in 2016. However, not all cases of NE are avoidable, but some are, and it is only through reflection, critical thinking and evaluation of care that improved outcomes can occur.

Neonatal Observations

In 2020, 72% of infants born requiring TH had an Apgar score of ≤3 at one minute of life. By ten minutes of life 18% of infants had an Apgar score of ≤3. There are knowledge gaps on the outcome of normally formed term infants who are born with no heart rate. However, with advanced Neonatal Resuscitation Programme (NRP) resuscitation techniques and progressions in neonatal intensive care long term outcomes for these newborns is improving.[1]

TH data for 2020 indicated that 81% of infants required PPV and 59% were intubated in the delivery room. The need for intensive resuscitation intervention in this cohort of infants again reinforces the need for staff involved in the delivery of infants to maintain their NRP certificate while also being afforded opportunities to be involved in skills and drills training to maintain this specific skill set. The need for effective and sustained resuscitation technique is paramount in terms of providing infants with improved outcomes. National standards in NRP are forthcoming and will provide sites with opportunities to audit and benchmark against standards to ensure the delivery of safe services.

In 46 cases in 2020 venous blood was drawn for the initial infant blood gas as part of the assessment for NE. This is a repeated trend from 2019 data and it is worth reiterating that venous blood samples are not optimal especially in terms of assessment for TH. In cases where an infant is compromised and suspected of requiring TH clinicians should aim to carry out a capillary sample as the first gas as this sample provides more meaningful information with regard to an infant's condition.

In 2020, 32% of infants requiring TH were born in either a level 1 or 2 hospital site and transferred to a level 3 for ongoing and active management of TH. The National Neonatal Transport Programme (NNTP) continues to perform an essential and integral role as it transferred 79% of outborn infants. It is encouraging to note that referral sites assessed, diagnosed, and initiated referral for 67% of cases in 2020 within 2 hours of life.

In line with practice guidelines, TH should be initiated within six 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 vast majority of all infants, both inborn and outborn, achieved optimum core temperature within six hours of birth (n=50 of 74, 67.6%, missing data for two infants). It is important to note that 25% of infants who received TH in 2020 had their 72-hour treatment initiated when they were outside the optimum core temperature. Continual education and guideline updates for staff working in Neonatal intensive care units and special care baby

units is advocated. A neonatal guideline developer has been employed by the National Women and Infants Health Programme (NWIHP) to address the paucity in national neonatal guidelines.

Consistent documentation continues to present as a challenge in terms of accurately recording the modified Sarnat assessment on a daily basis and thereafter assigning a grade of NE. Consistent and accurate documentation is fundamental in cases of infants requiring TH.[2] The Sarnat score provides a baseline score of the infant's neurological status and allows clinicians to easily assess whether the infants neurological condition is improving or deteriorating.[3] In 2020, 57% of infants were assigned a Sarnat grade on day 1, 36% on day 2 and 36% on day 3, respectively. Engagement with NCHDs and NDTP is warranted in terms of providing education and training in the modified Sarnat assessment.

The amplitude integrated electroencephalogram (aEEG) is another important tool in the assessment of neurological status. In 2020, 52% of infants undergoing TH had documented interpretation of the aEEG on day 1, on day 2, 63% and day 3, 55% of infants had recordings. Consistent documentation is required to determine infant's progress and aid in early identification of the deteriorating infant. Clinicians are encouraged to familiarise themselves with the online education and training platform provided by the Royal College of Physicians of Ireland (RCPI) website.[4]

Over the five-year period, data was available on 309 infants in terms of feeding patterns. It is noted that 11% of infants undergoing TH were fed during the three days of treatment. Recent research advocates that Enteral feeding during TH is safe and associated with beneficial outcomes compared with not feeding.[5]

Investigations

In 2020, there was a placenta report availability rate of 70%, which is significantly lower than the desired >95% rate. The relationship between NE and placenta pathology is complex. The current understanding of most clinicians is that pre-existing placental pathology may compromise the fetal ability to endure the stresses that can be associated with labour. Last year, two categories deserved special mention: The first of these is delayed villous maturation and it is this, that shows the most striking difference to last year. There is an almost a four-fold increase in cases from what was reported the previous year, although in some cases, a minor component of delayed villous maturation was identified. This certainly deserves further scrutiny going forward. The second special mention last year was of meconium induced vascular necrosis, which also showed an increase on cases identified from last year (although the numbers are very small) but this may reflect a greater familiarity with this pathology.

Going forward we will revert to analysing the collective data from cumulative years to ensure greater statistical significance. We also continue to stress the importance of sending placentas for analysis in all cases of neonatal encephalopathy. In some cases, the infant is well at birth but has a later deterioration and this may explain the difficulty in retrieving the placenta. An audit for the reasons of placental non-availability in this small but critical group is needed.

A brain MRI scan is routinely undertaken in all infants with NE treated with TH. It is an important predictor of both short term and long-term developmental outcome. In 2020, 98% of infants who underwent TH treatment had their MRI scan by day 10 of life. This is reassuring with respect to a previous TH recommendation that all MRI scans be undertaken before day 10 of life in order to attain optimal images to inform diagnosis. For the purposes of the TH report, the Barkovich scoring system has been applied to assess the MRI reports. In 2020 the Barkovich scoring system yielded that 41% of the brain MRI results were abnormal.

Follow-up

In 2020, in this report we were again able to table some results from national Bayley Scale of Infant Development III (BSD-III) assessments carried out at 2-3 years of age. Based on the limited assessment carried out in 2019 and 2020, more than 23% of the TH cohort infants presented with Language Delay, and more than a quarter of the group (25.9%) demonstrated Gross Motor Delay with just over one fifth (21.2%) demonstrating Receptive and Expressive Communication Delay. Early intervention in this cohort of infants is fundamental in order to minimise long term effects of NE and contribute to improved quality of life. it is noted that both expressive communication and motor development may require concentrated attention when providing early intervention to this cohort of infants. Overall, the application of the Bayley III remains inconsistent nationally. However, it is hoped that with the funding and hiring of Neonatal Psychologists in each of the maternity networks a standardised approach will be adopted nationally leading to better outcome data which will inform both NICU and early intervention care.

Key Messages

- NE is a significant cause of enduring morbidity and is the main cause of mortality in normally formed infants. The total mortality rate for infants in the TH cohort for the time period 2016-2020 was 14%.

- During the years 2016-2020, 357 NE infants were treated with TH, indicating an incidence rate of 1.2 per 1,000 births. Consistent data collection, analysis, action and shared learning is needed to reduce the national incidence of NE requiring TH intervention.[6]

- The antenatal detection of intrauterine growth restriction is important. During the five-year period 2016-2020, approximately 18% of infants who underwent TH were small for dates (birthweight <10th centile).

- Over the five year period, 30% of TH infants were born in a peripheral hospital and required transfer to one of the four tertiary centres that deliver TH intervention. The National Neonatal Transport Programme (NNTP) plays an important role in the retrieval of NE infants requiring TH intervention from peripheral hospitals. The data in this report reinforces that the Irish Health Service is providing TH in Ireland by way of a continuum of care between referral hospital, NNTP and tertiary centres.

- The diagnosis of labour can be a challenge.[7] The accurate and consistent application to diagnosing labour is warranted to ensure appropriate level of care and monitoring is provided to mothers and their infants.

- Nulliparous mothers, induction of nulliparous mothers, shoulder dystocia, ethnicity and obesity with BMI >30 are risk factors for TH which require particular attention in their clinical management.

- Good documentation is the platform for improvement in the assessment, categorisation, and management of infants with NE. Use of the cooling candidacy checklist and daily Sarnat assessment ensures accurate clinical measurement and is is the best pathway to improve outcomes for this group of infants.

- To continue to broaden the understanding of NE and the antecedent factors which contribute to disturbed neurological function it is noted that parity, sentinel events and mode of delivery have a significant role in the causation of NE with first time mothers representing for 60% of cases, sentinel events accounting/contributing to for 36% of cases and events surrounding labour contributing to for 73%.

- The TH report is valuable in that it is wholly representative of the Republic of Ireland thereby eliminating population bias. NE remains a challenging condition, the continued national dataset collection aims to contribute to the improvement in perinatal outcome through the provision of epidemiological evidence.

- Observing outcomes presents the opportunity to measure interventions and benchmark. The mortality rate amongst the TH cohort of infants has been consistent throughout the TH project at 14% over the five-year period.

- BSD III outcome data displays that, of the whole cohort (n=85), 29 infants had an impairment and 56 of infants were within normal ranges in all the composite scores (Figure V). Among the infants who had any type of impairment, 41% had an impairment in all the composite scores, 14% in two of them, 28% had an impairment in language composite scores only, and 17% in motor composite scores only (Figure VI).

- Figures I to VI, from the aggregate TH data 2016-2020, are summarised and presented below in terms of parity, sentinel events and mode of delivery to highlight the recurring themes and their incidence. Mortality and outcome data is documented to highlight the life-long implications the effects of NE can have on infants and their families.

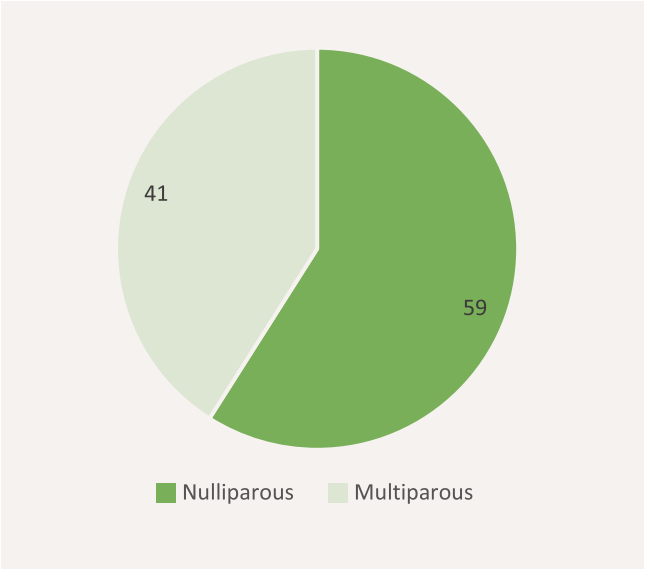


Figure I: Parity for mothers who delivered and infant requiring TH

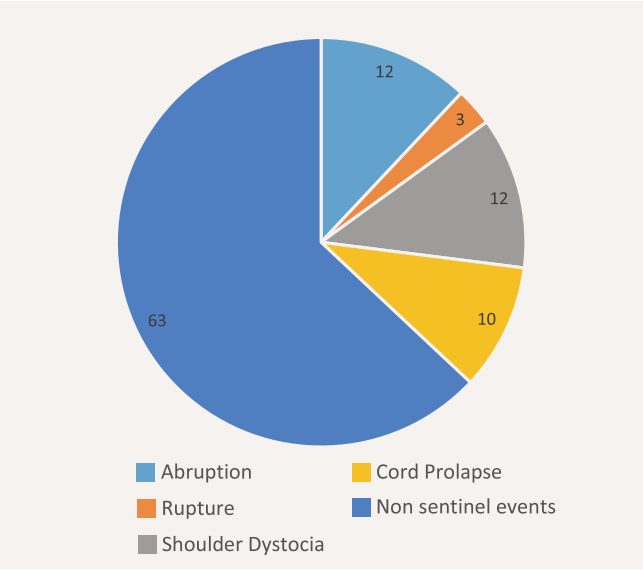


Figure II: Sentinel events for mothers who delivered and infant requiring TH

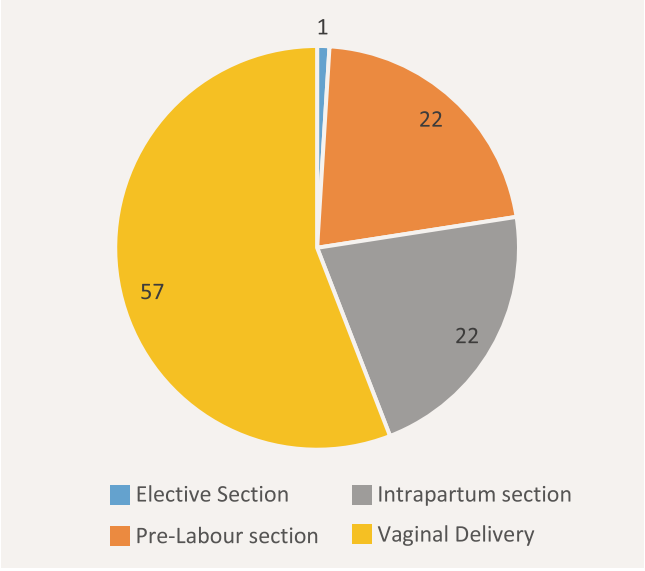


Figure III: Mode of delivery for TH infants

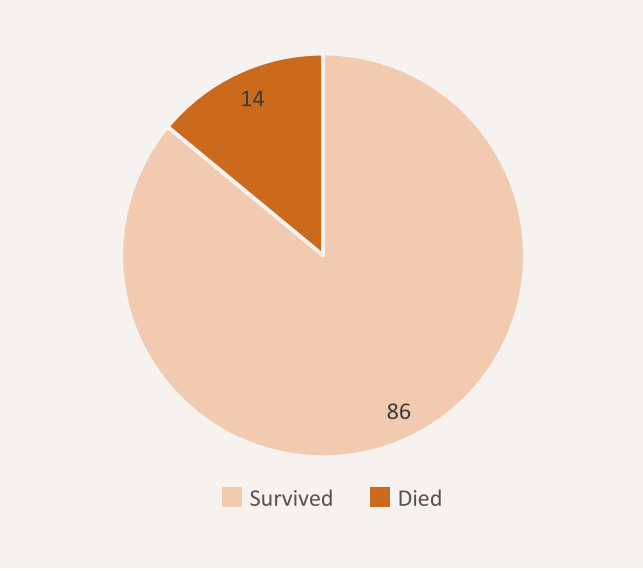


Figure IV: Mortality of TH infants

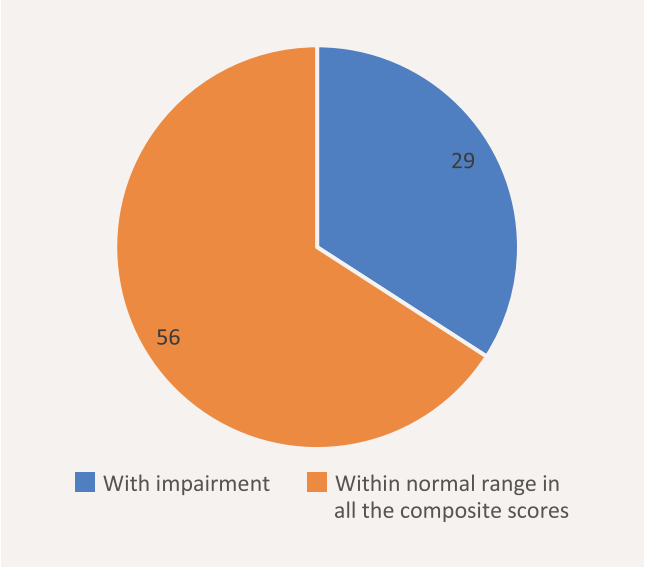


Figure V: BSD Assessment outcomes for infants treated with TH

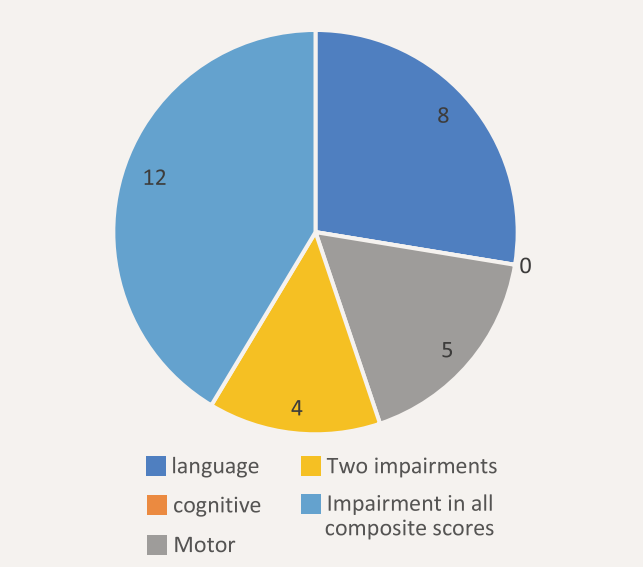


Figure VI: BSD Assessment outcomes for infants with impairments and treated with TH

NWIHP responses to 2019 Report recommendations

2019 Recommendation	NWIHP Response
1.1 Multi-disciplinary skills and drills training to deal with obstetric sentinel events are required	A Project Coordinator for Fetal Monitoring & Obstetric Emergencies was appointed in September 2021. The purpose of the post is to undertake a review of the current baseline practices, models of training and compliance of obstetric emergencies and fetal monitoring, adopted in each of the 19 maternity hospitals. It is anticipated this review process will assist in developing a national strategy for the provision of training in obstetric emergencies and fetal monitoring and will include the provision of support for the maternity services.
1.2 Front line staff responsible for CTG interpretation are recommended to undertake annual training as appropriate to experience	
2.0 Not all cases of TH can be avoided but some could be. A comprehensive review of each case of TH is recommended	The Serious Incidence Management Forum (SIMF) for each hospital group comprising of senior clinical personal and quality and risk staff are being established to review serious incidents/SREs to determine if further reviews are required to ensure safer standards in practice. In 2021 the NWIHP launched the Obstetric Event Support Team (the OEST). The OEST consists of a Consultant Obstetrician, a senior Midwife and a Quality & Safety Manager with additional backroom support based in the NWIHP. The OEST aims to support maternity services when an adverse event occurs and takes the opportunity to harvest the learning to form a national response. This is primarily a support service for hospitals and offers a second set of eyes, which are external, to assist in the incident review process.
3.0 The Neonatal Resuscitation Programme (NRP) certification is required for all midwives, nurses, and paediatric doctors working in maternity and neonatal units	In 2020, a baseline assessment exercise was commenced by the national NRP coordinator regarding the provision and organisation of neonatal resuscitation training across the 19 maternity sites and services. A number of areas were looked at including number of trainers, training facilities, training equipment, training capacity and on-site governance arrangements regarding NR training. In August 2021, the baseline assessment report was published and disseminated across the system from which key next steps were identified. Work is now underway to action the recommendations of the report with the development of governance structures for NRP, a suite of national NRP standards and a national audit of NRP training equipment.
4.0 Bayley Scales of Infant Development and Toddler Bayley III Neurodevelopmental follow-up	The Bayley Scales of Infant Development Bayley III is an individually administered test instrument to assess the developmental function of infants, toddlers and young children between 1 and 24 months. The Bayley III provides standardised outcome composite scores for the following domains: cognitive, language and motor development. The three additional posts funded to provide this service are now in place. It is the intention of NWIHP to develop a psychology network so as to continue to grow the follow-up data and design services to meet the needs of this cohort of infants. Furthermore, the NWIHP have funded Speech and Language Therapists (SLTs) in 2021 and Occupational Therapists (OTs) in 2022 to facilitate early assessment and intervention as appropriate both for TH infants and preterm infants. This wrap around service is vital in terms of development for these cohort of infants
5.0 Brain MRIs should be performed between days 5-10 after birth and the reporting should be standardised using the Barkovich Score	In the 2020 TH report 95% of MRIs (n=61) were carried out within 10 days of life. Data in relation to the age of the infant when the MRI is undertaken will continue to be collected to monitor this key performance indicator.

Of note, the NWIHP have invested in 2021 and 2022 in guideline developers both in obstetrics and neonatology to ensure care throughout the country is standardised and reduce variance in practice from site to site. The remaining 2019 recommendations require further engagement to progress and will continue to be sighted as recommendations in the TH reports until such a time the recommendations have been actioned.

Recommendations

1. **Enhanced awareness of the important risk factors for NE (first time mothers, intrauterine growth restriction (IUGR) etc.) through standardisation of care pathways and multi-disciplinary training among front line staff is needed**

   The findings from this report provide additional information to help improve the understanding of the risk factors associated with NE. Improving knowledge through the introduction of training programmes and tools for front line staff are essential to help develop strategies for minimising delays and initiating interventions if appropriate. This enhanced awareness should facilitate an ongoing evaluation particularly in labour and take account of the rapidly changing environment and the fact that most cases have no presenting risk factors.

2. **A National standardised assessment for the diagnosis of fetal growth restriction (FGR) is warranted and should include multi-disciplinary training**

   International evidence illustrates that suboptimal fetal growth is linked to both short and long-term adverse outcomes. Findings from this report illustrates there was some evidence of poor fetal growth with almost 20% of the infants born below the 10th centile. A multidisciplinary working group to address a national standardised approach for the detection of FGR has been established through the national encephalopathy action group and work is ongoing.

3. **Umbilical cord blood gas measurements are helpful in cases where an infant requires TH**

   The findings from this report have indicated that cord blood gas measurements were not taken in 19% (n=12) of cases. The cord blood gas measurements are an important part of the assessment in infants with NE requiring TH and should be recorded in each case of NE.

4. **Serum lactate on the cord blood or first Infant blood gas for infants requiring TH**

   The anaerobic metabolism in response to hypoxia and poor tissue perfusion leads to an increase in the production of lactate. Raised serum lactate levels especially over 15 mmol/L can be a marker for adverse outcome. In every case of NE, the serum lactate should be part of the infant's assessment.

5. **The Cooling Candidacy Assessment Checklist should be used as the decision-making tool in the evaluation of the infant for therapeutic hypothermia to promote standardised assessment and documentation.**

   The Cooling Candidacy Checklist is the assessment tool that should be applied when deciding to commence an infant on TH. The use of this tool promotes consistent documentation thereby potentially minimising incidence of therapeutic creep. The findings of the evaluation should be entered in the infant's case notes. Our aggregate findings indicate that it is only being used in 74% of cases. A copy of the checklist is included in this report (Appendix C).

6. **All infants receiving TH require a daily Sarnat assessment during the three days of cooling**

   The Sarnat grading scale is an internationally recognised classification assessment tool for NE in the newborn infant. Daily assessment is necessary to assess the progression of encephalopathy. The 2020 TH report similar to 2016/2017/2018/2019 reports has found incomplete Sarnat assessment.

7. **All infants receiving TH require a daily amplitude integrated electroencephalogram (aEEG) report during the three days of cooling**

   The following aEEG parameters should be recorded daily during the period of cooling: Amplitude – Continuity – Sleep/Wake Cycling – Presence of seizures. An e-learning programme on aEEG interpretation is available on the RCPI web site.[8] An appendix on the interpretation of aEEG is attached (Appendix X).

8. **The retention of the placenta for histopathology examination in all cases where the infants requires admission to the neonatal unit**

   The findings of this report indicate that placental examination is not being undertaken in 30% of cases requiring TH. Given that a decision to treat an infant with TH does not always occur at birth, it is reasonable to recommend that placentas are retained and examined for all infants requiring a NICU admission. With the increasing use of the Amsterdam criteria[9,10] for placental reporting, the potential for exploring the associations of placental pathology, neonatal course and developmental outcome is enhanced. It is therefore critically important that placental submission rates in TH reach if not exceed the excellent rates of >95% achieved for stillbirth.

Introduction

NE is a disorder consisting of abnormal neurological behaviour and seizures present in infants from birth. Most of the cases of NE are due to the lack of oxygen to the infant either before or during labour. It is worth reflecting that up to the late '90s there was no treatment for these infants. Following scientific advances and well conducted Randomized Control Trials (RCTs) a treatment has been available since 2009 [11–13] and has become a standard of care in Ireland since 2012. This treatment is induced Neonatal Therapeutic Hypothermia. Infants undergo total body cooling at 33-34°C for a period of 72 hours, commencing within six hours of birth. TH is now considered the standard of care for infants suffering from moderate and severe NE. All the cases of NE reported in this document received TH.

The NWIHP, National Clinical Programme for Neonatology (NCPN) and the National Perinatal Epidemiology Centre (NPEC) presents its successive report on neonatal TH in the Republic of Ireland for 2020. We now have five years 2016/2017/2018/2019/2020 cumulative comprehensive data to determine the current status and outcomes for infants who underwent TH during this timeframe.

This report presents the 2020 data alongside the 2016/2017/2018/2019 data for comparative analysis. By laying out the report in this format it is anticipated that patterns and trends will begin to emerge.

The report is presented in the following format for your convenience;

SECTION 1
Maternal Demographics
Maternal Antenatal Course
Labour
Delivery

SECTION 2
Infant Characteristics
Resuscitation
Assessment for Therapeutic Hypothermia
Transfer to Tertiary Centre
Treatment days 1-3
Investigations
Rewarming
Feeding
Discharge diagnosis and Death
Placenta findings
BSID-III

Methods

Purpose of this report

The primary aim of this report is to present an overview and national statistics on Neonatal TH in the Republic of Ireland for the year 2020. TH is administered in four centres only (National Maternity Hospital, Rotunda Hospital, Coombe Women and Infants University Hospital and Cork University Maternity Hospital). All babies born in other local and regional hospitals needing this treatment are transferred to one of these four centres.

The review will examine the clinical details around each case of Neonatal TH. This will include the mothers' demographics, antenatal details, labour and delivery. The infant's resuscitation, neurological assessment, treatment, the supportive clinical care, the examination of the placenta and follow up data 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 TH review, medical records were considered the primary source of information. Data were collected on site and/or via MNCMS 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, NPEC and NWIHP collected data on all cases of neonatal TH in 2020 by taking an active case ascertainment approach.

Processing of the data

Data on all infants who received TH were collected on site in the 2020 maternity units/hospitals. The data was uploaded to the electronic register facilitated by NPEC and were processed in a pseudonymised format. No hospital identifiers were included in the dataset, which means these data cannot be attributed to a specific hospital or to a specific individual.

Missing data

To ensure accuracy of information, missing or incomplete data were sought from the respective maternity hospitals/units by the TH Co-Ordinators. The extent of missing data is reported in the results section.

Continuous CTG review

A review of CTGs was undertaken for a randomly selected 25 infants who had fetal monitoring undertaken in the one-hour period before delivery in the year 2020. During the review process a random sample of five infants delivered in 2020 who did not require TH were also included for the CTG group to review. The review group consisted of two consultant obstetricians, one midwife, and one senior obstetric registrar. For the review process, the group were given a short vignette and shown images of the CTG recorded in the one-hour period before birth. The vignette provided included the following details when available; maternal age, parity, any documented pre-existing medical and or obstetric conditions, augmentation of labour, length of labour and gestation at delivery. The full medical reports were not made available to the teams for this review process. Once the CTG was shown to the group, they had to document their decision before discussion began. The group were directed to categorise the CTG as; normal, suspicious, pathological or, unsure request input from a colleague. Once the initial decision was documented by each group member a discussion then occurred amongst the group to achieve consensus.

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

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 Hypoxic-Ischaemic Encephalopathy (HIE) is 1.5 per 1,000 live births.[14] 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 HIE. 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[15] 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 occurring 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 of life.

(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 NE by inhibiting various events in this cascade of HIE injury. Major randomized clinical trials[11–13] involving induced neonatal hypothermia have demonstrated a reduction in death and disability.[16–18] These trials have shown improved outcomes for babies with NE 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 with rewarming to normothermic temperature occurring over a 6–12 hour period thereafter. TH is considered to be the standard of care for infants with moderate-to-severe NE who meet all the 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 (Appendix C).

Main Findings

The following analysis is based on 76 infants who underwent neonatal TH treatment in 2020, and on the total numbers of infants who underwent neonatal TH between 2016 to 2019.

Maternal Demographics

Age

The age of mothers whose infants underwent TH was known for all 76 of the mothers in 2020. The mothers whose infants underwent TH ranged in age from teenage years (the youngest being 18 years of age) through to mid-forties (the eldest being 44 years of age), with an average age of 31.8 years old. Their age distribution reflected that of the population of mothers who gave birth in Ireland (Table 1).

Table 1: Age distribution of mothers whose infants underwent TH in 2016-2020 versus all births in 2016-2020

Age group	2016-2019* N=280	2020 N=76	All births 2016-2020 (%) N=301,940
<20yrs	5(1.8)	1(1.3)	1.6
20-24yrs	25(8.9)	11(14.5)	8
25-29yrs	50(17.9)	10(13.2)	17.2
30-34yrs	102(36.4)	29(38.2)	34.8
35-39yrs	79(28.2)	16(21.1)	30.8
≥40yrs	19(6.8)	9(11.8)	7.5

Note: Values are shown as N(%) unless otherwise stated. *Age unknown for one mother in 2018. Population data from the Central Statistics Office (CSO) for all births 2016-2020.[19]

As outlined in Table 2 there is no statistical difference in the risk of TH by maternal age. There were slight variations observed, with slightly higher risk among births to mothers aged under 25 years and lower risk for births to older mothers.

Table 2: Risk ratios for infants who underwent TH in 2016-2020 by maternal age

Age group	TH cases 2016-2020* N=356	Total N=301,940	Rate (95% CI)	Rate ratio (95% CI)	P-value
<20yrs	6	4783	1.25 (0.46-2.73)	1.23 (0.54-2.81)	0.624
20-24yrs	36	24296	1.48 (1.04-2.05)	1.45 (0.99-2.13)	0.057
25-29yrs	60	52035	1.15 (0.88-1.48)	1.13 (0.82-1.56)	0.459
30-34yrs	131	105066	1.25 (1.04-1.48)	1.22 (0.94-1.59)	0.137
35-39yrs	95	93099	1.02 (0.83-1.25)	1.00 (ref.)	-
≥40yrs	28	22661	1.24 (0.82-1.79)	1.21 (0.79-1.85)	0.374

Note: Values are shown as N(%) unless otherwise stated. *Age unknown for one mother. Population data from the CSO for all births 2016-2020.[19]

Ethnicity

Assessment of risk associated with ethnic groups is impeded by the paucity of national data on ethnicity for the pregnant population in Ireland. The majority of mothers whose infants underwent TH in 2020 were of white Irish ethnicity (n=62, 79.5%) (Table 3). This is similar to the proportion of white Irish women in the female population aged 15-49 years (77.3%), enumerated by the National Census 2016.[20] While the numbers involved were small, Irish Traveller, Asian and Black ethnicities were overrepresented in the mothers whose infants underwent TH in 2020 (9.0%) compared to 5.5% of the female 15-49-year-old population in the Irish Traveller, Asian and Black ethnicities from the National Census in 2016.[20]

Table 3: Ethnicity of mothers whose infants underwent TH in 2016-2020 versus 15-49 year-old female population, 2016

Ethnicity	2016-2019* N=278	2020 N=76	15-49 year-old female population, 2016 (%) N=781,392
White Irish	205(73.7)	60(78.9)	77.3
Irish Traveller	4(1.4)	2(2.6)	0.8
Other white background	39(14)	7(9.2)	15.1
Asian/Asian Irish	13(4.7)	3(3.9)	3.1
Black/Black Irish	14(5)	2(2.6)	1.6
Other/mixed	3(1.1)	2(2.6)	2.1

Note: Values are shown as N(%) unless otherwise stated. *Ethnicity unknown for two mothers in 2017 and for one mother in 2018. Population data from the National Census 2016.[20]

Employment and insurance status

Table 4 provides a high-level overview of the data provided on mother's employment status, alongside data available for the most comparable occupation categories for mothers of all births in Ireland in 2016-2020.[21–25] Employment status was specified for all of the mothers for whom data were recorded in 2020 (n=76, 100%). It can be seen that unemployed status was recorded for 23.7% of the mothers whose infants underwent TH in 2020 compared to 21.3% of mothers of all births in Ireland in 2016-2020 (Table 4).

Table 4: Employment status at booking of mothers whose infants underwent TH in 2016-2020 versus all maternities in 2016-2020

	2016-2019* N=256	2020 N=76		Maternities 2016-2020 (%) N=298,389
Employed	193(75.4)	56(73.7)	**Employed**	73.42
Unemployed	26(10.2)	10(13.2)	**Unemployed**	4.60
Home duties	23(9)	8(10.5)	**Home duties**	16.71
Student	13(5.1)	1(1.3)	**Not stated**	2.10
Others not in labour force	1(0.4)	1(1.3)	**Not classifiable**	3.18

Note: *Data not known on employment for 10 mothers in 2016, for 12 mothers in 2017 and for two mothers in 2018. Population data from the Perinatal Statistics reports, 2016-2020.[21–25]

Public or private status was recorded for the 76 mothers whose infants underwent TH in 2020. More than 80% (n=63 of 76) of mothers whose infants underwent TH in 2020 availed of public services. In total, 2018-2020, 87% of TH mothers were public patients (n=184 of 211, 87.2%) while 12.8% attended a consultant obstetrician privately (n=27) in

this timeframe. According to HIPE data, 82.2% and 17.8% of all mothers who gave birth in hospital in 2018-2020 were public and private patients, respectively. The risk of TH for the infants of public patients was 1.30 (95% CI=1.12-1.50) per 1,000 women, which was 43% higher than the risk of 0.91 (95% CI=0.60-1.31) per 1,000 women among private patients (Risk ratio=1.43, 95%=0.96-2.13, p-value=0.077).

Individual Patient Factors

Body Mass Index

Body Mass Index (BMI) was available for the 76 mothers whose infants underwent TH in 2020 (Table 5). The BMI for 36% was classified as overweight (25.0-29.9kgm-2) in the TH cohort, compared with 29% in the general population of women giving birth in Ireland in 2020, based on comparison data collated from seven maternity units.

Table 5: Body mass index of mothers whose infants underwent TH in 2016-2020 versus body mass index of mothers in Ireland in 2020

BMI Category (kg/m²)	2016-2019* N=265	2020 N=76	Maternities 2020 (%) N=35,122
Underweight (<18.5)	3(1.1)	1(1.3)	1.3
Healthy (18.5-24.9)	108(40.8)	26(34.2)	46.2
Overweight (25.0-29.9)	78(29.4)	27(35.5)	31.3
Obese (>30.0)	76(28.7)	22(28.9)	21.1

Note: Values are shown as N(%) unless otherwise stated. *BMI value missing for six mothers in 2016, for five mothers in 2017 and 2018, and for three mothers in 2019. Data on BMI were collated for 35,122 maternities in 2020 from seven maternity units.

Smoking and substance abuse

Of the 76 mothers whose infants underwent TH in 2020, 14 mothers (18.7%) were smokers at the time of booking, and six were ex-smokers (8.0%, missing information for one mother); this is higher than all female smokers in the Irish population in 2019 (16%).[26] Of the 14 mothers who were smoking at booking, one mother stopped smoking during pregnancy. Among the mothers with a documented history of drug abuse in 2020, one woman used cannabis, one woman used cocaine and Benzodiazepine drugs and one woman used Methadone and Benzodiazepine drugs.

Previous pregnancy

In terms of parity of mothers who delivered infants requiring TH in 2020, there was an overrepresentation of nulliparous mothers (57.9%) compared to the general population of mothers who gave birth in 2016-2020[21–25] (n=117822 of 303,135, 38.9%, Table 6).

Table 6: Distribution of parity, 2016-2020

Parity	2016-2019 N=281	2020 N=76	All births 2016-2020(%) N=303,135
Nulliparous	166(59.1)	44(57.9)	38.88
Para 1	67(23.8)	17(22.4)	34.83
Para 2	28(10)	6(7.9)	17.51
Para 3+	20(7.1)	9(11.8)	8.79

Note: Values are shown as N(%) unless otherwise stated. Population data from the Perinatal Statistics reports, 2016-2020.[21–25]

Considering all infants born to multiparous mothers as one group, there were 147 cases of TH in 2016-2020 and their risk of TH was 0.80 (95% CI=0.63-0.99) per 1,000 births. Compared to these infants, the risk of TH was 2.78 times higher among those born to nulliparous mothers (Risk ratio=2.78, 95% CI=1.94-4.0, p-value<0.001) (Table 7).

Table 7: Risk ratios for infants who underwent TH in 2016-2020 by parity

Parity	TH cases N=357 2016-2020	All births 2016-2020 (%) N=303,135	Rate (95% CI)	Rate ratio (95% CI)	P-value
Nulliparous	210	117822	1.78(1.55-2.04)	2.78(1.94-4.0)	<0.001
Para 1	84	105561	0.80(0.63-0.99)	1.24(0.83-1.85)	0.285
Para 2	34	53087	0.64(0.44-0.89)	1.00 (ref.)	-
Para 3+	29	26665	1.09(0.73-1.56)	1.7(1.03-2.79)	0.036

Note: Population data from the Perinatal Statistics reports, 2016-2020.[21–25]

Previous Pregnancy-related problem

In 2020, 36 mothers had at least one previous pregnancy. Of these, 33.3% (n=12 of 36) had a previous pregnancy-related problem reported. As outlined in Table 8, in 2020, multiple miscarriages (three or more) was the most common pregnancy-related problem in mothers who had a previous pregnancy (n=3, 8.1%). This was followed up by both having previous caesarean delivery and having preterm births or mid-trimester pregnancy losses (n=2, 5.6%).

Table 8: Previous pregnancy-related problems in mothers whose infants underwent TH in 2016-2020

	2016-2019 N=145	2020 N=36
Previous pregnancy-related problems	**48(33.1)**	**12(33.3)**
• Previous caesarean delivery	23(15.9)	2(5.6)
• Three or more miscarriages	10(6.9)	3(8.3)
• Infant requiring intensive care	9(6.2)	1(2.8)
• Pre-term birth or mid-trimester loss	4(2.8)	2(5.6)
• Neonatal death	2(1.4)	1(2.8)
• Pre-eclampsia	3(2.1)	0(0)
• Stillbirth	3(2.1)	1(2.8)
• Placenta abruption	3(2.1)	0(0)
• Post-partum haemorrhage requiring transfusion	1(0.7)	0(0)
• Infant with congenital anomaly	1(0.7)	0(0)
• Placenta praevia	0(0)	0(0)
• Previous infant with HIE	0(0)	0(0)
• Other	6(4.1)	4(11.1)

Note: Percentage relates to the total number of mothers who had a previous pregnancy (n=181).
Categories are not mutually exclusive. Values are shown as N(%) unless otherwise stated.

Pre-existing medical problems

Less than half of the mothers whose infants underwent TH in 2020, had one or more pre-existing medical problems (n=34, 44.7%). The most common type of pre-existing medical problems were psychiatric disorders, with 17.1% of mothers (n=13) suffering from conditions of this type (Table 9). Endocrine disorders had the second highest percentage of occurrence (n=8, 10.5%).

Table 9: Pre-existing medical problems in mothers whose infants underwent TH in 2016-2020

	2016-2019 N=281	2020 N=76
Pre-existing medical problems	**85(30.2)**	**34(44.7)**
• Endocrine disorder	29(10.3)	8(10.5)
• Psychiatric disorder	18(6.4)	13(17.1)
• Hypertension	5(1.8)	0(0)
• Haematological disorder	3(1.1)	1(1.3)
• Diabetes	3(1.1)	2(2.6)
• Cardiac disease	5(1.8)	1(1.3)
• Inflammatory disorder	1(0.4)	1(1.3)
• Renal disease	0(0)	0(0)
• Epilepsy	4(1.4)	0(0)
• Other	51(18.1)	17(22.4)

Note: Percentage relates to total number of mothers, categories are not mutually exclusive

Antenatal care

Currently in Ireland, there is limited national data on the number of births as a result of fertility treatment. Information was available for almost 99% of the mothers whose infants underwent TH in 2020 (n=75, 98.7%). In five of these cases (6.7%), the pregnancy was reported to be the result of fertility treatment. In terms of parity the majority of this cohort of mothers were nulliparous (n=3 of 5, 60.0%).

During the associated pregnancy, the majority of the 76 mothers intended on delivering in an obstetric unit (n=75, 98.7%) with obstetric-led care (n=71, 93.4%) being the main intended type of delivery care at booking. All mothers had completed bookings for 2020 with the gestation at official booking appointments unknown for one woman. Estimated Date of Delivery (EDD) was documented for all 76 of the mothers.

Gestation at last antenatal hospital visit

Information on the last antenatal visit was available for 75 of the 76 mothers whose infants underwent TH in 2020 (98.7%). These 75 mothers last attended the hospital clinic between 25 and 41 weeks of gestation. The majority of mothers had their last antenatal visit at 37 weeks or later (n=56 of 75, 74.7%, Figure 1). Of the 75 mothers, one mother was transferred from another maternity unit with the fetus in utero at 17 gestational weeks.

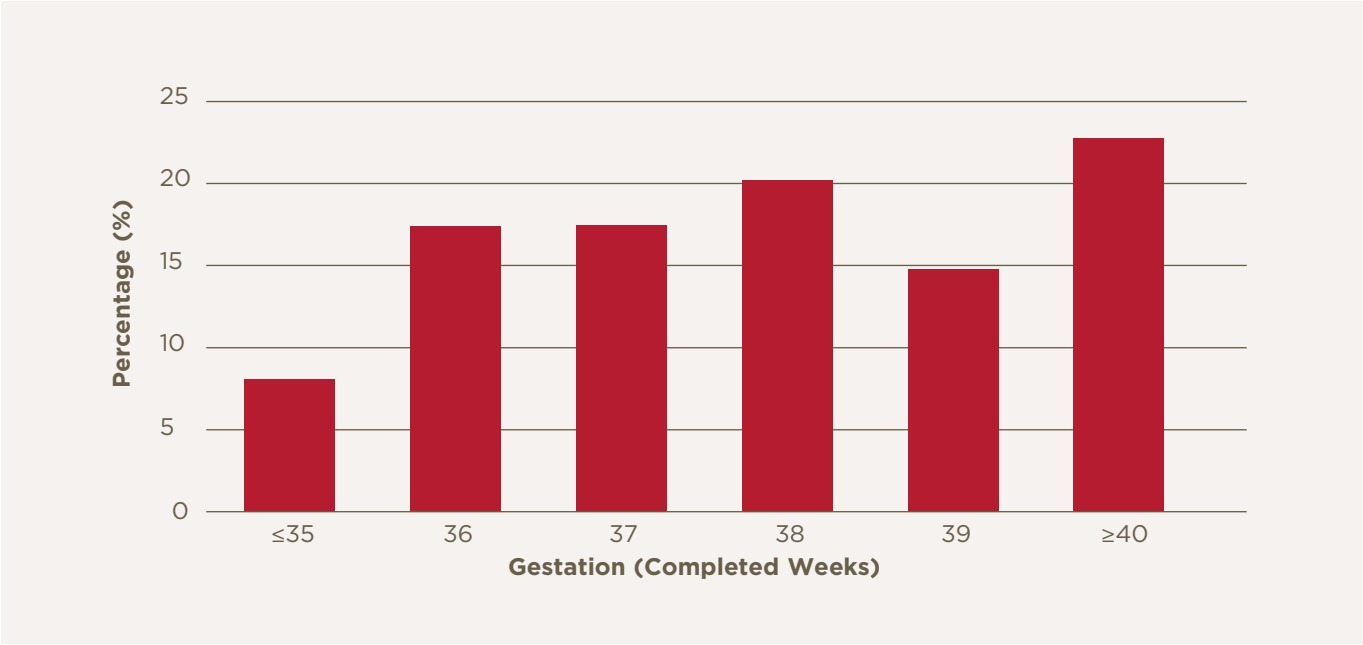


Figure 1: Weeks of gestation at last antenatal visit, 2020

Concern documented during pregnancy

Of the 76 cases, there were concerns documented during the pregnancy for 45 (57.7%) of the mothers whose infants underwent TH in 2020. More than half of these mothers had two or more concerns documented (n=26 of 45, 57.7%). The most common concerns documented were:

- Gestational diabetes mellitus with 14.4% (n=11 of 76) of mothers developing this condition during pregnancy
- This was followed by suspected intrauterine growth restriction (n=10 of 76, 13.1%)
- High BMI (n=8 of 76, 10.5)
- Hypertensive disorders were referred for 4% of these women (n=2 of 76, 2.6%).

Labour

Information on the onset of labour was available for all 76 mothers whose infants underwent TH in 2020 (Table 10). One third of the mothers laboured spontaneously (n=25, 32.9%), more than 40% of mothers were induced (n=34, 44.7%) and 22.4% of mothers were never in labour (n=17 of 76).

Table 10: Onset of labour for mothers whose infants underwent TH in 2016-2020

	2016-2019 N=281	2020 N=76
Spontaneous	135(48)	25(32.9)
Induction	97(34.5)	34(44.7)
Never in labour	49(17.4)	17(22.4)

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

As outlined in Table 11 below, approximately 60% of mothers who laboured spontaneously presented to the emergency department in 2020 (n=15 of 24, 62.5%, information missing for one mother). Of these mothers, the majority presented with spontaneous onset of labour (n=14 of 15), and one woman had spontaneous rupture of membranes (n=1 of 15).

Table 11: The department that mothers attended when presenting to the hospital for admission for queried onset of spontaneous labour 2020

	Total N=75	Spontaneous N=24	Induce N=34	Never in labour N=17
Maternity Emergency Department	31(41.3)	15(62.5)	5(14.7)	11(64.7)
Antenatal Wards	33(44)	1(4.2)	29(85.3)	3(17.6)
Labour Wards	6(8)	5(20.8)	0(0)	1(5.9)
Other	5(6.7)	3(12.5)	0(0)	2(11.8)

Note: Values are shown as N(%) unless otherwise stated. *Missing information for one mother. This report presents the following departments for standardisation purposes, even though this might not be reflective of different pathways of care or departments available at each maternity hospital in Ireland.

From 2019, documented times were sought relating to when the mother was admitted to hospital, diagnosed as being in labour, admitted to the labour ward, when she commenced active pushing and when the baby was born.

In 2020, of the 59 mothers with spontaneous and induced onset of labour, data in relation to timings for diagnosis of labour data was available for 71.1% (n=42 of 59, n=16 for spontaneous and 26 for induced onset of labour). For mothers who had a spontaneous onset of labour, more than 80% had their labour diagnosed after admission less than or equal to one hour (n=13 of 16, 81.25%). For mothers who had an induced onset of labour, almost 54% of the mothers had their labour diagnosed less than or equal to one hour (n=14 of 26, 53.8%) after admission, 8 mothers (30.8%) had had their labour diagnosed approximately two to four hours after hospital admission, and for four mothers (15.4%) labour diagnosis was made five or more hours before or after admission to the hospital.

The mean time from labour diagnosis to labour ward admission was 2.2 hours for both spontaneous and induced mothers. On average, time from labour diagnosis to labour ward admission was longer for nulliparous mothers either in spontaneous or induced mothers (Table 12).

The mean time from labour ward admission to commencing active pushing was 6.7 hours. The mean time was more than twice as long for nulliparous mothers, at approximately 9.3 hours, versus 4.6 hours for parous mothers among induced mothers. The general mean time for mothers with spontaneous onset of labour was lower than for induced mothers, although nulliparous mother still having a higher average of hours from labour ward admission to starting to commencing active pushing compared to parous women (Table 12).

Time from commencing active pushing until delivery of the baby was 45.4 minutes, on average. Again, this varied by parity, with a mean of 53 minutes for nulliparous mothers and 35 minutes for parous mothers, overall. The average timings for spontaneous and induced onset of labours of these mothers can be seen in Table 12.

Table 12: Mean time of stages of labour for mothers with spontaneous and induced onset of labour in 2020

Stage	Spontaneous			Induced		
	All mean (SD, range)	Nulliparous mean (SD, range)	Parous mean (SD, range)	All mean (SD, range)	Nulliparous mean (SD, range)	Parous mean (SD, range)
From labour diagnosis to labour ward admission, hours	1.6 (3.0, 0-10)	1.6 (3.5, 0-10)	1.5 (1.7, 0-4)	1.8 (3.0, 0-12)	2.4 (3.6, 0-12)	1.0 (1.2, 0-3)
From labour ward admission to commencing active pushing	5.3 (7.4, 0-20)	7.6 (8.2, 0-20)	0.5 (1.0, 0-2)	7.6 (6.0, 0-26)	9.3 (6.4, 2-26)	4.6 (3.9, 0-10)
From commencing active pushing to delivery of the baby, minutes	37.3 (31.7, 1-108)	47.6 (33.1, 12-108)	14.8 (10.7, 1-30)	50.4 (32.5, 7-127)	56.4 (25.5, 13-127)	43.5 (39.1, 7-113)

Note: Time values are shown in mean (standard deviation, range). Total number of mothers with spontaneous onset of labour N=12 (n=8 nulliparous and n=4 multiparous). Total number of mothers with induced onset of labour N=22 (n=14 nulliparous and 8 multiparous).

Spontaneous

Less than one third of the mothers who laboured spontaneously in 2020 had their labour accelerated (n=7 of 25, 28.8%), either by artificial rupture of membranes (ARM, n=2 of 7, 28.6%) or oxytocin (n=3 of 7, 42.9%). Two mothers (n=2 of 7, 28.6%) had their labour accelerated with both (Table 13).

Table 13: Method of acceleration for mothers who laboured spontaneously by parity in 2016-2020

	Total	Nulliparous		Parous	
	N=68	2016-2019 N=41	2020 N=6	2016-2019 N=20	2020 N=1
ARM	36(52.9)	17(41.5)	1(16.7)	17(85)	1(100)
Oxytocin	25(36.8)	19(46.3)	3(50)	3(15)	0(0)
Both	7(10.3)	5(12.2)	2(33.3)	0(0)	0(0)

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

Induction

Induction Reasons

There was a documented reason for induction for 100% of the 34 mothers whose onset of labour was induced in 2020. As indicated in Table 14, the common reasons to induce labour were associated with post maturity (n=9 of 34, 26.5%), gestational diabetes mellitus (GDM, (n=5 of 34, 14.7%) and intra-uterine growth restriction (n=4 of 34, 11.8%). Hypertensive disorders and large for gestational age accounted for almost 9% of common reasons to induce labour (n=3 of 34, 8.8% irrespectively). Under the "Other" category a range of indications were captured including twin pregnancy, symphysis pubis dysfunction (SPD), maternal anxiety, cholestasis and previous pregnancy complications.

Table 14: Reason for induction of mothers whose infants underwent TH in 2020

	Total N=34	Nulliparous N=19	Parous N=15
Post maturity	9(26.5)	7(36.8)	2(13.3)
Hypertensive disorders	3(8.8)	2(10.5)	1(6.7)
Large for gestational age	3(8.8)	1(5.3)	2(13.3)
Oligohydramnios	0(0)	0(0)	0(0)
Polyhydramnios	0(0)	0(0)	0(0)
Intra-uterine growth restriction	4(11.8)	4(21.1)	0(0)
Prolonged SROM	1(2.9)	0(0)	1(6.7)
Reduced fetal movements	2(5.9)	1(5.3)	1(6.7)
Gestational Diabetes Miellitus	5(14.7)	1(5.3)	4(26.7)
Other	7(20.6)	3(15.8)	4(26.7)

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

Cervical Assessment

It was documented that 33 of the 34 mothers who were induced had a cervical assessment carried out in 2020 (97.1%, Table 15). More than 80% of mothers had neither favourable or not favourable results (n=27 of 33, 81.8%). There was a documented Bishop score for just over 50% of the mothers who were induced n=19 of 34, 55.9%). Of these 19 mothers, the median Bishop score was 3.

Table 15: Results of the cervical assessment carried out on mothers who were induced whose infants underwent TH in 2020*

	Total N=33	Nulliparous N=19	Parous N=14
Favourable	3(9.1)	3(15.8)	0(0)
Not favourable	3(9.1)	2(10.5)	1(7.1)
Neither	27(81.8)	14(73.7)	13(92.9)
Bishop Score	**N=19**	**N=14**	**N=5**
0-6 score	18(94.7)	13(92.9)	5(100)
7-10 score	1(5.3)	1(7.1)	0(0)

Note: Values are shown as N(%) unless otherwise stated. *Missing data of the assessment for one parous woman in 2020. Missing data for the bishop score for 15 women in 2020 (five nulliparous and 10 parous).

Induction Method

The method of induction was known for all 34 mothers who were induced in 2020 (100%). Approximately 85% of mothers had their labour induced using multiple methods of induction As illustrated in Table 16, in 2020 more than 70% of mothers had their labour induced with the artificial rupture of membranes (n=25 of 34, 73.5%). The second most common method of induction was oxytocin (n=24 of 34, 70.6%) followed by prostaglandin gel (n=18 of 34, 52.9%).

Table 16: Method of induction for mothers whose infants underwent TH in 2016-2020

	Total	Nulliparous		Parous	
	2016-2020 N=131	2016-2019 N=63	2020 N=19	2016-2019 N=34	2020 N=15
Oxytocin	22(58.8)	38(60.3)	14(73.7)	15(44.1)	10(66.7)
Artificial rupture of membranes	5(60.3)	36(57.1)	14(73.7)	18(52.9)	11(73.3)
Prostaglandin gel	(55)	37(58.7)	8(42.1)	17(50)	10(66.7)
Propess	(28.2)	20(31.7)	10(52.6)	3(8.8)	4(26.7)
Other	(0.8)	1(1.6)	0(0)	0(0)	0(0)

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

Liquor colour

As outlined in Table 17, liquor was clear in 34 of the 57 documented cases for women whose onset of labour was spontaneous or induced (59.6%). One in every three mothers had meconium-stained liquor (n=18 of 57, 31.6%). The grade of meconium was specified for the 18 cases (100%), with 38.9% of these mothers having Grade 1 (n=7 of 18), 33.3% of mothers having Grade 2 (n=6 of 18) and the remaining five mothers having Grade 3 (27.8%).

Table 17: Liquor colour in 2016-2020

	Total N=338	2016-2019 N=281	2020 N=57
Clear	166(49.1)	132(47)	34(59.6)
Meconium	89(26.3)	71(25.3)	18(31.6)
Other	28(8.3)	23(8.2)	5(8.8)
Missing/Non-applicable	55(16.3)	55(19.6)	0(0)

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

Never in labour

In 2020, the proportion of mothers who were never in labour and whose infants underwent TH (n=17 of 76, 22.4%) was similar to the figures for 2016-2019 (n=60 of 281, 21.4%). A consistent trend since the onset of data collection in 2016 again revealed in 2020 a slightly higher proportion of parous mothers (n=9 of 32, 28.1%) who were never in labour compared to nulliparous mothers (n=8 of 44, 18.2%).

The indication for admission to the hospital was recorded for all 17 mothers in 2020.

- 47% of mothers who were never in labour were admitted following a non-reassuring CTG (n=8 of 17, 47.1%),
- 17% of women were admitted with a query of pain (n=3 of 17, 17.6%),
- 12% of women had antepartum haemorrhage (n=2 of 17, 11.8%).
- The remaining four mothers were admitted due to cord prolapse (n=1), prolonged spontaneous rupture of membranes (n=1), oligohydramnios (n=1) and hypertensive disorders (n=1).

Fetal heart monitoring

Fetal heart monitoring was undertaken for 72 of the 76 mothers whose infants underwent TH in 2020 (94.7%). The method of fetal heart monitoring was documented for all 72 mothers (100%). As illustrated in Table 18, external continuous fetal heart monitoring was the most common method of monitoring used during labour (n=61 of 72, 84.7%). More than half of all mothers who had fetal monitoring undertaken had external intermittent fetal heart monitoring (n=41 of 72, 56.9%) and of these mothers, the majority also underwent external continuous fetal heart monitoring during labour (n=30 of 72, 41.7%).

Table 18: Method of fetal heart monitoring for infants who underwent TH in 2016-2020

				Nulliparous		Parous	
	Total N=314	2016-2019 N=240	2020 N=72	2016-2019 N=154	2020 N=44	2016-2019 N=86	2020 N=32
External continuous	257(81.3)	196(81.7)	61(80.3)	132(85.7)	35(79.5)	64(74.4)	26(81.3)
External intermittent	146(46.2)	105(43.8)	41(53.9)	64(41.6)	21(47.7)	41(47.7)	20(62.5)
Internal continuous	27(8.5)	23(9.6)	4(5.3)	13(8.4)	4(9.1)	10(11.6)	0(0)

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

Data on cardiotocography (CTG) was interpreted for 30 cases. Of them, 25 were TH cases and 5 were controls. Of the 25 cases, 75% were interpreted as pathological (n=20), 15% were undetermined (n=3), 5% were interpreted as suspicions (n=1) and another 5% as non-pathological (n=1). Of the 5 controls, 60% were interpreted as pathological, and 20% were interpreted as suspicious and non-pathological for each one (n=20, respectively).

Delivery

Time of Day

Information on both the day and time of birth was available for all 76 infants who underwent TH in 2020. The timing of birth was categorised between 08:00 and 19:59 hours and 20:00 and 07:59hrs. As illustrated in Figure 2, almost 59% of births happened between 20:00 and before 07:59 (n=45 of 76, 59.2%).

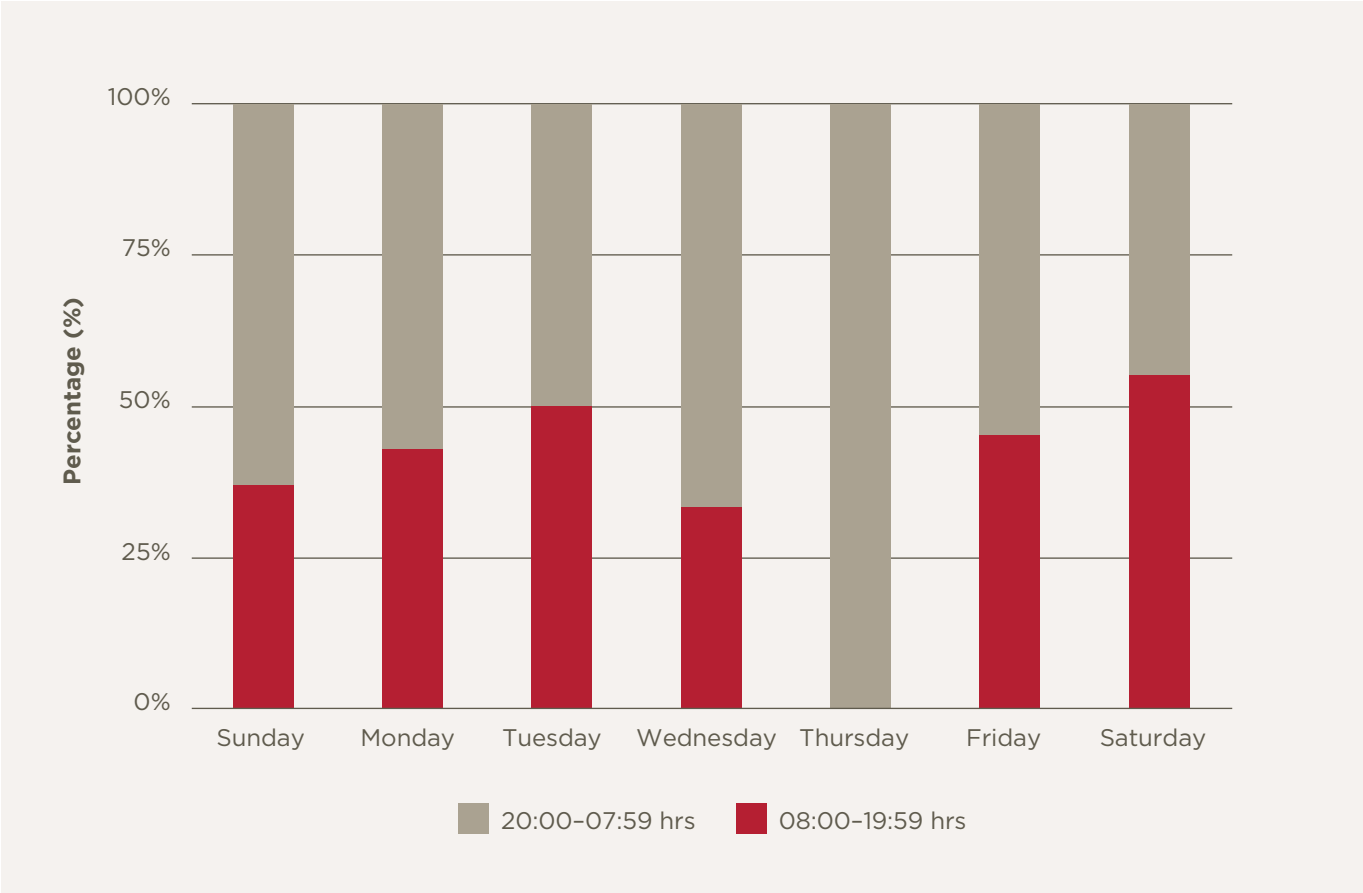


Figure 2: Day of week and time of birth (08:00 – 19:59 and 20:00 – 07:59) for infants who underwent TH in 2020

Presentation at delivery was known for 100% of mothers who laboured before delivery (n=59 of 76, n=25 for spontaneous deliveries and n=34 for induction of labour). The majority of presentations at delivery were vertex presentations (n=57 of 59, 96.6%), in one case the presentation was breech (n=1 of 59, 1.7%), and in the last case the presentation was compound (i.e. includes transverse and shoulder presentations; n=1 of 59, 1.7%).

Mode of delivery was known for all mothers (n=76) whose infants underwent TH in 2020 (Table 19). Caesarean section was the most common mode of delivery for all 76 of these infants (n=33 of 76, 43.4%). One in five of infants had a spontaneous vaginal delivery (n=20 of 76, 26.3%), which is considerably lower than the proportion of vaginal deliveries of all births occurring in Ireland for 2016-2019 (51.4%). One third of the deliveries were instrumental (n=22 of 76, 28.9%), with two mothers who had a combination of a ventouse and a forceps delivery. The interval time from decision to the instrumental delivery was known in 18 of the 22 cases. The median interval time to delivery was 9.28 minutes and ranged from one to 41 minutes.

Table 19: Mode of delivery for mothers whose infants underwent TH in 2020 versus all births in 2016-2019*

	2020 N=76	Nulliparous N=44	Parous N=32		All births** 2016-2019 N(%)
Spontaneous Vaginal Cephalic	20(26.3)	12(27.3)	8(25)	**Vaginal birth+**	151,936 (51.4)
Spontaneous Vaginal Breech	1(1.3)	1(2.3)	0(0)		
Pre-labour Caesarean Section	17(22.4)	8(18.2)	9(28.1)	**Caesarean section++**	99,483 (33.6)
Caesarean Section*	16(21.1)	10(22.7)	6(18.8)		
Assisted breech	0(0)	0(0)	0(0)	**Assisted breech**	327 (0.1)
Ventouse**	19(25)	11(25)	8(25)	**Ventouse**	33,116 (11.2)
Forceps	5(6.6)	3(6.8)	2(6.3)	**Forceps**	10,891 (3.7)

Note: Values are N(%) unless otherwise stated. Categories are not mutually exclusive. *Two mothers had a caesarean section following failed instrumental deliveries in 2020. Two mothers who had a ventouse delivery, also had a forceps delivery in 2020. **All birth data are based on HIPE data and therefore relate to all mothers who gave birth in hospital rather than all births. The value for forceps includes mothers whose delivery involved both Ventouse and forceps. +Vaginal births in this category include mothers who had both a Spontaneous Vaginal Cephalic and a Spontaneous Vaginal Breech delivery. ++Caesarean section in this category includes mothers who had a pre-labour caesarean section as well as mothers who had a caesarean section after the onset of labour.

The type of caesarean section was documented for 32 of 33 mothers (Table 20). There were no elective caesarean sections in 2020 for this cohort of mothers. Emergency caesarean section delivery was the most common type of caesarean section delivery, accounting for 62.5% (n=20 of 32). Of the mothers who had an emergency caesarean section delivery, 60.0% (n=12 of 20) were pre-labour and 40.0% (n=8 of 20) occurred after the onset of labour.

Table 20: Type of caesarean section delivery for mothers whose infants underwent TH in 2020*

	Total N=32	Nulliparous N=18	Parous N=14
Elective – planned	0(0)	0(0)	0(0)
Urgent – maternal or fetal compromise which is not immediately life threatening	12(37.5)	7(38.9)	5(35.7)
Emergency – immediate threat to life of woman or fetus	20(62.5)	11(61.1)	9(64.3)

*Missing information for one mother in 2020.

For mothers who had their labours induced (n=34), almost half had an instrumental delivery (n=16 of 34, 47.1%). As outlined in Table 21, induced parous mothers were as likely to deliver vaginally as nulliparous women (n=4 of 15, 26.7% versus n=5 of 19, 26.3%). These findings differ from 2019 data which showed that induced parous mothers were twice as likely to deliver vaginally compared to induced nulliparous mothers (n=4 of 10, 40.0% versus n=3 of 16, 18.8%).

Table 21: Mode of delivery for mothers who were induced whose infants underwent TH in 2020

	Total N=34	Nulliparous N=19	Parous N=15
Vaginal delivery	9(26.5)	5(26.3)	4(26.7)
Vaginal breech delivery	1(2.9)	1(5.3)	0(0)
Caesarean Section*	9(26.5)	5(26.3)	4(26.7)
Ventouse**	12(35.3)	6(31.6)	6(40)
Forceps	4(11.8)	3(15.8)	1(6.7)

Note: Values are N(%) unless otherwise stated. Categories are not mutually exclusive. *One mother had a caesarean section following failed instrumental deliveries in 2020. **One mother who had a ventouse delivery, also had a forceps delivery in 2020.

Labour Events

Sentinel Events

Of the mothers in 2020 who delivered a baby requiring TH intervention, 26.3% (n=20) experienced a sentinel event as described in Table 22.

Table 22: Sentinel events for mothers whose infants underwent TH in 2020

	2016-2019 N=281	2020 N=76
Shoulder dystocia	36(16.5)	6(7.9)
Placental Abruption	36(16.5)	6(7.9)
Uterine Rupture	9(4.1)	3(3.9)
Cord Prolapse	32(14.7)	5(6.6)

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

Recurring Factors

Induction and instrumental delivery were the most common recurring factors, followed by maternal pyrexia and meconium aspiration in 2020 as per Table 23.

Table 23: Recurring factors for mothers whose infants underwent TH in 2020

	2016-2019 N=281	2020 N=76
Maternal pyrexia in labour	36(12.8)	7(9.2)
Prolonged rupture of membranes	26(9.3)	1(1.3)
Meconium aspiration	19(6.8)	8(10.5)
Subgaleal haematoma	4(1.4)	5(6.5)
Spontaneous premature labour	1(0.4)	0(0)
Birth trauma	1(0.4)	0(0)
Instrumental Delivery	92(32.7)	22(28.9)
Induction	97(34.5)	34(44.7)
Other	7(2.5)	6(7.8)

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

Shoulder dystocia infants

Shoulder dystocia was reported as affecting the delivery of six of the 76 infants (7.9%) who received TH in 2020, which is the lowest incidence compared to previous years. In total, shoulder dystocia was associated with the delivery of 42 of the 357 infants (11.8%) who received TH in 2016-2020.

According to HIPE data for 2016-2020, shoulder dystocia was recorded for 2,278 (0.8%) of the 295,753 women who gave birth in hospital. Based on these data, the risk of an infant receiving TH was 18.4 (95% CI=13.3-24.9) per 1,000 women if the delivery was affected by shoulder dystocia compared to 1.1 (95% CI=1.0-1.2) per 1,000 women if there was no reported should dystocia, a 17-fold difference (Risk ratio=17.18, 95% CI=12.45-23.70, p-value<0.001).

Table 24 details maternal, infant and delivery characteristics for the 42 cases of TH associated with shoulder dystocia compared to the other 315 cases during 2016-2020. Cases associated with shoulder dystocia were similar to other cases with respect to maternal age (p-value=0.752) and mode of delivery (p-value=0.436). The most significant

differences were observed in relation to induction of labour (59.5% vs. 33.7%; p-value=0.001) and birthweight (54.8% ≥4kg vs. 11.7%, p-value<0.001; 33.3% ≥90th centile vs. 8.9%, p-value<0.001).

The most common manoeuvre utilised for deliveries with shoulder dystocia was a combination of McRoberts and suprapubic pressure (n=29 of 42, 69.0%). Thirty four of the 42 mothers had an instrumental delivery (81.0%). Time between decision to use instrumentation and delivery of the baby was recorded for the TH cases with shoulder dystocia in 2020. The median time was 31.8 minutes, and the range was 18-63 minutes.

Table 24: Maternal, infant and delivery characteristics for deliveries with and without shoulder dystocia 2016-2020

Characteristic	Cases with shoulder dystocia in 2020 N=6	Cases without shoulder dystocia in 2020 N=70	Cases with shoulder dystocia in 2016-2020 N=42	Cases without shoulder dystocia in 2016-2020 N=315
Age Group				
<30yrs	2(33.3)	20(28.6)	12(28.6)	90(28.6)
30-34yrs	4(66.7)	25(35.7)	18(42.9)	113(35.9)
35-39yrs	0(0)	16(22.9)	10(23.8)	85(27)
>40yrs	0(0)	9(12.9)	2(4.8)	26(8.3)
BMI Category (kg/m²)				
Underweight (<18.5)	0(0)	1(1.4)	0(0)	4(1.3)
Healthy (18.5-24.9)	3(50)	23(32.9)	11(26.2)	123(41)
Overweight (25.0-29.9)	1(16.7)	26(37.1)	13(31)	92(30.7)
Obese (≥30.0)	2(33.3)	20(28.6)	18(42.9)	81(27)
Parity				
Nulliparous	3(50)	41(58.6)	28(66.7)	182(57.8)
Parous	3(50)	29(41.4)	14(33.3)	133(42.2)
Induction of labour	4(66.7)	30(42.9)	25(59.5)	106(33.7)
Mode of delivery				
Spontaneous vaginal cephalic	1(16.7)	19(27.1)	8(19)	79(25.1)
Instrumental delivery	5(83.3)	18(25.7)	34(81)	202(64.1)
Caesarean section	0(0)	33(47.1)	0(0)	33(10.5)
Manoeuvres				
McRoberts	4(66.7)	0(0)	8(19)	-
McRoberts and suprapubic pressure	4(66.7)	0(0)	29(69)	-
Other*	6(100)	0(0)	15(35.7)	-
Birthweight (grams)				
<3000	0(0)	26(37.1)	1(2.4)	99(31.4)
3000-3499	0(0)	21(30)	4(9.5)	91(28.9)
3500-3999	3(50)	13(18.6)	14(33.3)	88(27.9)
≥4000	3(50)	10(14.3)	23(54.8)	37(11.7)
Birthweight centile				
<10th	0(0)	14(20)	0(0)	63(20.1)
10-49th	0(0)	30(42.9)	10(23.8)	130(41.4)
50-89th	2(33.3)	17(24.3)	18(42.9)	93(29.6)
≥90th	4(66.7)	8(11.4)	14(33.3)	28(8.9)
Total	6(100)	70(100)	42(100)	315(100)

Note: Values are shown as N(%) unless otherwise stated. Maternal age, body mass index (BMI) and mode of delivery were not recorded for one, 15 and one case, respectively in 2019. *Other types of manoeuvres include suprapubic only (n=5) and rubin (n=1). Categories are not mutually exclusive.

Infant characteristics

Half of the infants who received TH in 2020 were female (n=38 of 76, 50.0%). In the overall population of births from 2016 to 2020, 51.3% were male and 48.7% female (Table 25). There were three infants who underwent TH from multiple births in 2020 (3.9%).

Table 25: Sex of infants who underwent TH in 2016-2020

	2016-2019 N=357	2020 N=76	All births 2016-2020 (%) N=278,460
Male	158(56.2)	38(50)	51.30
Female	123(43.8)	38(50)	48.70

Note: Values are shown as N(%) unless otherwise stated. Population data for all births in Ireland from the National Census in 2016-2020 [27]

Gestation at delivery

Figure 3 outlines the gestational age at delivery for infants who underwent TH in 2020 versus all infants born from 2016-2019.[28] Almost two thirds of infants were born between 36 and 39 completed weeks of gestation in 2020 (n=46 of 76, 60.5%).

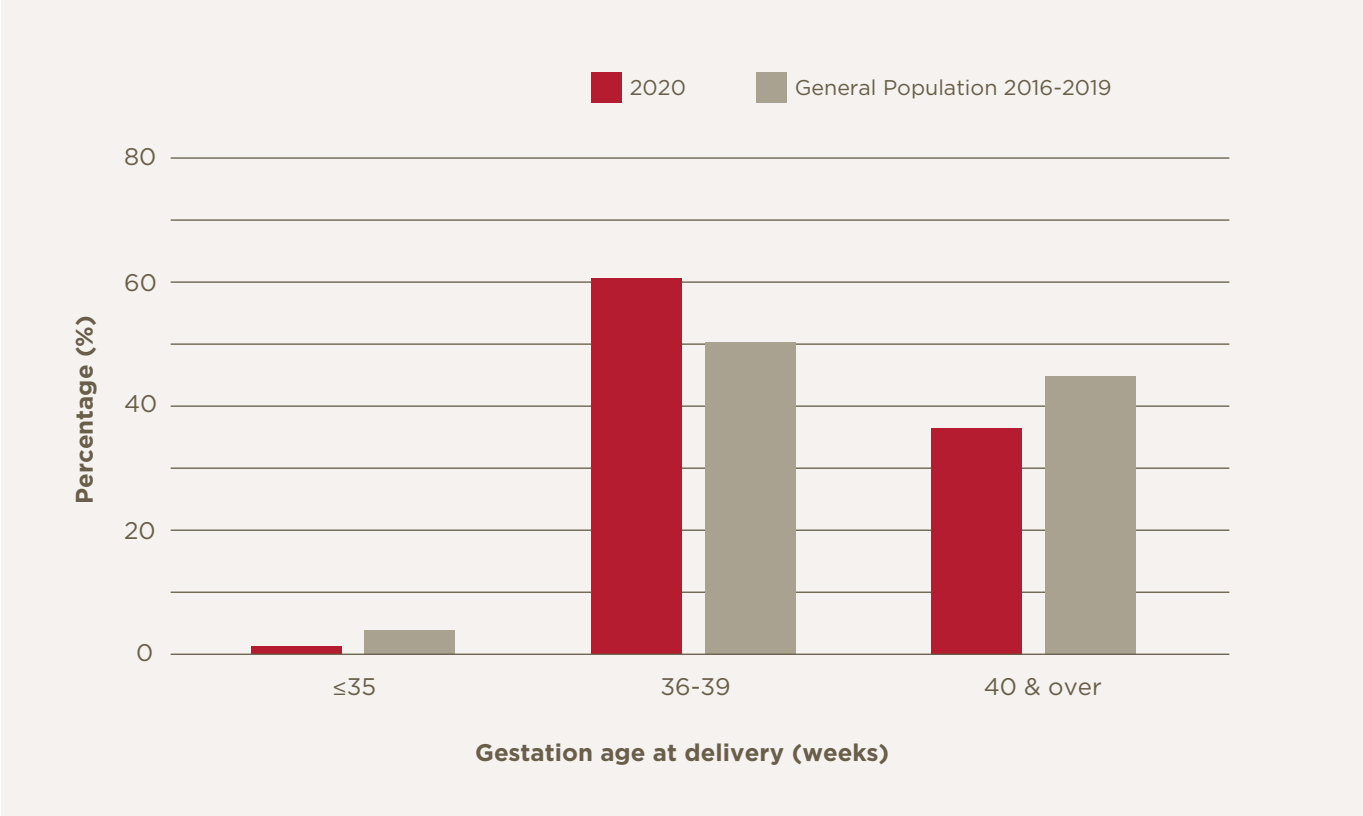


Figure 3: Gestational age at delivery (weeks) for infants who underwent TH in 2020 versus all infants born in 2016-2019

Birthweight at delivery

The mean birthweight for infants who underwent neonatal TH in 2020 was 3,353 grams (Standard Deviation: 76.5 grams). The birth weight ranged from 2,050 grams to 4,920 grams.

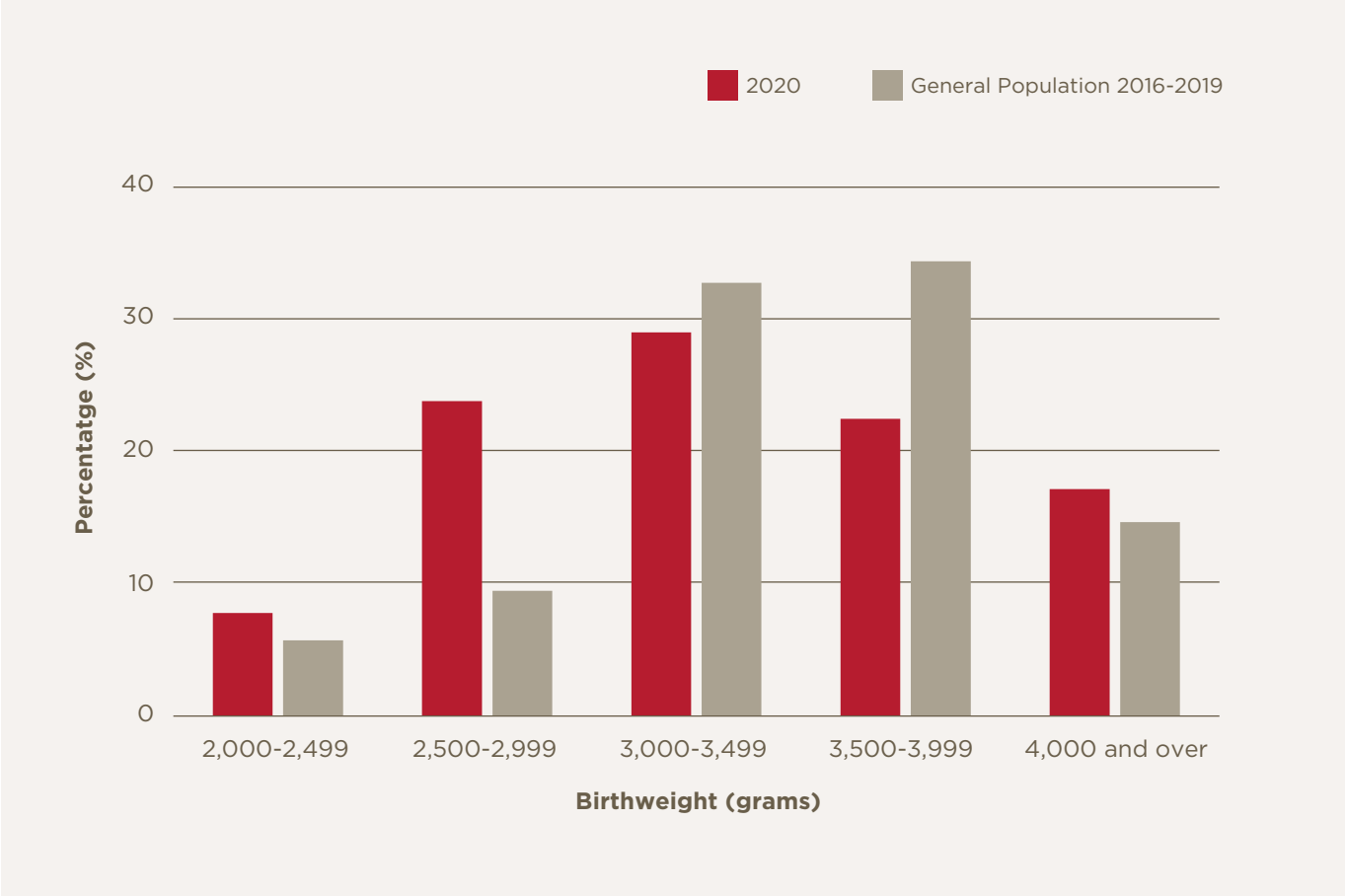


Figure 4: Distribution of birthweight for infants who underwent TH in 2020 versus all infants born in 2016-2019.[28]

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,[29] was used to produce Figure 5 which illustrates the optimal birthweight and normal range compared to the recorded birthweights of infants who underwent neonatal TH in 2020.

The optimal weight and normal range for all gestations are plotted with the actual birthweights of the infants in Figure 6.

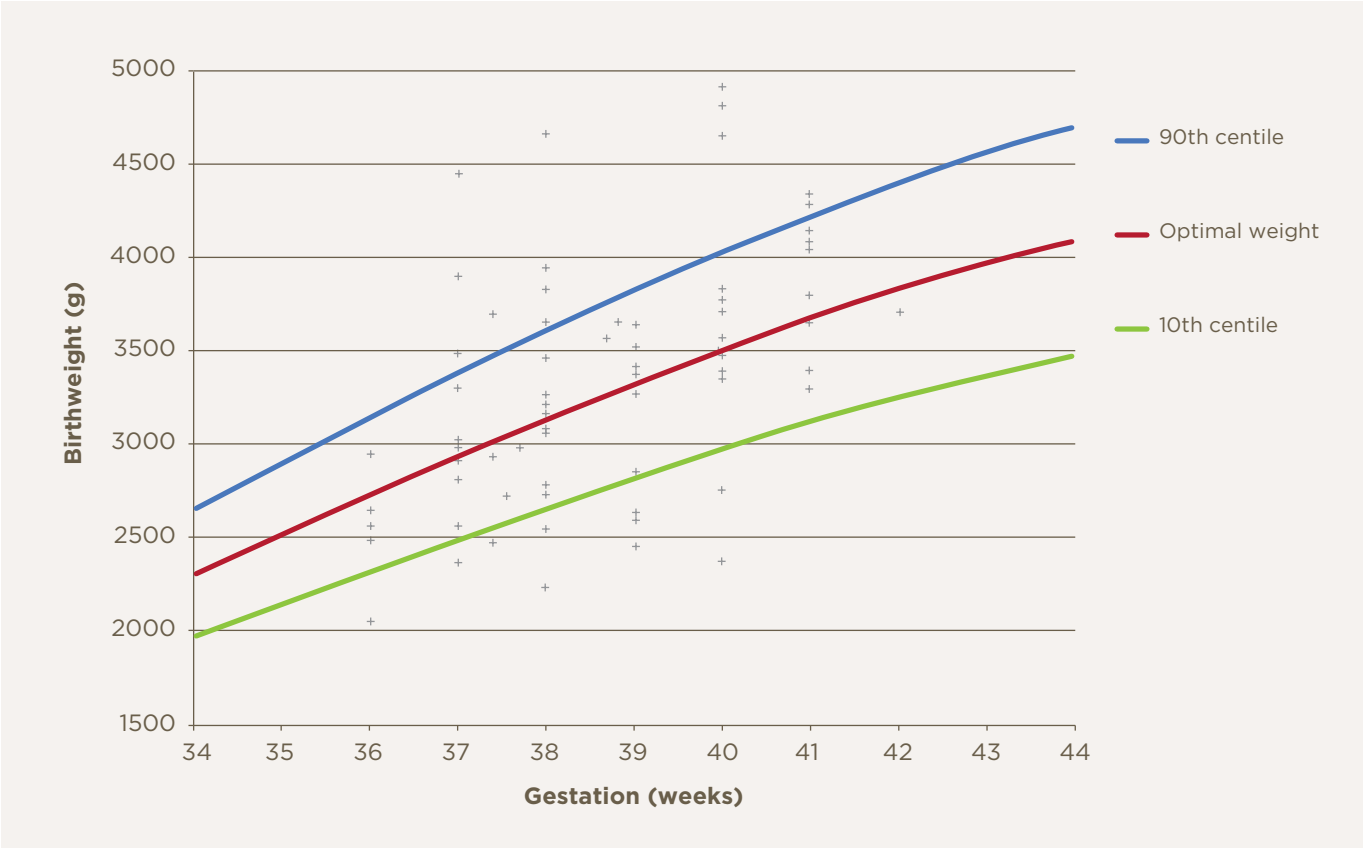


Figure 5: Optimal birthweight and normal range compared to actual birthweights for infants who underwent TH in 2020

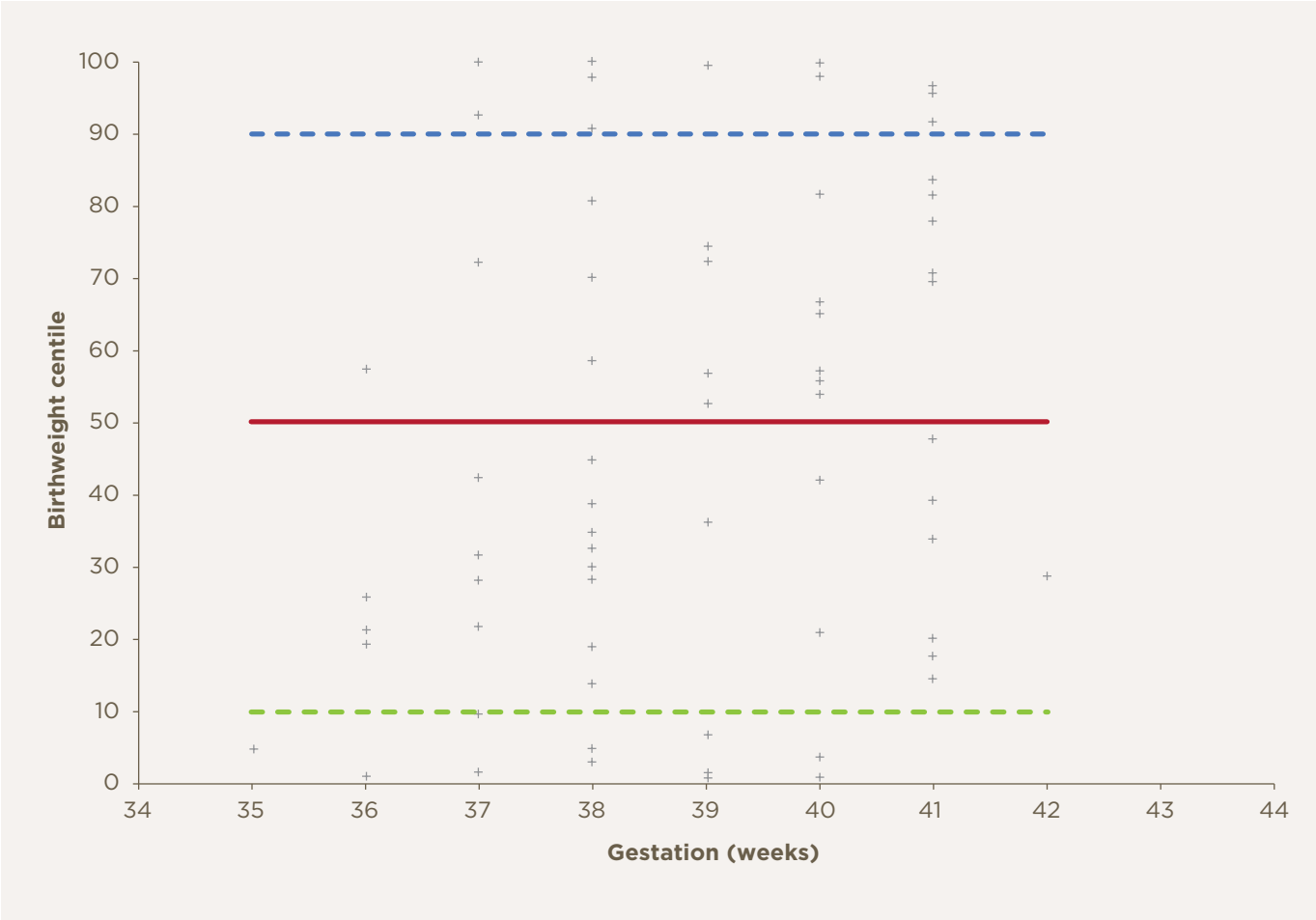


Figure 6: Distribution of customised birthweight centiles for infants who underwent TH in 2020

As can also be seen in Table 26, 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=14 of 75, 18.6%) in 2020 and (n=49 of 281, 17.4%) in 2016-2019 were below the 10th centile.

Table 26: Birth weight centiles for infants who underwent TH in 2016-2020*

Centiles	2016-2019 N=281	2020 N=75
<3rd	15(5.3)	8(10.7)
3rd to 9th	34(12.1)	6(8)
10-49th	112(39.9)	30(40)
50-89th	90(32)	19(25.3)
>90th	30(10.7)	12(16)

Note: Values are shown as N(%) unless otherwise stated. *Missing information for one infant in 2020.

Based on the four years of data from 2016-2019, there was significant variation in risk of TH associated with birthweight centile (Table 27). Infants with a birthweight in the 50-89th centile range had the lowest risk of TH, at 0.9 per 1,000 births. The risk was 30% and 54% higher among infants in the 10-49th and >90th birthweight centile ranges, respectively, but the risk was doubled for infants with a birthweight under the 10th centile.

Table 27: Birth weight centiles for infants who underwent TH in 2016-2020

Centiles	2020 N=75	2016-2020 N=356	Rate (95% CI)	Rate ratio (95% CI)	P-value
<3rd	8(10.7)	23(6.5)	2.54 (1.61-3.81)	2.81 (1.79-4.41)	<0.001
3rd to 9th	6(8)	40(11.2)	1.89 (1.35-2.58)	2.1 (1.46-3.01)	<0.001
10-49th	30(40)	142(39.9)	1.18 (0.99-1.39)	1.3 (1.02-1.67)	0.028
50-89th	19(25.3)	109(30.6)	0.9 (0.74-1.09)	1.00 (ref.)	-
>90th	12(16)	42(11.8)	1.39 (1-1.88)	1.54 (1.08-2.2)	0.017

Note: Values are shown as N(%) unless otherwise stated. *Missing information for one infant in 2020.

Diagnosis of fetal growth restriction (FGR)

There were 14 (18.4%) infants who underwent TH in 2020 born with a birth weight below the 10th centile (Table 26). Nine (11.8%) of the 76 infants in 2020 had a diagnosis of FGR in their medical records. For eight of them, the diagnosis was made in the antenatal period (n=8 of 9, 88.9%, Table 28).

Table 28: Diagnosis of fetal growth restriction for infants who underwent TH in 2016-2020

	2016-2019* N=206	2020 N=76
No diagnosis documented	190(92.2)	67(88.2)
Diagnosis of fetal growth restriction	16(7.8)	9(11.8)
Fetal growth restriction suspected antenatally	9(4.4)	8(10.5)

Note: Values are shown as N(%) unless otherwise stated. Percentage of infants with fetal growth restriction suspected antenatally or postnatally based on total number of infants with a diagnosis of fetal growth restriction.
*Missing data for three infants in 2017.

Resuscitation

As outlined in Table 29, in the vast majority of births there was paediatric support present at resuscitation in 2020.

Table 29: Medical staff present for the resuscitation of infants who underwent TH in 2016-2020

	2016-2019* N=277	2020 N=76
Consultant (Neonatology/Paediatrics)	105(37.9)	27(35.5)
Registrar	253(91.3)	63(82.9)
Senior House Officer	235(84.8)	64(84.2)
Neonatal Nurse	123(44.4)	37(48.7)
Midwife	60(21.7)	21(27.6)

Note: Values are shown as N(%) unless otherwise stated. *Data missing for two infants in 2016, one infant for 2018, and one infant for 2019. Categories are not mutually exclusive. These data should be interpreted with caution as documentation related to the grade of those in attendance was poorly recorded in maternity notes.

In 2020, the majority of infants had positive pressure ventilation (PPV) during resuscitation (n=61 of 75, 81.3%, data missing for one infant) which began between 20 seconds and four minutes and was sustained between 30 seconds and six hours and 30 minutes. Spontaneous breathing was established by almost half of infants (n=34 of 75, 45.3%). Of these infants, the age at which spontaneous breathing was sustained was recorded for 28 of the 34 infants (66.3%) and began between zero and 14 minutes (mean 5 minutes).

As illustrated in Table 30, 58.7% of the 75 infants were intubated (n=44) which occurred between 1 and 19 minutes. One third of infants had chest compressions (n=21, 28.0%), which began between 0 and 14 minutes (data missing for four infants). FiO2 was administered to the majority of infants (n=71, 94.7%).

Table 30: Resuscitation for infants who underwent TH in the years 2016-2020

	2016-2019 N=281	2020* N=75
Positive pressure ventilation*	66(23.5)	61(81.3)
Spontaneous breathing established	143(50.9)	34(45.3)
Intubation	169(60.1)	44(58.7)
Chest compressions	98(34.9)	21(28)
FiO2	254(90.4)	71(94.7)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive. Information about positive pressure ventilation was not collected until 2019; therefore, this data is for 2019 only. *Data missing for one infant in 2020.

As illustrated in Table 31, 26% of the 76 infants who underwent TH had saline as a fluid treatment administered at birth in 2020 (n=20). Adrenaline was administered for almost 12% of the infants (n=9 of 76), and only two infants had O negative blood.

Table 31: Drugs or fluid treatment administered at birth for infants who underwent TH in 2016-2020

	2016-2019 N=281	2020 N=76
Adrenaline	42(14.9)	9(11.8)
Saline	70(24.9)	20(26.3)
O negative blood	19(6.8)	2(2.6)

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

As indicated in Table 32, at one minute after birth almost three quarters of infants (n=53 of 74, 71.6%) had an Apgar score of between zero and three in 2020. At ten minutes, the proportion of infants with an Apgar score of between zero and three had reduced to 18.3% (n=11 of 60). At twenty minutes, only six infants had an Apgar score recorded; only one infant had a score lower than three (16.7%).

Table 32: Apgar Scores at 1, 5, 10, 15 and 20 minutes for infants who underwent TH in 2020

	1 minute N=74	5 minutes N=74	10 minutes N=60	15 minutes N=23	20 minutes N=6	Total N=237
0	11(14.9)	6(8.1)	4(6.7)	2(8.7)	0(0)	23(9.7)
1	19(25.7)	7(9.5)	0(0)	0(0)	1(16.7)	27(11.4)
2	13(17.6)	7(9.5)	2(3.3)	0(0)	0(0)	22(9.3)
3	10(13.5)	9(12.2)	5(8.3)	0(0)	0(0)	24(10.1)
4	9(12.2)	16(21.6)	10(16.7)	5(21.7)	1(16.7)	41(17.3)
5	2(2.7)	6(8.1)	7(11.7)	1(4.3)	0(0)	16(6.8)
6	5(6.8)	9(12.2)	13(21.7)	6(26.1)	1(16.7)	34(14.3)
7	3(4.1)	6(8.1)	6(10)	6(26.1)	2(33.3)	23(9.7)
8	1(1.4)	6(8.1)	9(15)	2(8.7)	0(0)	18(7.6)
9	1(1.4)	2(2.7)	3(5)	1(4.3)	1(16.7)	8(3.4)
10	0(0)	0(0)	1(1.7)	0(0)	0(0)	1(0.4)

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

An Apgar chart was completed for 69.7% (n=53) of infants at one and five minutes; for 55.3% (n=42) of infants at 10 minutes of life, for 25.0% (n=19) of infants at 15 minutes of life, and 7.9% (n=6) of infants at 20 minutes of life (Table 33).

Table 33: Apgar Charts at 1, 5, 10, 15 and 20 minutes for infants who underwent TH in 2020

		1 minute N=53	5 minutes N=53	10 minutes N=42	15 minutes N=19	20 minutes N=6
Heart rate	Absent	9(17)	5(9.4)	3(7.1)	3(15.8)	1(20)
	<100	23(43.4)	10(18.9)	2(4.8)	0(0)	1(20)
	<100	21(39.6)	38(71.7)	37(88.1)	16(84.2)	3(60)
	Total	53	53	42	19	5
Respiration effort	Absent	36(67.9)	26(49.1)	10(23.8)	6(33.3)	3(75)
	Slow irregular	16(30.2)	23(43.4)	25(59.5)	8(44.4)	0(0)
	Regular crying	1(1.9)	4(7.5)	7(16.7)	4(22.2)	1(25)
	Total	53	53	42	18	4
Muscle tone	Limp	42(79.2)	34(64.2)	18(42.9)	10(55.6)	3(75)
	Some flexion	11(20.8)	19(35.8)	21(50)	8(44.4)	0(0)
	Active Movement	0(0)	0(0)	3(7.1)	0(0)	1(25)
	Total	53	53	42	18	4
Stimulus catheter	Nil	35(67.3)	26(50)	14(34.1)	7(38.9)	5(83.3)
	Grimace	13(25)	20(38.5)	19(46.3)	9(50)	0(0)
	Cough/sneeze	4(7.7)	6(11.5)	8(19.5)	2(11.1)	1(16.7)
	Total	52	52	41	18	6
Colour	Nil	33(62.3)	12(22.6)	5(11.9)	4(21.1)	4(66.7)
	Pink body, blue extremities	19(35.8)	28(52.8)	18(42.9)	6(31.6)	1(16.7)
	Pink	1(1.9)	13(24.5)	19(45.2)	9(47.4)	1(16.7)
	Total	53	53	42	19	6

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

One of the key indicators for intrapartum asphyxia is severe metabolic acidosis evident in umbilical cord blood at delivery.[30] A cord blood gas measurement was available for 84.2% of infants (n=64). An initial infant blood gas measurement was available for 88.2% of infants (n=67) in 2020.

Table 34: pH level from cord and initial infant blood gases for infants who underwent TH in 2020

	Cord Blood Gas			Initial Infant Blood Gas		
	Venous N=60	Capillary N=59	Unknown N=1	Venous N=46	Capillary N=16	Arterial N=12
pH level						
<=6.5	0(0)	0(0)	0(0)	2(4.3)	0(0)	0(0)
6.51-6.6	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
6.61-6.7	2(3.3)	4(6.8)	0(0)	2(4.3)	0(0)	0(0)
6.71-6.8	9(15)	10(16.9)	1(100)	2(4.3)	3(18.8)	1(8.3)
6.81-6.9	2(3.3)	11(18.6)	0(0)	6(13)	1(6.3)	2(16.7)
6.91-7.0	5(8.3)	10(16.9)	0(0)	11(23.9)	6(37.5)	2(16.7)
7.01-7.1	8(13.3)	9(15.3)	0(0)	14(30.4)	4(25)	2(16.7)
7.11-7.2	17(28.3)	11(18.6)	0(0)	8(17.4)	2(12.5)	4(33.3)
7.21-7.3	15(25)	4(6.8)	0(0)	1(2.2)	0(0)	1(8.3)
7.31-7.4	2(3.3)	0(0)	0(0)	0(0)	0(0)	0(0)

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

Assessment for TH

In almost three-quarters of cases the NNTP Cooling Candidacy Checklist was used when making an assessment for TH in 2020 (n=56 of 76, 73.7%). More than 80% of the mothers, whose infants underwent TH in 2020, were recorded as experiencing an acute perinatal event (n=61 of 76, 80.3%, Table 35).

Table 35: Assessment for TH in 2020

	TH cases 2020 N=76
>36 completed weeks gestational age	**74(97.4)**
Apgar score ≤5 at 10 minutes	29(42)
Weight ≥1800 grams	76(100)
Continued need for PPV or Intubation at 10 mins	43(56.6)
Did an acute perinatal event occur?	**61(81.3)**
Variable / late fetal heart rate decelerations	51(67.1)
Prolapsed / ruptured / tight nuchal cord	5(6.6)
Uterine Rupture	3(3.9)
Maternal haemorrhage / placental abruption	6(7.9)
Maternal trauma	1(1.3)
Other	4(5.3)
Acidosis present in umbilical cord, or any blood sample within 60 minutes of birth	**44(57.9)**
Base Deficit >16.0 mmol/L in umbilical cord, or any blood sample, within 60 minutes of birth	**41(54.7)**

Note: Values are shown as N(%) unless otherwise stated. Data missing for seven infants for Apgar scores, and for one infant for continued need for PPV and base deficit, respectively.

During assessment, the majority of the infants in 2020 (n=62 of 76, 81.6%) had a diagnosis of encephalopathy based on having an altered state of consciousness, (lethargy, stupor or coma). Of these, 69.4% (n=43) used the NNTP Cooling Candidacy Checklist to diagnose the encephalopathy. Although not a requirement for assessment, 34.9% (n=15) of infants were graded (See Table 36). Of the remaining infants, 62.8% (n=27) had a diagnosis of encephalopathy but were not graded (n=27 of 62, 43.5%).

Table 36: Grade of encephalopathy during assessment for therapeutic hypothermia in 2016-2019

	2016-2019 N=118	2020 N=15
Mild	13(11)	1(6.7)
Moderate	72(61)	7(46.7)
Severe	33(28)	7(46.7)

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

The NNTP Cooling Candidacy Checklist was not used for approximately 30% of infants (n=19 of 62, 30.7%), but a grade was given for seven infants (n=6 had a moderately grade of encephalopathy, and one had severe encephalopathy). Information in relation to grade of encephalopathy was not documented for the remaining 12 infants.

Transfer to Tertiary Unit

For reasons of safety and expertise, the provision of Neonatal TH by means of active servo-controlled cooling, is limited in Ireland to the four tertiary neonatal intensive centres. In order to ensure that infants born outside these centres are not delayed in accessing TH within the six-hour window, TH in Ireland is delivered by way of a continuum of care between the referring hospital, transport team and tertiary TH centre.

Utilising national guidelines and documentation,[31] TH by means of passive (or active) cooling is commenced at the referring hospital as soon as the criteria for cooling have been met.[31] The time the target temperature is reached is recorded. TH via passive cooling can then be continued during transport by own hospital teams or in those cases transported by the NNTP, utilising active servo-controlled cooling. On arrival at the tertiary centre TH via active cooling is either continued from an NNTP transfer or initiated after an own hospital transfer.

Just over two-thirds of the 76 infants who underwent neonatal TH in 2020 were born in a tertiary hospital (n=52 of 76, 68.4%, Table 37). The other 24 infants required transfer to a tertiary unit for TH treatment (31.6%). Of the 24 infants who required transfer to a tertiary unit in 2020, the majority of them were transported by the NNTP (n=19 of 24, 79.2%) with the remaining five (20.8%) infants being transported by the referring hospital's team.

Of the 357 infants who received TH during the five-year period 2016-2020, 62.5% of the infants were born in a tertiary hospital (n=223 of 357). During the same period, according to HIPE data, 53% of all the mothers who gave birth in hospital did so in a tertiary hospital (n=156,278 of 295,753, 52.8%). Thus, TH was provided to 1.43 infants per 1,000 mothers who gave birth in a tertiary hospital (95% CI=1.25-1.63) and 0.98 infants per 1,000 mothers who gave birth in a non-tertiary hospital (95% CI=0.82-1.15), a 46% difference (Risk ratio=1.46, 95% CI=1.18-1.81, p-value<0.001). In 2020, there was a slight increase in the provision of TH, which appeared to be related to babies born in tertiary hospitals as there has been no increase for babies born in non-tertiary hospitals.

Table 37: Transfer of infants to a tertiary unit for TH treatment in 2020*

	2020 N=76
Inborn at tertiary unit	52(68.4)
Out-born requiring transfer*	24(31.6)
Transferred by the NNTP	19(79.2)
Transferred by referring hospital's team	5(20.8)

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

For the majority of infants who required transfer, a referral call was made to the tertiary cooling centre within two hours of birth in 2020 (n=16 of 24, 66.7%). The average time for transporting the infants from the referral centre to the tertiary centre was 1.5 hours (SD 33 minutes). The shortest transfer was 34 minutes long, and the longest transfer was 2 hours and 33 minutes.

All infants who were transferred to a tertiary centre in 2020, except one infant, were passively cooled initially (n=23 of 24, 95.8%). The decision to cool the infant, who was not passively or actively cooled at the referring centre, was made only upon arrival to the tertiary site. Passive cooling was initiated within the first hour of birth for almost 45% of infants (n=10 of 23, 43.5%, missing data for one infant), and within six hours for almost 90% of infants (n=20 of 23, 86.9%, data missing for one infant). Active cooling was initiated within six hours of birth for more than 80% of the infants (n=15 of 18, 83.3%).

As illustrated in Figure 7, 71% of the infants transferred had a core temperature within the target range of 33°C to 34°C on departure from the referring hospital (n=17 of 24, 70.8%), and 29% of infants (n=7 of 24, 29.2%) had a core temperature ranging from 34.1°C to 37.5°C.

Half of the infants were transferred within 6 hours of birth (n=12 of 24, 50.0%).

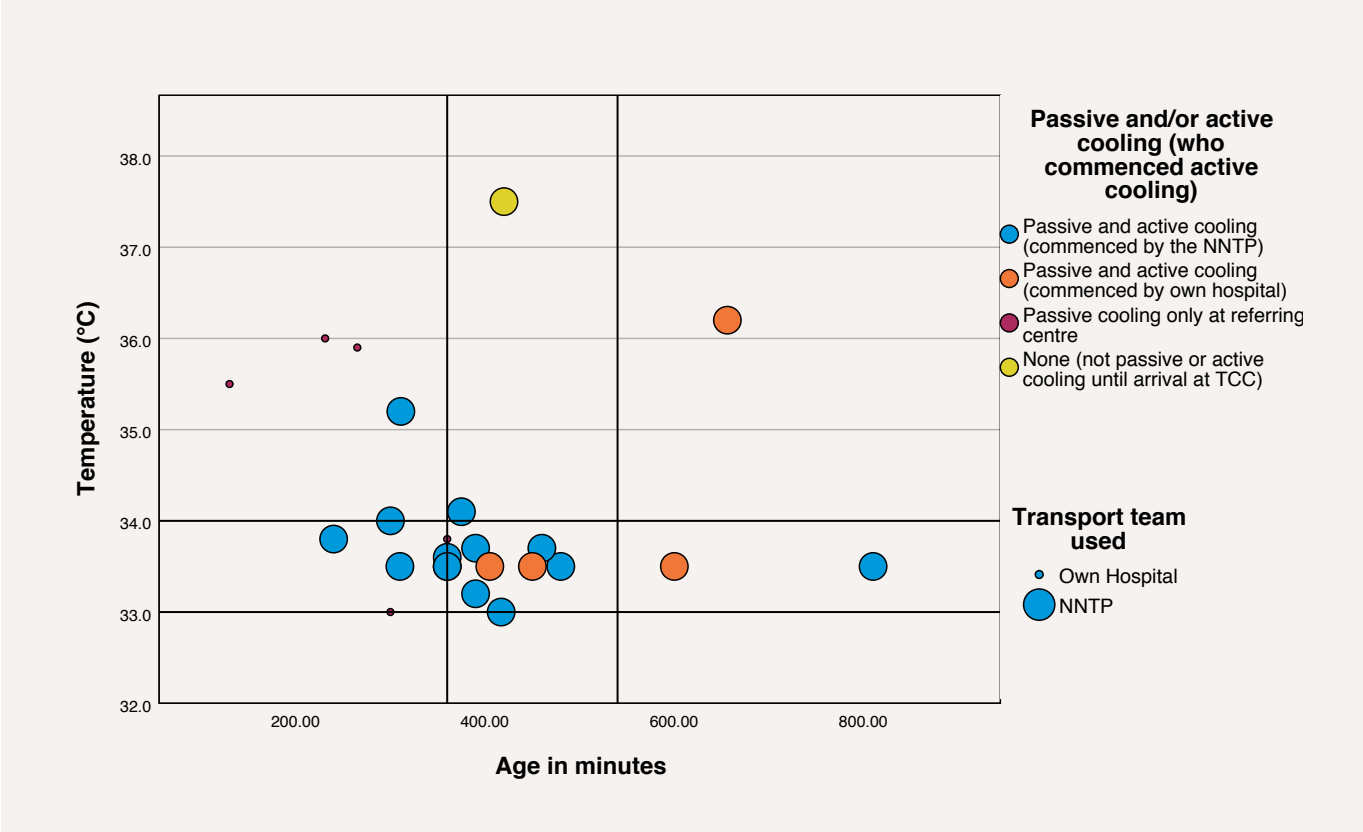


Figure 7: Temperature (°C) of infant by age (mins) on departure from referring hospital in 2020

Note: First vertical line refers to 360 mins which is equal to 6 hours and the second vertical line refers to 540 mins which is equal to 9 hours. Tertiary Care Centre (TCC). Two infants had the same temperature (33.5 °C) and age (360 mins) at departure from the referring centre, and therefore, the two points in the graph overlapped and it seems like it was only one point.

More than 90% of the 24 infants transferred for neonatal TH treatment required respiratory support (n=22, 91.7%), and two-thirds required sedation (n=17 of 24, 70.8%) in-route to the tertiary unit (Table 38).

Table 38: Management during transfer of infants for TH in 2020 (n=24)

	NNTP N=19	Own Hospital Team N=6
Respiratory support	**17(89.5)**	**5(83.3)**
Ventilation	14(82.4)	3(60)
CPAP	4(23.5)	1(20)
Nasal prong O_2	0(0)	1(20)
Sedation	**14(73.7)**	**3(50)**
IV access	**19(100)**	**5(83.3)**
Peripheral	19(100)	5(100)
Umbilical	12(63.2)	0(0)
Other*	1(5.3)	0(0)

Note: Values are shown as N(%) unless otherwise stated. *Other included radial arterial lines.

The average age for infants at admission to the tertiary unit was eight hours (Figure 8). More than 60% of infants requiring transfer for TH treatment were admitted to the tertiary centre between more than six hours and nine hours after birth (n=15 of 24, 62.5%).

As illustrated in Figure 8, the majority of infants had a core temperature within the target range of 33°C to 34°C (n=17 of 24, 70.8%) on admission to a tertiary unit. Among the remaining cases, 20.8% (n=5) had a core temperature ranging from 34.1°C to 37.4°C, and two infants had a core temperature below 33°C on admission to a tertiary unit from a referring hospital.

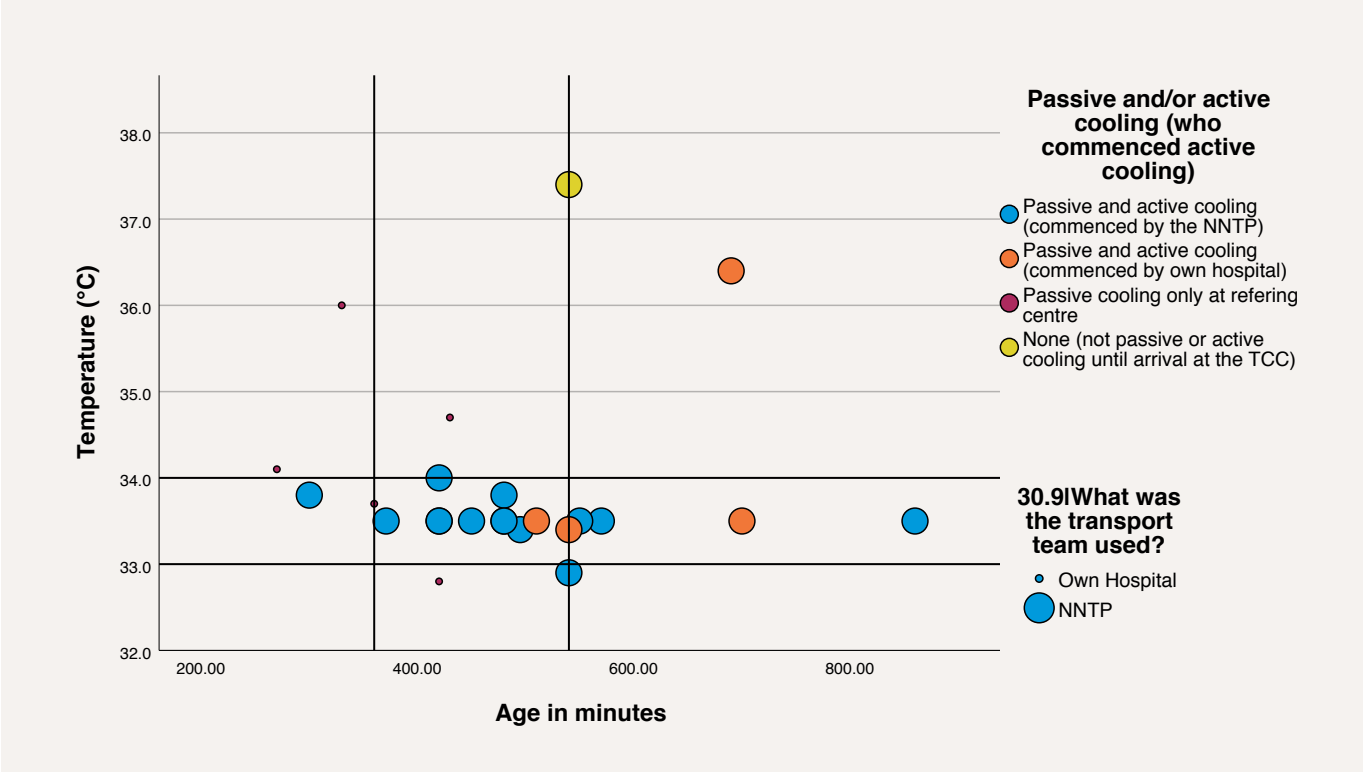


Figure 8: Temperature (°C) of infant by age (mins) on admission to a tertiary unit from a referring hospital

Note: First vertical line refers to 360 mins which is equal to 6 hours and the second vertical line refers to 540 mins which is equal to 9 hours. Tertiary Care Centre (TCC). Two infants had the same temperature (33.5 °C) and age (420 mins) at departure from the referring centre, and another two infants had the same temperature (33.5 °C) and age (480 mins). Therefore, there are four points in the graph which are overlapped and it seems like there are only two points.

Initiating Treatment

In line with practice guidelines, TH should be initiated within six 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. Core temperature was recorded for the first twelve hours of birth.

Figure 9 illustrates the average temperatures for the first twelve hours of life of TH infants at each hour. This shows that infants born in a tertiary hospital reached optimum core temperature (33.0-33.4C) sooner than infants that were outborn requiring transfer. Specifically, infants born in a tertiary hospital reached the targeted optimum core temperature at 3 hours compared to the six ours for the infants who were born in a regional hospital. This report also assessed the average age of the infants when they reached the target temperature. The average age for inborn infants, measured as time from birth (hh:mm), at when the target temperature (33.0-34.0C) was reached, was 4:26 hours (median: 4:00 hours) (SD=2:36) compared to the average age for outborn infants that was 11:07 hours (median: 11:23 hours) (SD=7:53). This difference was statistically significant p<0.001.

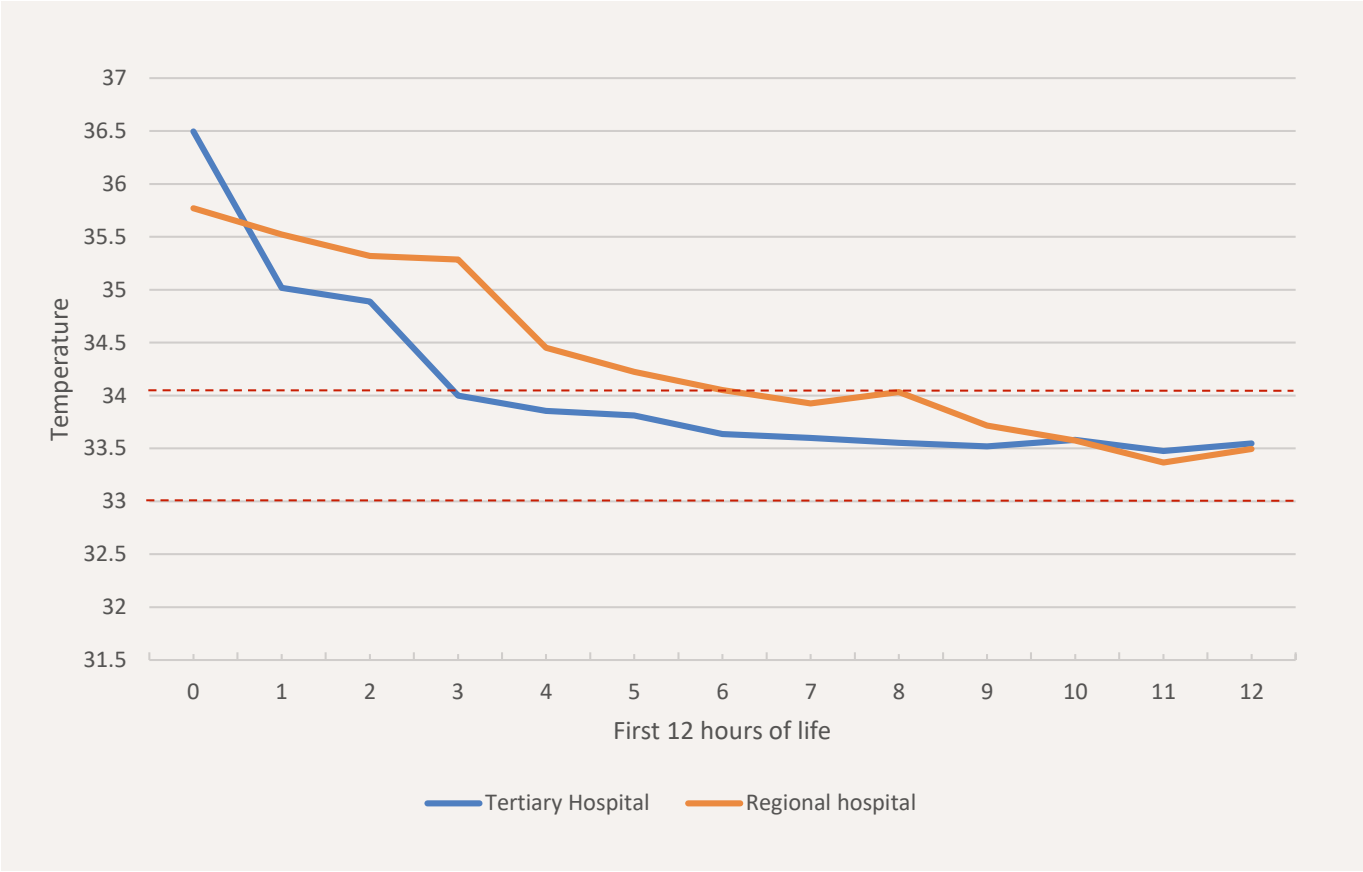


Figure 9: Infant core temperature for the first twelve hours of life for infants born in a tertiary hospital (inborn, n=52) compared to infants born in a regional hospital (outborn, n=24) in 2020

The 72-hour treatment clock should begin when the infant reaches the targeted 33-34°C rectal temperature. As illustrated in Figure 10, more than 70% of infants (n=53 of 73, 72.6%; data missing for three infants) began TH at the optimum core temperature of 33°C to 34°C, approximately 25% over the optimum core temperature (n=18 of 73, 24.7%), and two cases were below optimum core temperature (n=2 of 73, 2.7%).

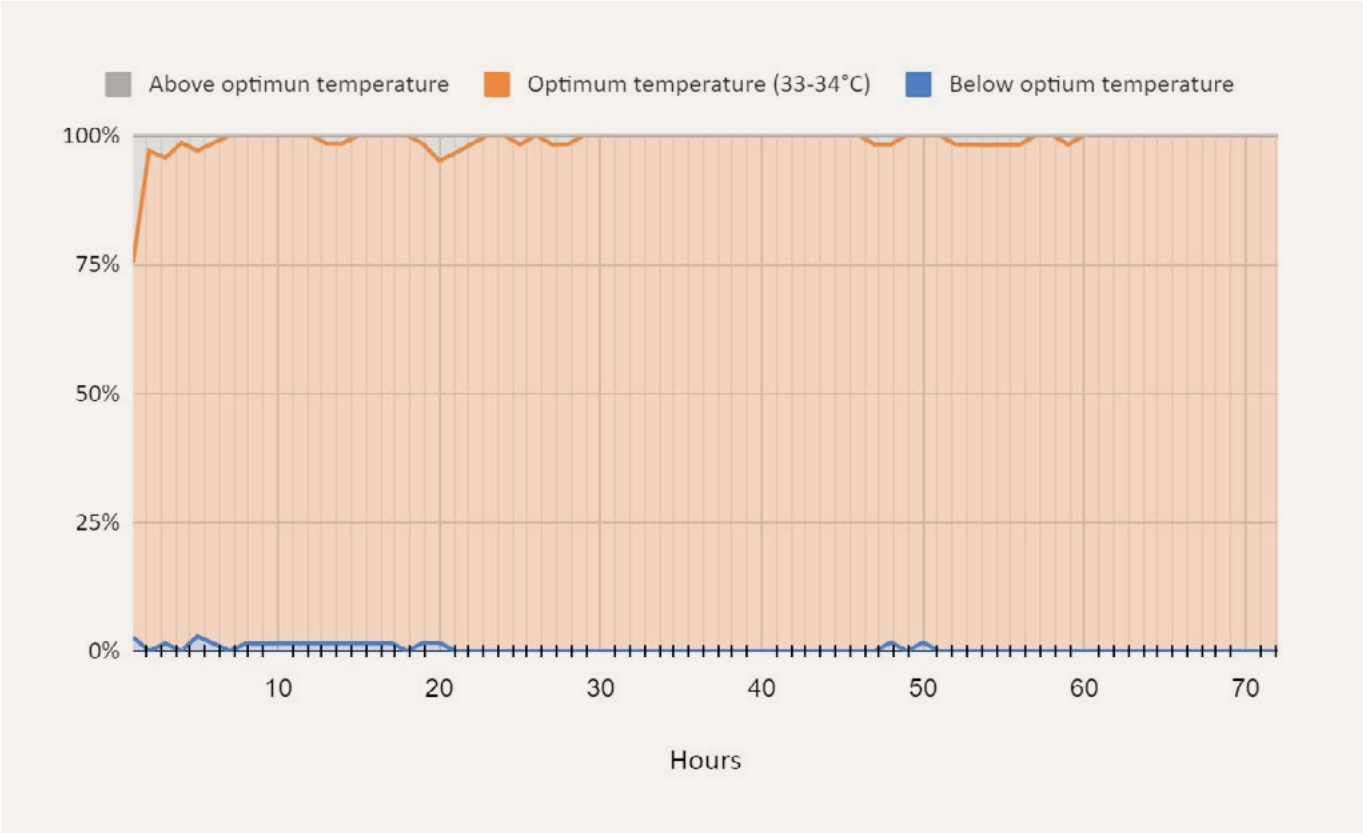


Figure 10: Percentage of infants at optimum temperature (33-34°C) over 72 hours of TH in 2020

Note: Recordings were not always available for the full 72 hours in all the tertiary centres.

Treatment Days 1-3

As outlined in Table 39, almost all infants admitted for TH received sedation on Day 1 (n=74 of 76, 97.4%), Day 2 (n=67 of 76, 88.2%) and Day 3 (n=64 of 76, 84.2%) of treatment in 2020. The most common type of sedation was Morphine (n=66 of 74, 86.8%), followed by Fentanyl (n=18 of 76, 23.7%).

More than 90% of infants were administered antibiotics on Day 1 (n=72 of 76, 94.7%), on Day 2 (n=52 of 76, 68.4%) and Day 3 (n=29 of 76, 38.2%). Nineteen infants required blood products on Day 1 of treatment (25%) of which the majority had fibrinogen administered (n=10 of 19, 52.6%) and 37% had fresh frozen plasma administered (n=7 of 19, 36.8%).

Table 39: Drugs and Volume Replacement Day 1, 2 & 3 in 2020

	Day 1 N=76	Day 2 N=76	Day 3 N=76
Sedation	74(97.4)	67(88.2)	64(84.2)
Antibiotics	72(94.7)	52(68.4)	29(38.2)
Anticonvulsants	28(36.8)	19(25)	15(19.7)
Inotropes	25(32.9)	20(26.3)	16(21.1)
Blood products	19(25)	3(3.9)	0(0)
Volume replacement (normal saline)	33(43.4)	5(6.6)	3(3.9)
Other	20(26.3)	10(13.2)	9(11.8)

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

Over the course of treatment and for those infants whose fluid input was measured for a full 24hr period in 2020, the mean fluid input in milligrams per kg was 51.9mg/kg (SD=14.9, Range 28-135) on Day 1, 48.0mg/kg (SD=11.7, Range 30-116) on Day 2 50.9mg/kg (SD=12.4, Range 33-88) on Day 3. In 2020, the lowest blood sugar level reported was between 0mmol/L and 3mmol/L for over a third of infants on Day 1 (n=31 of 76, 40.8%), Day 2 (n=29, 38.2%) and Day 3 (n=28, 36.8%, Table 40). Sodium levels were 124 mmol/L or lower for more than 17% of infants on Day 1 (n=13 of 76, 17.1%), for just under one quarter of infants on Day 2 (n=18, 23.7%) and for 15% of infants on Day 3 (n=11, 14.5%, Table 40).

Table 40: Laboratory Parameters Day 1, 2 & 3 in 2019-2020*

	2019 Day 1 N=72	2020 Day 1 N=76	2019 Day 2 N=72	2020 Day 2 N=76	2019 Day 3 N=72	2020 Day 3 N=76
Coagulation (mg/dL)	23(31.9)	44(57.9)	7(9.7)	10(13.2)	1(1.4)	4(5.3)
Blood sugars (mmol/L)						
0-3	28(38.9)	31(40.8)	22(30.6)	29(38.2)	23(31.9)	28(36.8)
4-7	37(51.4)	37(48.7)	38(52.8)	30(39.5)	33(45.8)	35(46.1)
≥8	5(6.9)	6(7.9)	3(4.2)	7(9.2)	2(2.8)	2(2.6)
Not documented	2(2.8)	2(2.6)	9(12.5)	10(13.2)	14(19.4)	11(14.5)
Sodium (mmol/L)						
≤124	13(18.1)	13(17.1)	7(9.7)	18(23.7)	9(12.5)	11(14.5)
125-128	19(26.4)	25(32.9)	15(20.8)	20(26.3)	7(9.7)	11(14.5)
129–131	15(20.8)	18(23.7)	19(26.4)	14(18.4)	15(20.8)	17(22.4)
132–136	18(25)	16(21.1)	16(22.2)	10(13.2)	18(25)	19(25)
≥137	6(8.3)	2(2.6)	6(8.3)	3(3.9)	8(11.1)	6(7.9)
Not documented	1(1.4)	2(2.6)	9(12.5)	11(14.5)	15(20.8)	12(15.8)

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive. *Prior to 2019, this audit collected all sodium results over the 3 days period. For 2019 onwards, sodium was collected as the lowest result on each day; therefore, comparisons with previous years are not available.

SARNAT Scoring

A diagnosis of encephalopathy, consisting of an altered state of consciousness (lethargy, stupor or coma) was assigned to 57.3% (n=44 of 75) of infants who had a SARNAT completed on Day 1, for 35.8% (n=24 of 67) on Day 2 and 36.4% (n=24 of 66) of infants on Day 3. One infant in 2020 was initially cooled but rewarmed very quickly hence information for this section was not applicable. Infants were assigned a SARNAT score[32] based on clinical behaviour on Day 1, Day 2 and Day 3 of treatment (Table 41).

Table 41: SARNAT Scoring on Treatment Day 1, 2 & 3 in 2020

		Day 1 N=75	Day 2 N=67	Day 3 N=66
Level of consciousness				
	Hyperalert	5(6.7)	3(4.5)	2(3)
	Lethargic or obtunded	32(42.7)	29(43.3)	22(33.3)
	Stupor or Coma	8(10.7)	5(7.5)	5(7.6)
	Normal	16(21.3)	11(16.4)	13(19.7)
	Undocumented	14(18.7)	19(28.4)	24(36.4)
Activity				
	Normal	15(20)	10(14.9)	6(9.1)
	Decreased	36(48)	27(40.3)	24(36.4)
	Absent	6(8)	6(9)	4(6.1)
	Normal	4(5.3)	6(9)	9(13.6)
	Undocumented	14(18.7)	18(26.9)	23(34.8)
Neuromuscular Control				
Muscle tone	Normal	5(6.7)	6(9)	8(12.1)
	Mild hypotonia	40(53.3)	32(47.8)	32(48.5)
	Flaccid	10(13.3)	6(9)	4(6.1)
	Normal	2(2.7)	3(4.5)	2(3)
	Undocumented	18(24)	20(29.9)	20(30.3)
Posture	Mild distal flexion	14(18.7)	4(6)	12(18.2)
	Strong distal flexion	8(10.7)	12(17.9)	10(15.2)
	Intermittent decerebration	6(8)	3(4.5)	4(6.1)
	Normal	6(8)	6(9)	6(9.1)
	Undocumented	41(54.7)	42(62.7)	34(51.5)
Stretch reflexes	Overactive Stage 1	4(5.3)	2(3)	10(15.2)
	Overactive Stage 2	6(8)	7(10.4)	5(7.6)
	Decreased or absent	8(10.7)	5(7.5)	6(9.1)
	Normal	7(9.3)	9(13.4)	7(10.6)
	Undocumented	49(65.3)	43(64.2)	37(56.1)
	Deferred	1(1.3)	1(1.5)	1(1.5)
Complex Reflexes				
Suck	Weak	18(24)	10(14.9)	15(22.7)
	Weak or absent	7(9.3)	8(11.9)	3(4.5)
	Absent	15(20)	10(14.9)	10(15.2)
	Normal	11(14.7)	14(20.9)	11(16.7)
	Undocumented	22(29.3)	24(35.8)	26(39.4)
	Deferred	2(2.7)	1(1.5)	1(1.5)
Moro	Strong; low threshold	2(2.7)	1(1.5)	0(0)
	Weak; incomplete high threshold	9(12)	1(1.5)	1(1.5)
	Absent	5(6.7)	3(4.5)	3(4.5)
	Normal	9(12)	8(11.9)	5(7.6)
	Undocumented	40(53.3)	45(67.2)	50(75.8)
	Deferred	10(13.3)	9(13.4)	7(10.6)

Tonic Neck	Slight	1(1.3)	2(3)	1(1.5)
	Strong	1(1.3)	1(1.5)	0(0)
	Absent	1(1.3)	0(0)	0(0)
	Normal	0(0)	0(0)	0(0)
	Undocumented	69(92)	61(91)	60(90.9)
	Deferred	3(4)	3(4.5)	5(7.6)
Autonomic Function				
Pupils	Dilated	2(2.7)	3(4.5)	3(4.5)
	Constricted	14(18.7)	9(13.4)	8(12.1)
	Variable; often unequal, poor light reflex, fixed, dilated	6(8)	3(4.5)	6(9.1)
	Normal	17(22.7)	18(26.9)	17(25.8)
	Undocumented	35(46.7)	34(50.7)	30(45.5)
	Deferred	1(1.3)	0(0)	2(3)
Heart rate	Tachycardia	0(0)	0(0)	0(0)
	Bradycardia	20(26.7)	17(25.4)	15(22.7)
	Variable	2(2.7)	2(3)	1(1.5)
	Normal	51(68)	46(68.7)	46(69.7)
	Undocumented	2(2.7)	2(3)	4(6.1)
Respiratory rate	Regular	23(30.7)	19(28.4)	20(30.3)
	Periodic breathing	37(49.3)	35(52.2)	35(53)
	Aponea	13(17.3)	9(13.4)	7(10.6)
	Normal	2(2.7)	3(4.5)	4(6.1)
	Not documented	0(0)	1(1.5)	0(0)
Seizures	None	56(74.7)	54(80.6)	64(97)
	Common; focal or multifocal	19(25.3)	11(16.4)	1(1.5)
	Uncommon (excluding decerebration)	0(0)	0(0)	1(1.5)
	Normal	0(0)	1(1.5)	0(0)
	Undocumented	0(0)	1(1.5)	0(0)

Note: Values are shown as N(%) unless otherwise stated. Missing data for one infant in day 1, nine infants for day 2 in 2020, and 10 infants for day 3 in 2020.

As outlined in Table 42, less than a third of infants were graded as severely encephalopathic on the three days: Day 1 (n=13 of 43, 30.2%), Day 2 (n=7 of 24, 29.2%), and Day 3 (n=7 of 24, 29.2%) of treatment.

Table 42: Grade of Encephalopathy on Treatment Day 1, 2 & 3 in 2020

	Day 1 N=43	Day 2 N=24	Day 3 N=24
Mild	6(14)	7(29.2)	7(29.2)
Mild to moderate	1(2.3)	0(0)	0(0)
Moderate	22(51.2)	9(37.5)	9(37.5)
Moderate to Severe	1(2.3)	1(4.2)	1(4.2)
Severe	13(30.2)	7(29.2)	7(29.2)

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

Over the course of the 72 hours of treatment, amplitude-integrated electroencephalography (aEEG) interpretation was documented for over half of cases on Day 1 (n=39 of 75, 52.0%) in 2020, under two thirds of cases on Day 2 (n=42 of 67, 62.7%) and 54.7% of cases on Day 3 (n=35 of 66). Electrical seizures were identified in 22 of the 39 infants (56.4%) on Day 1, in 14 of the 42 infants (33.3%) on Day 2 and in 5 of 35 infants (14.3%) on Day 3 (Table 43).

Table 43: aEEG interpretation on Treatment Day 1, 2 & 3 in 2020

	Day 1 N=75	Day 2 N=67	Day 3 N=66
Background activity	**39(52)**	**42(62.7)**	**35(53)**
Normal (CNV, DNV)	14(35.9)	20(47.6)	16(45.7)
Abnormal (BS)	6(15.4)	6(14.3)	3(8.6)
Moderately abnormal (CLV)	5(12.8)	3(7.1)	3(8.6)
Severely abnormal (FT)	2(5.1)	1(2.4)	0(0)
Not documented	12(16)	12(17.9)	13(19.7)
Sleep wake cycle			
Present	8(20.5)	8(19)	14(40)
Absent	6(15.4)	8(19)	11(31.4)
Not documented	25(64.1)	26(61.9)	10(28.6)
Electrical seizures	**22(56.4)**	**14(33.3)**	**5(14.3)**

Investigations

In relation to neuroimaging, 65.8% (n=50 of 76) of infants had a cranial ultrasound in 2020 that occurred between Day 1 and Day 5 of life (Table 44). Of the 50 cranial ultrasounds undertaken, 19 (38.0%) were reported as abnormal.

Table 44: Cranial ultrasound undertaken in 2020 (N=76)

	Day 1	Day 2	Day 3	Day 4 or later
Cranial ultrasound*	28(36.8)	13(17.1)	8(10.5)	1(1.3)

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

Just over one third of the infants who received TH in 2020 had an echocardiogram during their hospital admission (n=26 of 76, 34.3%, Table 45). Almost all infants had microbiology bloods undertaken (n=75 of 76, 98.7%). Nine of the 76 infants had genetic bloods undertaken (11.8%).

Table 45: Investigations undertaken in 2020

	TH Cases N=76
Echocardiogram	26(34.2)
Lumbar puncture	12(15.8)
Microbiology bloods	75(98.7)
Genetic bloods	9(11.8)

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

Of the 76 infants who underwent TH treatment in 2020, 67 infants had an MRI of the brain undertaken, of which 57 infants (75%) had an MRI report available at time of data collection. Most of the infants had the MRI performed between days one and four of life (n=24 of 61, 31.6%, missing information for one case, Table 46). By day 10, 98.4% (n=60 of 61) had an MRI performed.

The 57 available MRI reports were assessed by adopting the Barkovich HIE scoring system in HIE.[33] Adopting the Barkovich HIE scoring system, 41% of this cohort had an abnormal MRI in 2020 (n=23). The full set of Barkovich HIE scores for infants with an abnormal result in 2020 are outlined in Appendix E.

Table 46: Day of life MRI undertaken in 2019 and 2020

	TH Cases N=59 2019	TH Cases N=61 2020	TH Cases N=120 2019-2020
1-3	2(3.4)	5(8.2)	7(5.8)
4	7(11.9)	19(31.1)	26(21.7)
5	15(25.4)	14(23)	29(24.2)
6	12(20.3)	10(16.4)	22(18.3)
7	3(5.1)	5(8.2)	8(6.7)
8	9(15.3)	4(6.6)	13(10.8)
9	5(8.5)	1(1.6)	6(5)
10-15	6(10.2)	3(4.9)	9(7.5)

Note: Values are shown as N(%) unless otherwise stated. Missing data for one infant in 2020.

Rewarming

Of the 76 infants who underwent TH treatment, 12 infants (15.8%) did not complete 72 hours of TH in 2020. As outlined in Table 47, half of these infants had their care redirected to end of life care (n=6 of 12, 50.0%).

Table 47: Indications to cease TH intervention in infants who underwent TH in 2016-2020 before 72 hours completed therapy

	2016-2019* N=33	2020 N=12
Redirection of care	23(69.7)	6(50)
PPHN	7(21.2)	3(25)
Sepsis	2(6.1)	0(0)
Cooling criteria not met	1(3)	2(16.7)
Contraindicated	0(0)	1(8.3)

Note: Values are shown as N(%) unless otherwise stated. *Missing data for one infant in 2018.

Excluding the 12 infants whose treatment was ceased, data on rewarming was available for 100% of the 64 of the remaining infants in 2020. As outlined in Table 48, the majority of infants were rewarmed within 12 hours (n=48 of 64, 75.0%), and between 16 and 18 hours (n=15 of 64, 23.4%) in 2020. During the rewarming period, six of the 64 infants (9.4%) had seizures.

Table 48: Duration of rewarming for infants who underwent TH in 2016-2020*

	2016-2019 N=241	2020 N=64
Up to 12 hours	201(83.4)	48(75)
13–15 hours	8(3.3)	1(1.6)
16–18 hours	30(12.4)	15(23.4)
Greater than 19 hours	2(0.8)	0(0)

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

Feeding

After excluding data for the 12 neonatal deaths and two infants whereby the first one was transferred to the hospital of birth before feeding was commenced, and the second infant was rewarmed on day 1, therefore data on the introduction of feeding was available for 62 of the 76 infants who underwent TH treatment (81.6%) in 2020. As outlined in Table 49, the majority of infants had feed introduced on Day 4 (n=32 of 62, 51.6%) or Day 5 (n=17 of 62, 27.4%). Ten of the mothers breastfed breastfeed on introduction of feed (16.4%, missing information for one infant), half of infants were fed with expressed breast milk (n=33 of 61, 54.1%) and 18 were fed with formula (29.5%).

Table 49: Age that infants who underwent TH in 2016-2020 had feed introduced

	2016-2019 N=247	2020 N=62
Up to Day 3	26(10.5)	9(14.5)
Day 4	99(40.1)	32(51.6)
Day 5	81(32.8)	17(27.4)
Day 6	29(11.7)	3(4.8)
Day 7+	12(4.9)	1(1.6)

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

Of these 62, almost three-quarters of infants were initially fed with a nasogastric tube in 2020 (n=45, 73.8%, missing information for one case). Of the 45 infants that were initially fed with a nasogastric tube, data was available on 40 in terms of duration of feed. More than 50% were fed for more than 72 hours (n=21 of 40, 52.5%, information missing for five infants). As indicated in Table 50, no infant was discharged home with a nasogastric tube.

Table 50: Duration of feeding with a nasogastric tube for infants who underwent TH in 2016-2020

	2016-2019 N=136	2020 N=40
Less than 24 hours	30(22.1)	1(2.5)
24-47 hours	25(18.4)	8(20)
48-71 hours	22(16.2)	10(25)
Greater than 72 hours	45(33.1)	21(52.5)
Discharged home with a nasogastric tube	14(10.3)	0(0)

Note: Values are shown as N(%) unless otherwise stated. *Missing data for five infants in 2020.

Specific placental conditions

In 2020, 76 infants underwent TH Of this cohort, 51 placentas were available for analysis, and 14 cases did not have placentas sent for histological examination (Table 51). The remainder did not have a report on file at the time of data collection. This yields an availability rate of 70%, which is similar to last year's 2019 report and remains disappointingly low in comparison to the Stillbirth yield of 95%.

Placental disease categories are divided into major subsections and the more widespread use of the Amsterdam Criteria[9] for placental reporting means it is easier to compare data from different institutions. The major subsections include: maternal vascular malperfusion (MVM), fetal vascular malperfusion (FVM), isolated cord pathology, cord pathology with distal disease, chorioamnionitis, villitis and other.

Table 51: Placental histology findings for infants who underwent neonatal TH in 2016-2019 versus infants who underwent neonatal TH in 2020 and Stillbirths in 2016-2020 in Ireland

	2016-2019 N=162	2020 N=51	Stillbirth* 2016-2020 N=1,172
Maternal Vascular Malperfusion (MVM)	37	9	28.41%
Low Grade	13	8	
High Grade	5	1	
Fetal Vascular Malperfusion (FVM)	27	10	25.60%
Low Grade	5	6	
High Grade	6	4	
Any Cord Pathology	45	9	22.95%
Isolated	21	7	
Cord Pathology with distal FVM	6	0	
Cord Pathology with distal High Grade FVM	4	2	
Chorioamnionitis	44	19	8.62%
Chorioamnionitis FIR Stage 2	1	0	-
Villitis	13	5	3.41%
Other Placental Condition	53	21	16.30%
Other	6	4	
Delayed Villous Maturation	4	16	
Meconium-associated vascular Necrosis	3	5	
Normal	11	8	-

Note: Values are shown as N(%) unless otherwise stated. Categories are not mutually exclusive. *Perinatal Mortality in Ireland Annual Report 2016-2020, NPEC.[‡] [34–37]

[‡]San Lazaro Campillo I, Manning E, Corcoran P, Keane J, O'Farrell IB, McKernan J, White E, Greene RA, on behalf of the Perinatal Mortality National Clinical Audit Governance Committee. Perinatal Mortality National Clinical Audit in Ireland Annual Report 2020. Cork: National Perinatal Epidemiology Centre, 2022. [In press]

Discharge diagnosis and neonatal death

At discharge, results for neurological examination were available for 62 infants in 2020. Of the 62 infants who had an MRI scan undertaken, 69.4% (n=43 of 62) had normal results for the neuro examination, 25.8% (n=16 of 62) had an abnormal result, and three infants had no information documented at discharge.

There was a grade of encephalopathy assigned to 52 infants during their admission out of the 76 infants of this cohort in 2020 (n=52 of 76, 68.4%). The overall grade of encephalopathy assigned to an infant during their admission is the worst grade of encephalopathy achieved during admission. A grade of moderate encephalopathy was assigned to less than half of infants (n=26 of 52, 50.0%, Table 52). Over one fourth of infants had a grade of severe HIE on discharge (16 of 52, 30.8%).

Table 52: Grade of encephalopathy on discharge in 2016-2020

	2016-2019 N=281	2020 N=76
HIE – assigned	183(65.1)	52(68.4)
Mild HIE	17(6)	6(11.5)
Mild-Moderate HIE	17(6)	2(3.8)
Moderate HIE	104(37)	26(50)
Moderate to Severe HIE	5(1.8)	2(3.8)
Severe HIE	40(14.2)	16(30.8)
HIE – no grade assigned	62(22.1)	24(31.6)
HIE not documented	24(8.5)	0(0)

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

The survival rate for the infants who underwent TH in 2020 was 84.2%, as 12 of the 76 infants died, which is similar to the survival rate of last year (n=15 of 72, 79.2%). Eleven of deaths occurred within 7 completed days of birth and were classified as early neonatal deaths (n=11 of 12, 91.7%). As outlined in Table 53, one death occurred after the 7th day and within 28 completed days of birth and were classified as late neonatal deaths (n=1 of 12, 8.3%). Eleven of the infants were referred to the coroner (91.7%) and 11 infants had an autopsy performed (91.7%). It is important to note that data on the findings of these reports, and on the infants' respective causes of death, were not collected for this report.

Table 53: Perinatal and infant mortality for infants who underwent TH in 2016-2020

	2016-2019* N=38	2020 N=12
Early neonatal death	19(50)	11(91.7)
Late neonatal death	12(31.6)	1(8.3)
Infant death	7(18.4)	0(0)

Note: Values are shown as N(%) unless otherwise stated. *Age at death for one neonatal death in 2019 was unknown. % based on data available (n=14 neonatal deaths).

An assessment of the mortality risk for infants who received TH compared to all infants born in Ireland was based on the risk of neonatal death (early and late neonatal death combined). There were 43 neonatal deaths among the 357 infants who had TH in 2016-2020, a neonatal mortality risk of 120.5 neonatal deaths per 1,000 infants. There were 700 neonatal deaths among the 303,838 infants born in Ireland in 2016-2020,[‡(34-37)] which gives a neonatal mortality rate of 2.3 neonatal deaths per 1,000 births. Thus, there is a 50-fold difference in the relative risk of neonatal death.

[‡]San Lazaro Campillo I, Manning E, Corcoran P, Keane J, O'Farrell IB, McKernan J, White E, Greene RA, on behalf of the Perinatal Mortality National Clinical Audit Governance Committee. Perinatal Mortality National Clinical Audit in Ireland Annual Report 2020. Cork: National Perinatal Epidemiology Centre, 2022. [In press]

As outlined in Table 54, first infant blood lactate level was strongly associated with risk of death among infants treated with TH. As expected, infants with a higher blood lactate were at a higher risk of death. The continued need for PPV or intubation at 10 mins was also strongly associated with mortality with these infants being 4.5 times more at risk. Infants with acidosis present in umbilical cord, or any blood sample, within 60 minutes of birth had 4.09 times higher risk of death compared to the other infants. Similarly, infants with a base deficit greater than 16.0 mmol/L in umbilical cord, or any blood sample, within 60 minutes of birth had 4.76 times higher risk of death compared to the other infants. Similarly, low Apgar score was an indicator of mortality risk. Twenty-four percent of the infants with an Apgar score ≤5 at 10 minutes died, which was 4.49 times higher than the risk of deaths compared to the other infants.

Table 54: Maternal and infant characteristics and mortality risk for infants who underwent TH in 2016-2020

		Number of infants	Number (%) who died	Risk ratio (95% CI)	P-value
All		357	51 (14.3)		
Parity	Nulliparous	210	30 (14.3)	1.00 (ref.)	
	Parous	147	21 (14.3)	1 (0.57-1.75)	1.000
Mode of delivery	Vaginal delivery	89	12 (13.5)	1.00 (ref.)	
	Instrumental	215	25 (11.6)	0.86 (0.43-1.72)	0.673
	CS pre labour	31	9 (29)	2.15 (0.91-5.11)	0.082
	CS after the onset of labour	29	5 (17.2)	1.28 (0.45-3.63)	0.644
Birthweight centile	<10th	63	9 (14.3)	1.95 (0.75-5.04)	0.170
	10-49th	142	28 (19.7)	2.69 (1.22-5.89)	0.014
	50-89th	109	8 (7.3)	1.00 (ref.)	
	>90th	42	6 (14.3)	1.95 (0.68-5.61)	0.218
Sex	Male	196	21 (10.7)	1.00 (ref.)	
	Female	161	30 (18.6)	1.74 (1-3.04)	0.052
First infant blood lactate	0 to 4	19	1 (5.3)	1.06 (0.14-8.31)	0.953
	5 to 14	202	10 (5)	1.00 (ref.)	
	15+	99	26 (26.3)	5.31 (2.56-11)	<0.001
	Undocumented	40	14 (35)	7.07 (3.14-15.92)	<0.001
Assessment for TH		0			
>36 completed weeks gestational age	Yes	347	51 (14.7)	1.00 (ref.)	
	No	10	0 (0)	0.00 (--)	
Apgar score ≤5 at 10 minutes	Yes	164	40 (24.4)	4.49 (2.24-8.97)	<0.001
	No	184	10 (5.4)	1.00 (ref.)	
Weight ≥1800 grams	Yes	354	51 (14.4)	1.00 (ref.)	
	No	3	0 (0)	0.00 (--)	
Continued need for PPV or Intubation at 10 mins	Yes	220	44 (20)	4.5 (1.92-10.56)	<0.001
	No	135	6 (4.4)	1.00 (ref.)	
Did an acute perinatal event occur?	Yes	233	42 (18)	2.48 (1.21-5.1)	0.013
	No	124	9 (7.3)	1.00 (ref.)	
Acidosis present in umbilical cord, or any blood sample within 60 minutes of birth	Yes	231	45 (19.5)	4.09 (1.75-9.59)	<0.001
	No	126	6 (4.8)	1.00 (ref.)	
Base Deficit >16.0 mmol/L in umbilical cord, or any blood sample, within 60 minutes of birth	Yes	183	41 (22.4)	4.76 (2.23-10.16)	<0.001
	No	170	8 (4.7)	1.00 (ref.)	
Diagnosis of encephalopathy during assessment for TH	Yes	262	41 (15.6)	1.47 (0.74-2.94)	0.274
	No	94	10 (10.6)	1.00 (ref.)	

Neurodevelopmental Outcomes using the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III)

The Bayley-III is an ability test of global development, individually administered to assess infants, toddlers and young children from 1 month to 42 months of age. It comprises of a series of play tasks and language stimulus books broken up into 3 composite scales with 5 sub-categories – Cognitive Development (Cognitive Scale), Receptive and Expressive Communication (Language Scale) and Fine Motor and Gross Motor development (Motor Scale). The cognitive scale evaluates sensorimotor development, object relatedness, memory, exploration, manipulation and concept formation. The language scale is the sum of the receptive and expressive scores. The receptive scale measures comprehension and responses to requests. The expressive scale evaluates the child's ability to name objects and actions, respond to questions, communicate wants, and use multiword sentences. Similarly, the motor assessment includes both a fine motor score (e.g., "pincer" grasp, block stacking, lego play and early writing skills) and a gross motor score (e.g., locomotion, balance, and climbing steps). All scales have normative values (standard deviation [SD]) of 10 and composite scores of 100. The Bayley Scales can classify delayed or advanced development within the specific sub-categories.

Of the whole cohort assessed, a total of 37 infants were assessed for the 2019 TH report, and 48 infants in the 2020 TH report. Outlined in Table 55 and 56 is the amalgamated results of the 2019 and 2020 TH report, the composite scores and scaled scores are presented as per day of birth; therefore, 20 children, who were treated with TH at birth and assessed either in 2019 or 2020, were born in 2016, 45 children were born in 2017 and 20 children were born in 2018. The categories used to represent the composite score outcomes across the cohort have been divided into the following: Above Average, Average, Mild/Moderate Delay and Extremely Delayed Performance using the Bayley Manual classifications.[39] These classifications demonstrate a broad range of outcomes. Children performing within the Mild Delayed Range would be expected to benefit from appropriate and tailored intervention thus improving their outcome over time while children performing within the Moderate and Extremely Delayed categories will still face many developmental challenges.[39]

Scaled scores have also been presented for each domain as these facilitate further breakdown of the results, for example, for the language scale we can now look at receptive communication and expressive communication skills separately. For the motor scale we can measure fine motor and gross motor separately as a delay in one subset can be missed if the other subset scaled score is higher for example, a higher fine motor score can mask the low gross motor score / a low expressive communication score can be compensated by a higher receptive communication score giving a normal / average outcome when the composite scores are used. These standardised scaled scores have been very helpful to clinicians in terms of determining the type of intervention required to address the delay. These scaled scores have been broken down to measure Above Average (1-3 SD above the mean), Average and Below Average/Delayed (1-3 SD below the mean) performance in accordance with the Bayley III Manual classification.[39]

When the Composite Scores for the total group were analysed (n=85 children), this report found that above Average Performance was higher for Cognitive Development (N= 22 /25.9%) compared to Language (N=13/15.3%) and Motor Development (N=17/20.0%) (Table 55). Average Performance was similar for Cognitive (N= 49/57.6%) when compared with Motor Development (N= 50/58.8%) and Language (N=48/56.5%). Mild/Moderate Delay was highest for Language Development (N=20/23.5%) compared to Cognitive (N=12/14.1%) and Motor (N=14/16.5%). Extreme Delay noted for Motor, Language and Cognitive Development was Motor (N= 4/4.7%), Language (N=4/4.7%) Cognitive (N=2/2.4%).

While the cohort group was small only representing 85 children, 28.2% of this group of children presented with Language Delay (Table 55). There were two extremely delayed outcomes reported for the Composite Cognitive domain, four for the Composite Motor domain and four for the Composite Language domain representing that 4.7% delay in Motor and Language outcomes.

Table 55: Bayley III Composite Scores for TH infants

	2016 N=20	2017 N=45	2018 N=20	2016-2018 N=85
Cognitive Composite Score				
Mean (SD)	104(13.9)	98.9(15.2)	99.5(15.1)	100.2(14.9)
Range	70-130	55-130	70-130	55-130
Above average (≥110)	7(35)	10(22.2)	5(25)	22(25.9)
Normal range (90-109)	11(55)	27(60)	11(55)	49(57.6)
Mild/Moderate Delay (70-89)	2(10)	6(13.3)	4(20)	12(14.1)
Extremely Delay (≤69)	0(0)	2(4.4)	0(0)	2(2.4)
Language Composite Score				
Mean (SD)	99.5(15.2)	96(15.9)	98(19.1)	97.3(16.4)
Range	74-129	59-132	65-144	59-144
Above average (≥110)	4(20)	6(13.3)	3(15)	13(15.3)
Normal range (90-109)	11(55)	26(57.8)	11(55)	48(56.5)
Mild/Moderate Delay (70-89)	5(25)	10(22.2)	5(25)	20(23.5)
Extremely Delay (≤69)	0(0)	3(6.7)	1(5)	4(4.7)
Motor Composite Score				
Mean (SD)	102.2(16)	95(15.9)	99.4(14)	97.7(15.6)
Range	67-139	46-130	67-133	46-139
Above average (≥110)	6(30)	6(13.3)	5(25)	17(20)
Normal range (90-109)	12(60)	26(57.8)	12(60)	50(58.8)
Mild/Moderate Delay (70-89)	1(5)	11(24.4)	2(10)	14(16.5)
Extremely Delay (≤69)	1(5)	2(4.4)	1(5)	4(4.7)

Note: Values are shown as N(%) unless otherwise stated. SD (Standard Deviation). The BDS scores for nine infants were excluded for analysis because the data was incomplete, or the assessment was not performed.

When these Scaled Scores were analysed for the total group more than a quarter of the group (25.9%) demonstrated Gross Motor Delay with just over one fifth (21.2%) demonstrating Receptive and Expressive Communication Delay. Cognitive Delay was measured at 16.5% and Fine Motor Delay at 11.8% (Table 56).

Table 56: Bayley III Scaled Scores for TH infants

	2016 N=20	2017 N=45	2018 N=20	2016-2018 N=85
Cognitive Scaled Score				
Mean (SD)	10.8(2.8)	9.8(3)	10(3.1)	10.1(3)
Range	4-16	1-16	4-16	1-16
1SD above (≥13)	6(30)	6(30)	3(15)	15(17.6)
Normal range (8-12)	12(60)	31(155)	13(65)	56(65.9)
1SD below (≤7)	2(10)	8(40)	4(20)	14(16.5)
Receptive Communication (RC) Scaled Score				
Mean (SD)	10.2(3.2)	9.4(2.7)	9.7(3)	9.7(2.9)
Range	4-16	4-16	4-17	4-17
1SD above (≥13)	6(30)	5(25)	3(15)	14(16.5)
Normal range (8-12)	12(60)	29(145)	12(60)	53(62.4)
1SD below (≤7)	2(10)	11(55)	5(25)	18(21.2)
Expressive Communication (EC) Scaled Score				
Mean (SD)	9.6(2.4)	9.2(2.9)	9.6(3.8)	9.4(3)
Range	6-15	2-15	3-18	2-18
1SD above (≥13)	3(15)	5(25)	4(20)	12(14.1)
Normal range (8-12)	13(65)	31(155)	11(55)	55(64.7)
1SD below (≤7)	4(20)	9(45)	5(25)	18(21.2)
Fine Motor (FM) Scaled Score				
Mean (SD)	11.2(3.6)	9.7(2.6)	10.8(2.1)	10.3(2.8)
Range	4-19	1-16	7-14	1-19
1SD above (≥13)	6(30)	5(25)	5(25)	16(18.8)
Normal range (8-12)	12(60)	33(165)	14(70)	59(69.4)
1SD below (≤7)	2(10)	7(35)	1(5)	10(11.8)
Gross Motor (GM) Scaled Score				
Mean (SD)	10.1(3)	8.5(3.1)	9(3.2)	9(3.1)
Range	4-17	1-16	1-18	1-18
1SD above (≥13)	4(20)	5(25)	1(5)	10(11.8)
Normal range (8-12)	14(70)	24(120)	15(75)	53(62.4)
1SD below (≤7)	2(10)	16(80)	4(20)	22(25.9)

Note: Values are shown as N(%) unless otherwise stated. SD (Standard Deviation). The BDS scores for nine infants were excluded for analysis because the data was incomplete, or the assessment was not performed.

OBSTETRIC CASE REVIEW TOOL

To investigate the obstetric antecedents of an infant requiring therapeutic hypothermia intervention.

When reviewing cases of neonatal encephalopathy, the following types of data may be helpful to identify learning.

- MATERNAL DEMOGRAPHICS
- PREVIOUS PREGNANCY HISTORY
- CURRENT PREGNANCY HISTORY
- ANTENATAL RISK ASSESSMENT (including not undertaken)

SENTINEL EVENTS

Placental Abruption
Consider risks/aetiology – Previous abruption, hypertension, abdominal trauma, smoker, drug misuse.

Uterine Rupture
History of previous caesarean section or other uterine surgery. Was oxytocin/prostaglandin used?

Difficulties at delivery
1. Shoulder Dystocia.
   Consider risks/aetiology – History of shoulder dystocia, BMI, diabetes, macrosomia, failure to progress in labour.
2. Impacted Head at Caesaran Section.
   Caesaran Section at full dilation.

Cord Prolapse
Consider risks/aetiology – Abnormal presentation, unstable lie, ARM?

Maternal Collapse
Consider aetiology – Eclampsia, seizure, myocardial infarction, anaesthetic event, amniotic fluid embolus, etc.

Fetal Haemorrhage
Consider aetiology placenta previa, vasa previa, trauma, placental cause etc.

RECURRING FACTORS

Cardiotocograph Monitoring
Consider use and findings – Adequate monitoring, appropriate quality of trace, suspicious features, second eyes/second review/opinion undertaken, documented training of attending medical/ midwifery personnel.

Oxytocin
Consider use/misuse; tachyphylaxis, hyper stimulation, medical review of inadequate progress, response, etc.

Communication
Assess presence or absence of good practice as documented – Second eyes, documentation of maternal concerns, concerns escalated appropriately to senior midwifery/ senior medical staff, appropriate staff: patient ratios.

Pyrexia/PROM/MEC
Consider factors such as – Appropriate review, assessment and investigation, care plan, appropriate antibiotic therapy, was there an indication for urgent delivery, etc.

Failure to Progress
Consider risks/aetiology – Nulliparous or parous mother, abnormal presentation, primary or secondary FTP, issues with maternal care plan, maintenance of partogram, appropriate escalation, appropriate medical response, etc.

Diagnosis of Labour
Consider diagnosis of labour, timing – Did mother self-present, time after admission diagnosis of labour made, appropriate monitoring, etc.

Induction
Consider documentation – Indication and plan for induction, cervical assessment at time of planning, indication discussed with consultant if not per guideline. Consultant informed if cervix unfavourable and kept updated.

Instrumental
Delivery done by appropriate grade of doctor? Decision and timing of events documented, procedure(s) well documented, consequences of repeated attempts considered and understood.

GOVERNANCE

Who is responsible for all deliveries-at all times, from the start of labour/induction until delivery?

Document the review team including their discipline, specialty and grade.

Not every case that requires TH will be covered by this review – the above events and factors will cover the majority.

National Women & Infants Health Programme

Seirbhís Sláinte Níos Fearr á Forbairt | Building a Better Health Service

NATIONAL PERINATAL EPIDEMIOLOGY CENTRE

Gníomhaireacht Bainistíochta an Chisteáin Náisiúnta
National Treasury Management Agency
An Ghníomhaireacht um Éilimh ar an Stát
State Claims Agency

CANDIDACY CHECKLIST FOR NEONATAL THERAPEUTIC HYPOTHERMIA (COOLING)

PATIENT'S NAME: _____ **HOSP. NO:** _____

TIME of BIRTH: _____:_____ **hrs.** **CURRENT AGE in hours /minutes:** _____ **hrs.**_____**mins.**

If current age is greater than 6 hours, call tertiary cooling centre before proceeding.

Directions for the use of this checklist: Start at the top and work through each numbered component. When directed to proceed to the exam (neurological criteria), refer to the exam found on page 2. If there is missing data, (such as Apgar scores) and you are in doubt as to whether or not the patient qualifies for cooling, consult with the tertiary cooling centre promptly to discuss the patient.

Clinical Information	Criteria *(place a tick in the box that corresponds to the patient information)*	Instructions
Gestation	1 ≥ 36 weeks gestation ☐	Go to → 2 **Weight**
	= 35 weeks gestation ☐	May not be eligible *Contact cooling centre*
	< 35wks gestation ☐	Not Eligible
Weight	2 ≥ 1800 grams ☐	Go to → 3 **Blood Gas**
	< 1800 grams ☐	Not Eligible
Blood Gas pH = _____ Base Deficit = _____ Source: Cord ☐ Or 1st infant blood gas at <1hour of life ☐ Arterial ☐ Capillary ☐ Venous Time Obtained: _____:_____	3 pH < 7.0 ☐ or Base Deficit ≥ 16 ☐	Criteria met thus far. Go to **EXAM***
	No gas obtained ☐ or pH ≥ 7.0 ☐ or Base Deficit < 16 ☐	May not be eligible; Go to → 4 **History of acute perinatal event**
Acute Perinatal Event *(tick all that apply)*	4 Variable / late foetal HR decelerations ☐ Prolapsed / ruptured/tight nuchal cord ☐ Uterine Rupture ☐ Maternal haemorrhage / placental abruption ☐ Maternal trauma (eg. vehicle accident) ☐ Mother received CPR ☐	Any ticked, Go to → 5 **Apgar score**
	No perinatal event ☐ or Indeterminate what the event was because of home birth or missing information ☐	May not be eligible; Go to → 5 **Apgar score**
Apgar Score at 1 minute _____ 5 minute _____ 10 minute _____	5 Apgar ≤ 5 at 10 minutes ☐	Criteria met thus far. Go to **EXAM***
	Apgar > 5 at 10 minutes ☐	May not be eligible; Go to → 6 **Resuscitation after delivery**
Resuscitation after Delivery *(tick all that apply)* _____ PPV/intubated at 10 minutes _____ CPR _____ Adrenaline administered	6 Continued need for PPV or Intubated at 10 minutes? ☐	Criteria met thus far. Go to **EXAM***
	No PPV/not Intubated at 10 mins? ☐	Does not meet the current evidence based criteria for therapeutic hypothermia

Signature:_____ **Professional No.:**_____ **Date of Exam:**____/____/____ **Time of Exam:**____:____

Circle findings for each domain
PATIENT IS ELIGIBLE FOR COOLING WHEN 3 OR MORE DOMAINS HAVE FINDINGS IN COLUMNS 2 OR 3
Neurological criteria to be assessed between 1 and 6 hours after birth (Assessment of encephalopathy may be less accurate if performed prior to 1 hour of age)

Domain	1	2	3
Seizures	**No Seizures**	**Focal or Multifocal Seizures** (Multifocal: clinical activity involving > one site which is asynchronous and usually migratory) Note: If the patient is < 6 hours old and meets the gestation, weight and blood gas criteria and has a witnessed seizure, patient is eligible for cooling regardless of the rest of this exam	**Severe, Generalised Seizures** (Often resistant to conventional treatment) Note: If the patient is < 6 hours old and meets the gestation, weight and blood gas criteria and has a witnessed seizure, patient is eligible for cooling regardless of the rest of this exam
Level of Consciousness	**Normal** **or** **Hyperalert**	***Lethargic*** Decreased activity in an infant who is aroused and responsive **Definition of Lethargic:** • Sleeps excessively with occasional spontaneous eye opening • Responses are delayed but complete • Threshold for eliciting such responses increased • Can be irritable when disturbed	**Stuporous / Comatose** Demonstrates no spontaneous eye opening and is difficult to arouse with external stimuli **Definition of Stuporous:** • Aroused only with vigorous and continuous stimulation **Definition of Comatose:** • No eye opening or response to vigorous stimulation In both stupor and coma, the infant may respond to stimulation by grimacing/ stereotyped withdrawal / decerebrate posture
Spontaneous activity when awake or aroused	**Active** **Vigorous, doesn't stay in one position**	**Less than active, not vigorous**	**No activity**
Posture	**Moving around and does not maintain only one position**	**Distal flexion, complete extension or "frog-legged" position** Term infants with HIE often exhibit • Weakness in hip-shoulder distribution (eg proximal part of extremities) • Distal joints, fingers and toes often exhibit strong flexion • Thumbs strongly flexed and adducted. • Wrists often flexed • Above postures are enhanced by any stimulation	**Decerebrate with or without stimulation (all extremities extended)**
Tone	**Normal** • Resists passive motion **Hypertonic, jittery** • Lowered threshold to all types of minimal stimuli eg light touch, sudden noises • Infant may even respond to his/her own sudden movements	**Hypotonic or floppy,** • Axial hypotonia and/or limb hypotonia	**Completely flaccid**
Primitive reflexes	***Suck:*** Vigorously sucks finger or ETT ***Moro:*** Normal: Limb extension followed by flexion with stimulus	***Suck:*** Weak ***Moro:*** Incomplete	***Suck:*** Completely absent ***Moro:*** Completely absent
Autonomic system	***General Activation of Sympathetic nervous system*** ***Pupils:*** • Normal size (-1/3 of iris diameter) • Reactive to Light ***Heart Rate:*** • Normal, > 100bpm ***Respirations:*** • Regular spontaneous breathing	***General Activation of Parasympathetic nervous system*** ***Pupils:*** • Constricted (< 3mm estimated) • but reactive to light ***Heart Rate:*** • Bradycardia (< 100bpm, variable up to 120) ***Respirations:*** • Periodic, irregular breathing effort • Often have more copious secretions and require frequent suctioning	***Pupils:*** • Skew gaze, fixed, dilated, • not reactive to light ***Heart Rate:*** • Variable, inconsistent heart rate, irregular, may be bradycardic ***Respirations:*** • Completely apnoeic, requiring PPV & / or ET intubation and ventilation

Signature:_____ **Professional No.:**_____ **Date of Exam:** ____/____/____ **Time of Exam:** ____:____

This checklist, adapted from the 'STABLE Program', 6th edition, 2013, has been produced by the National Neonatal Transport Programme (NNTP) and endorsed by the Faculty of Paediatrics, Royal College of Physicians, Ireland. 1st edition, March 2014. This 2nd edition, July 2017. Also referenced: 1.*The TOBY Study. Whole body hypothermia for the treatment of perinatal asphyxial encephalopathy: A randomised controlled trial.* Dennis Azzopardi and The TOBY Study Group. BMC Pediatrics 2008, 8:17
2. *Optimizing Therapeutic Hypothermia for Neonatal Encephalopathy*. Steven L. Olsen et al. Pediatrics Feb 2013, 131 (2) e591-e603

Appendix C. Sarnat Teaching Cards

Modified Sarnat Staging for Neonatal Encephalopathy			
Severity	**Stage 1 (mild)**	**Stage 2 (Moderate)**	**Stage 3 (Severe)**
Level of consciousness	Hyperalert	Lethargic / Obtunded	Stupor or coma
Activity	Normal	Decreased	Absent
Neuromuscular Control:			
Muscle tone	Normal	Mild hypotonia/hypertonia	Flaccid/rigid
Posture	Mild distal flexion	Strong distal flexion	Intermittent decerebration
Tendon reflexes	Overactive	Overactive	Decreased or Absent
Complex reflexes			
Suck	Weak	Weak/absent	Absent
Moro	Strong, low threshold	Weak, incomplete,high threshold	Absent
Tonic neck	Slight	Strong	Weak or absent
Autonomic Nervous System			
Pupils	Dilated pupil	Constricted pupil	Variable: often unequal, poor light reflex, fixed, dilated
Heart rate	Tachycardia	Bradycardia	Variable
Respiratory rate	Regular	Periodic breathing	Apnoea
Seizure	None	Common; focal or multifocal	Uncommon (excluding decerebration)

Modified from Sarnat HB, Sarnat MS. Neonatal Encephalopathy Following Fetal Distress.A Clinical and Electroencephalographic Study. *Arch Neurol.* 1976;33(10):696–705

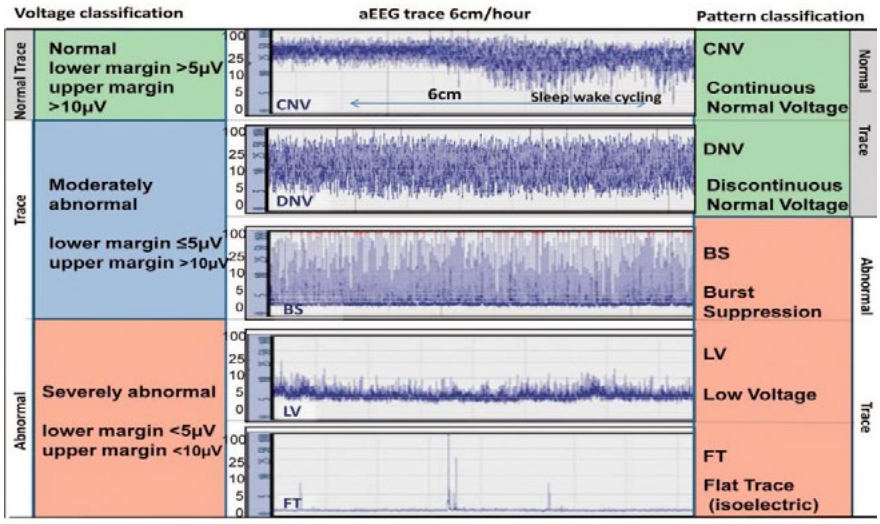
- ✓ **Key parameters to assess level of consciousness:** response to stimuli, corneal and gag reflex, motor activity
- ✓ **Stimulation technique:** Mild stimuli (tactile touch), Moderate stimuli (heel flick), Noxious stimuli (pinch of thumbnail/earlobe)

- **Hyperalert:** respond readily to stimuli, corneal and gag reflexes present, normal motor activity
- **Lethargy:** delayed response to stimuli, corneal and gag reflexes present, reduced motor activity
- **Obtunded:** delayed, incomplete response to stimuli, corneal and gag reflexes present, markedly reduced motor activity
- **Stupor**: only respond to strong noxious stimuli, Absent corneal and gag reflexes , no spontaneous motor activity, other – shallow ataxic breathing, apnoeic
- **Coma:** No response to noxious, vigorous stimulation, absent corneal and gag reflexes, no motor activity

- ➢ **Posture:** Normal posture = flexion and adduction of all limbs
- ➢ **Key deep tendon reflexes:** knee, supinator, biceps
- ➢ **Mean horizontal papillary diameter:** Term neonates: 3.8 mm +/- 0.8mm (SD)

Summary Document for aEEG Interpretation

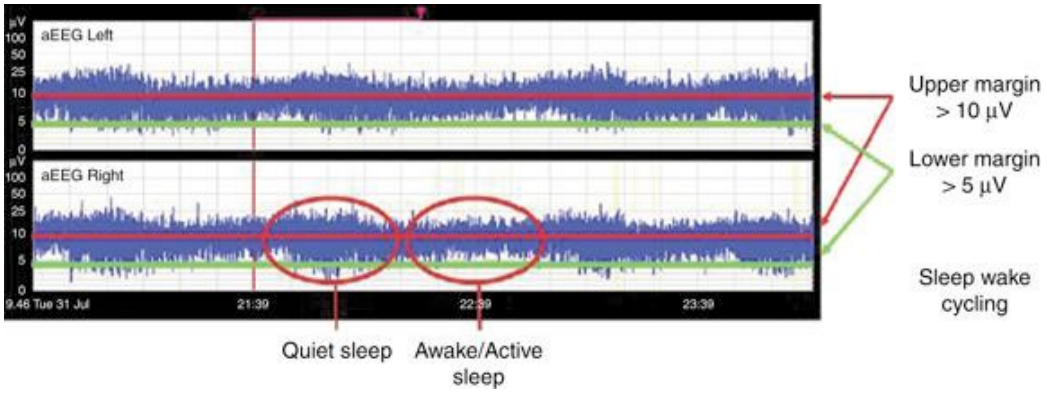
1. Background Voltage and Pattern Classification



From Thoresen M, et al. Effect of hypothermia on amplitude-integrated electroencephalogram in infants with asphyxia. Pediatrics. 2010 Jul;126(1):e131-9. PMID:9563847 Reprinted with permission of The American Academy of Pediatrics

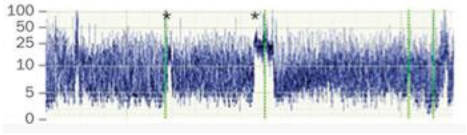
2. Presence of Sleep-Wake Cycling (SWC)

- SWC characterized by smooth sinusoidal variations, mostly in the minimum amplitude of the trace

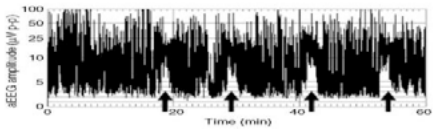


3. Presence of Seizures

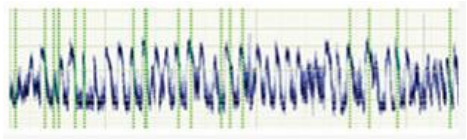
- Single seizure: solitary seizure



- Repetitive seizures: single seizures appearing more frequently than at 30 minute intervals



- Status Epilepticus: Continuous ongoing seizure activity for > 30 minutes



Appendix E. Barkovich Scoring in HIE

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

Appendix F. Neonatal TH Working Group Members

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Appendix G. Link Representatives from each of the Hospital Sites

Cavan General Hospital;
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Coombe Women & Infants University Hospital;
Dr Martin White/ Ms Anne O'Sullivan

Cork University Maternity Hospital;
Dr Peter Filan/ Ms Lucille Bradfield

Kerry General Hospital;
Dr Pervaiz/ Ms Maudie Creagh

Letterkenny General Hospital;
Dr Mathew Thomas/ Kathleen Greenough/ Ms Evelyn Smith

Mayo General Hospital;
Ms Andrea McGrail

Midland Regional Hospital, Mullingar;
Ms Geraldine Kavanagh

Midland Regional Hospital, Portlaoise;
Dr Gallagher/ Ms Yolanda Fennell

National Maternity Hospital;
Prof John Murphy/ Ms Julie McGinley

Our Lady of Lourdes Hospital, Drogheda;
Ms Claire Shannon*

Portiuncula Hospital;
Ms Priscilla Neilan/ Ms Deirdre Naughton

Rotunda Hospital;
Prof Adrienne Foran/ Kathy Conway

Sligo University Hospital;
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Ms Maura Grogan

St. Luke's General Hospital, Kilkenny;
Ms Breda O'Dwyer

University Hospital Galway;
Ms Jean James/ Ms Aine Binchy

University Hospital Limerick;
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University Hospital Waterford;
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*We would like to acknowledge the contributions of Ms Claire Shannon to the TH project and offer our sincere condolences to her family, friends and colleagues on her untimely passing. May she rest in eternal peace.

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