Queensland Clinical Guidelines

Translating evidence into best clinical practice

Maternity and Neonatal **Clinical Guideline**

Supplement: Hypoxic-ischaemic encephalopathy (HIE)

Queensland Government

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1 Introduction

This document is a supplement to the Queensland Clinical Guideline *Hypoxic-ischaemic encephalopathy (HIE)*. It provides supplementary information regarding guideline development, makes summary recommendations, suggests measures to assist implementation and quality activities and summarises changes (if any) to the guideline since original publication. Refer to the guideline for abbreviations, acronyms, flow charts and acknowledgements.

1.1 Funding

The development of this guideline was funded by Queensland Health, Healthcare Innovation and Research Branch. Consumer representatives were paid a nominal fee. Other working party members participated on a voluntary basis.

1.2 Conflict of interest

Declarations of conflict of interest were sought from working party members as per the Queensland Clinical Guidelines *Conflict of Interest* statement. No conflicts of interest were identified.

1.3 Guideline review

Queensland Clinical Guidelines are reviewed every 5 years or earlier if significant new evidence emerges. Table 1 provides a summary of changes made to the guidelines since original publication.

Table 1. Summary of change

Publication date *Endorsed by:*	**Identifier**	**Summary of major change**
6/05/2010	NN1005.11-V1-R13	• First publication
13/05/2010	NN1005.11-V2-R13	• IV Dextrose reworded to IV Glucose
22/08/2011	MN10.11-V3-R15	• New website. Name and format updates
26/10/2011	MN10.11-V4-R15	• Appendix D: Anticonvulsant therapy deleted. Reference to Queensland Maternity and Neonatal Clinical Guideline Neonatal Seizures added
2/03/2016 *Statewide Maternity and Neonatal Clinical Network (Queensland)*	MN16.11-V5-R21	• First full review of original publication • Removed sections on general medical neonatal intensive care management • Flow charts added • Inclusion criteria for therapeutic hypothermia amended • First Guideline Supplement published
16/03/2016	MN16.11-V6-R21	• Flow chart: Criteria for therapeutic hypothermia (cooling): “pH ≤ 7.00” amended to “pH <7.00”
4/8/2017	MN17.11-V7-R21	• Amendments to reference list (typos) • Format of medications updated (not capitalised) • Table 11 Temperature monitoring using axillary temperature and frequency clarified/reworded • Appendix D amended to align with Table 11
10/01/2018	MN17.11-V8-R21	• Checklist for therapeutic hypothermia (page 3) : re-ordered criteria. • Assessment of encephalopathy severity (page 4): Added assessment codes for normal and not applicable. Added space to record time of assessment. • Change requested by clinician. Supports clarity of therapeutic hypothermia criteria and documentation of Modified Sarnat assessment.

Publication date *Endorsed by:*	**Identifier**	**Summary of major change**
February 2018	MN16.11-V9-R21	• Change initiated by clinician to improve clarity around current evidence for therapeutic cooling criteria • Checklist for therapeutic hypothermia amended o Removed statement about criteria with limited evidence o Added standard criteria for cooling to checklist • Base deficit changed to base excess throughout document. • Description of base excess units of measure changed throughout document o **From** ≥ minus 12 mmol/L ‘ o **To** ‘equal to or worse than minus 12 mmol/L’

2 Methodology

Queensland Clinical Guidelines (QCG) follows a rigorous process of guideline development. This process was endorsed by the Queensland Health Patient Safety and Quality Executive Committee in December 2009. The guidelines are best described as 'evidence informed consensus guidelines' and draw from the evidence base of existing national and international guidelines and the expert opinion of the working party.

2.1 Topic identification

The topic was identified as a priority by the Statewide (Queensland) Maternity and Neonatal Clinical Network at a forum in 2009.

2.2 Scope

The scope of the guideline was determined using the PICO Framework (Population, Intervention, Comparison, Outcome) as outlined in Table 2.

Table 2. PICO Framework

PICO	
Population	Newborns, greater than or equal to 35 weeks, with a potential HIE diagnosis
Intervention	Management of neonates with HIE, including therapeutic hypothermia
Comparison	Original HIE guideline
Outcome	Decreased short and long term morbidity

2.3 Clinical questions

The following clinical questions were generated to inform the guideline scope and purpose:

- What is included in the recognition and assessment of HIE?
- What is the management for HIE?
- What is the prognosis associated with HIE?
- What are the parental considerations?

2.4 Exclusions

The following exclusions were identified in the guideline scope:

- Resuscitation [refer to Queensland Clinical Guideline: *Neonatal resuscitation*]
- Management of respiratory distress [refer to Queensland Clinical Guideline: *Respiratory distress including CPAP*]
- Neonatal seizures [refer to Queensland Clinical Guideline: *Neonatal seizures*]
- Newborn hypoglycaemia [refer to Queensland Clinical Guideline: *Newborn hypoglycaemia*]
- Newborn stabilisation for retrieval [refer to Queensland Clinical Guideline: *Neonatal stabilisation for retrieval*]

2.5 Search strategy

A search of the literature was conducted during April 2015. The QCG search strategy is an iterative process that is repeated and amended as guideline development evolves and the draft guideline is refined, additional areas of interest emerge, areas of contention requiring more extensive review are identified or new evidence is identified. All guidelines are developed using a basic search strategy. This involves both a formal and informal approach.

Table 3. Basic search strategy

Step		Consideration
1.	Review clinical guidelines developed by other reputable groups relevant to the clinical speciality	• This may include national and/or international guideline writers, professional organisations, government organisations, state based groups. • This assists the guideline writer to identify: o The scope and breadth of what others have found useful for clinicians and informs the scope and clinical question development o Identify resources commonly found in guidelines such as flowcharts, audit criteria and levels of evidence o Identify common search and key terms o Identify common and key references
2.	Undertake a foundation search using key search terms	• Construct a search using common search and key terms identified during Step 1 above • Search the following databases o PubMed o CINAHL o Medline o Cochrane Central Register of Controlled Trials o EBSCO o Embase • Studies published in English less than or equal to 5 years previous are reviewed in the first instance. Other years may be searched as are relevant to the topic • Save and document the search • Add other databases as relevant to the clinical area
3.	Develop search word list for each clinical question.	• This may require the development of clinical sub-questions beyond those identified in the initial scope. • Using the foundation search performed at Step 2 as the baseline search framework, refine the search using the specific terms developed for the clinical question • Save and document the search strategy undertaken for each clinical question
4.	Other search strategies	• Search the reference lists of reports and articles for additional studies • Access other sources for relevant literature o Known resource sites o Internet search engines o Relevant text books

2.5.1 Keywords

The following keywords were used in the basic search strategy. Other keywords may have been used for specific aspects of the guideline:

neonat*, newborn, infant, perinatal, HIE, hypoxic-ischaemic encephalopathy, hypoxi*, diagnosis, therapeutic hypothermia, cooling, passive cooling, active cooling, hypoxic insult, intrauterine hypoxia, encephalopathy, ischaemic injury, Clinical staging, rewarming, manual cooling, criteria, Sarnat criteria, encephalopathy, guideline, prognosis, morbidity, mortality, investigations, parent discussion, consumer information, side effects, PPHN, coagulopathy.

2.6 Consultation

Major consultative and development processes occurred between March 2015 and October 2015. These are outlined in Table 4.

Table 4. Major guideline development processes

Process	Activity
Clinical lead	• The nominated Clinical Lead was approved by QCG Steering Committee
Consumer participation	• Consumer participation was invited from a range of consumer focused organisations who had previously accepted an invitation for on-going involvement with QCG
Working party	• An EOI for working party membership was distributed via email to Queensland clinicians and stakeholders (~1000) in May 2015 • The working party was recruited from responses received • Working party members who participated in the working party consultation processes are acknowledged in the guideline • Working party consultation occurred in a virtual group via email
Statewide consultation	• Consultation was invited from Queensland clinicians and stakeholders (~1000) during June–July 2015 • Feedback was received primarily via email • All feedback was compiled and provided to the clinical lead and working party members for review and comment

2.7 Endorsement

The guideline was endorsed by the:

- Queensland Clinical Guidelines Steering Committee in October 2015
- Statewide Maternity and Neonatal Clinical Network [Queensland] in February 2016

2.8 Publication

The guideline and guideline supplement were published on the QCG website in March 2016.

The guideline can be cited as:

Queensland Clinical Guidelines. Hypoxic-ischaemic encephalopathy. Guideline No. MN16.11-V9-R21. Queensland Health. 2018. Available from: http://www.health.qld.gov.au/qcg

The guideline supplement can be cited as:

Queensland Clinical Guidelines. Supplement: Hypoxic-ischaemic encephalopathy. Guideline No. MN16.11-V9-R21. Queensland Health. 2018. Available from: http://www.health.qld.gov.au/qcg

3 Levels of evidence

The levels of evidence identified in the National Health and Medical Research Council (NHMRC), Levels of evidence and grades for recommendations for developers of guidelines (2009) were used to inform the summary recommendations]. Levels of evidence are outlined in Table 5. Summary recommendations are outlined in Table 6.

Note that the 'consensus' definition* in Table 4 is different from that proposed by the NHMRC and instead relates to forms of evidence not identified in the NHMRC's level of evidence and/or the clinical experience of the guideline's clinical lead and working party.

Table 5. Levels of evidence

Levels of evidence	
I	Evidence obtained from a systematic review of all relevant randomised controlled trials.
II	Evidence obtained from at least one properly designed randomised controlled trial**.**
III-1	Evidence obtained from well-designed pseudo randomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies including systematic review of such studies with concurrent controls and allocation not randomised (cohort studies), case control studies or interrupted time series with a control group**.**
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without parallel control group.
IV	Evidence obtained from case series, either post-test or pre-test and post-test.
Consensus*	Opinions based on respected authorities, descriptive studies or reports of expert committees or clinical experience of the working party.

3.1 Summary recommendations

Summary recommendations and levels of evidence are outlined in Table 5.

Table 6. Summary recommendations

Recommendation		Grading of evidence
1	Commence therapeutic hypothermia in all newborns who meet the criteria.	**Level I**
2	Commence therapeutic hypothermia within the first 6 hours of birth.	**Level I**
3	For any baby who meets the criteria for therapeutic hypothermia at a Level 1 to 5 neonatal service: • Discuss care with Retrieval Services Queensland and a Neonatologist	**Consensus**
4	Document shared decision making with the parents.	**Consensus**
5	Provide parents with applicable web addresses and/or written information on HIE.	**Consensus**
6	Include in parental discussions information on: • Resuscitation • Incidence • Consequences • Prognosis • Treatment including therapeutic hypothermia where applicable	**Consensus**
7	Enrol all babies with moderate to severe HIE into a follow-up program which can provide assessment, appropriate follow-up and data collection on outcomes.	**Consensus**

4 Implementation

This guideline is applicable to all Queensland public and private maternity facilities. It can be downloaded in Portable Document Format (PDF) from www.health.qld.gov.au/qcg

4.1 Guideline resources

The following guideline components are provided on the website as separate resources:

- Checklist: Criteria for therapeutic hypothermia (cooling)
- Flowchart: Criteria for therapeutic hypothermia (cooling)
- Flowchart: HIE clinical features, investigations and management
- Flowchart: Passive cooling flow chart
- Education resource: Hypoxic-ischaemic encephalopathy (HIE)
- Knowledge assessment: Hypoxic-ischaemic encephalopathy (HIE)
- Parent information: Hypoxic-ischaemic encephalopathy (HIE)

4.2 Suggested resources

During the development process stakeholders identified additional resources with potential to complement and enhance guideline implementation and application. The following resources have not been sourced or developed by QCG but are suggested as complimentary to the guideline:

- Parent information: Bliss and BeBop; Hope for HIE

4.3 Implementation measures

Suggested activities to assist implementation of the guideline are outlined below.

4.3.1 QCG measures

- Notify Chief Executive and relevant stakeholders
- Monitor emerging new evidence to ensure guideline reflects contemporaneous practice
- Capture user feedback
- Record and manage change requests
- Review guideline in 2021

4.3.2 Hospital and Health Service measures

Initiate, promote and support local systems and processes to integrate the guideline into clinical practice, including:

- Hospital and Health Service (HHS) Executive endorse the guidelines and their use in the HHS and communicate this to staff
- Promote the introduction of the guideline to relevant health care professionals
- Support education and training opportunities relevant to the guideline and service capabilities
- Align clinical care with guideline recommendations
- Undertake relevant implementation activities as outlined in the *Guideline implementation checklist* available at www.health.qld.gov.au/qcg

4.4 Quality measures

Auditing of guideline recommendations and content assists with identifying quality of care issues and provides evidence of compliance with the National Safety and Quality Health Service (NSQHS) Standards[1]. Suggested audit and quality measures are identified in Table 7. NSQHS Standard 1.

Table 7. NSQHS Standard 1

NSQHS Standard 1: Governance for Safety and Quality in Health Service Organisations	
Clinical Practice: Care provided by the clinical workforce is guided by current best practice	
Criterion 1.7:	**Actions required:**
Developing and/or applying clinical guidelines or pathways that are supported by the best available evidence	1.7.1 Agreed and documented clinical guidelines and/or pathways are available to the clinical workforce
	1.7.2 The use of agreed clinical guidelines by the clinical workforce is monitored

4.4.1 Therapeutic hypothermia audit criteria

The following clinical quality measures are suggested for babies who undergo therapeutic hypothermia.

Table 8. Clinical quality measures — therapeutic hypothermia

No.	Audit criteria — Therapeutic hypothermia
1.	Baby met the criteria for therapeutic hypothermia
2.	No contraindications were present
3.	Baby's condition and treatment options were discussed with parents and documented in the baby's medical record
4.	Continuous monitoring recording was commenced as soon as possible
5.	Baby achieved the target temperature of 33–34˚C
6.	The baby was not overcooled, that is, below 33˚C
7.	Hypothermia was maintained for 72 hours before rewarming
8.	The rectal temperature was monitored continuously
9.	Rectal temperature monitoring was ceased after the target rectal temperature of 37°C had been recorded for 6 hours
10.	A magnetic resonance imaging (MRI) was undertaken between 5 and 10 days of age, ideally at 7 days
11.	Parents were informed of the need for continued follow-up

4.5 Safety and quality

Implementation of this guideline provides evidence of compliance with the National Safety and Quality Health Service Standards and Australian Council on Healthcare Standards (ACHS) Evaluation and Quality Improvement Program (EQuIP) National accreditation programs.[2,3]

Table 9. NSQHS/EQuIPNational Criteria

NSQHS/EQuIPNational Criteria	Actions required	☑ Evidence of compliance
NSQHS Standard 1: Clinical governance		
Patient safety and quality systems Safety and quality systems are integrated with governance processes to enable organisations to actively manage and improve the safety and quality of health care for patients.	**Diversity and high risk groups** 1.15 The health service organisation: a. Identifies the diversity of the consumers using its services b. Identifies groups of patients using its services who are at higher risk of harm c. Incorporates information on the diversity of its consumers and higher-risk groups into the planning and delivery of care	☑ Assessment and care appropriate to the cohort of patients is identified in the guideline ☑ High risk groups are identified in the guideline ☑ The guideline is based on the best available evidence
Clinical performance and effectiveness The workforce has the right qualifications, skills and supervision to provide safe, high-quality health care to patients.	**Evidence based care** 1.27 The health service organisation has processes that: a. Provide clinicians with ready access to best-practice guidelines, integrated care pathways, clinical pathways and decision support tools relevant to their clinical practice b. Support clinicians to use the best available evidence, including relevant clinical care standards developed by the Australian Commission on Safety and Quality in Health Care	☑ Queensland Clinical Guidelines is funded by Queensland Health to develop clinical guidelines relevant to the service line to guide safe patient care across Queensland ☑ The guideline provides evidence-based and best practice recommendations for care ☑ The guideline is endorsed for use in Queensland Health facilities. ☑ A desktop icon is available on every Queensland Health computer desktop to provide quick and easy access to the guideline
	Performance management 1.22 The health service organisation has valid and reliable performance review processes that: a. Require members of the workforce to regularly take part in a review of their performance b. Identify needs for training and development in safety and quality c. Incorporate information on training requirements into the organisation's training system	☑ The guideline has accompanying educational resources to support ongoing safety and quality education for identified professional and personal development. The resources are freely available on the internet http://www.health.qld.gov.au/qcg
Patient safety and quality systems Safety and quality systems are integrated with governance processes to enable organisations to actively manage and improve the safety and quality of health care for patients.	**Policies and procedures** 1.7 The health service organisation uses a risk management approach to: a. Set out, review, and maintain the currency and effectiveness of, policies, procedures and protocols b. Monitor and take action to improve adherence to policies, procedures and protocols c. Review compliance with legislation, regulation and jurisdictional requirements	☑ QCG has established processes to review and maintain all guidelines and associated resources ☑ Change requests are managed to ensure currency of published guidelines ☑ Implementation tools and checklist are provided to assist with adherence to guidelines ☑ Suggested audit criteria are provided in guideline supplement ☑ The guidelines comply with legislation, regulation and jurisdictional requirements

NSQHS/EQuIPNational Criteria	Actions required	☑ Evidence of compliance
NSQHS Standard 2: Partnering with Consumers		
Health literacy Health service organisations communicate with consumers in a way that supports effective partnerships.	**Communication that supports effective partnerships** 2.8 The health service organisation uses communication mechanisms that are tailored to the diversity of the consumers who use its services and, where relevant, the diversity of the local community 2.9 Where information for patients, carers, families and consumers about health and health services is developed internally, the organisation involves consumers in its development and review 2.10 The health service organisation supports clinicians to communicate with patients, carers, families and consumers about health and health care so that: a. Information is provided in a way that meets the needs of patients, carers, families and consumers b. Information provided is easy to understand and use c. The clinical needs of patients are addressed while they are in the health service organisation d. Information needs for ongoing care are provided on discharge	☑ Consumer consultation was sought and obtained during the development of the guideline. Refer to the acknowledgement section of the guideline for details ☑ Consumer information is developed to align with the guideline and included consumer involvement during development and review ☑ The consumer information was developed using plain English and with attention to literacy and ease of reading needs of the consumer
Partnering with consumers in organisational design and governance Consumers are partners in the design and governance of the organisation.	**Partnerships in healthcare governance planning, design, measurement and evaluation** 2.11 The health service organisation: a. Involves consumers in partnerships in the governance of, and to design, measure and evaluate, health care b. Has processes so that the consumers involved in these partnerships reflect the diversity of consumers who use the service or, where relevant, the diversity of the local community 2.14 The health service organisation works in partnership with consumers to incorporate their views and experiences into training and education for the workforce	☑ Consumers are members of guideline working parties ☑ The guideline is based on the best available evidence ☑ The guidelines and consumer information are endorsed by the QCG and Queensland Statewide Maternity and Neonatal Clinical Network Steering Committees which includes consumer membership

NSQHS/EQuIPNational Criteria	Actions required	☑ Evidence of compliance
NSQHS Standard 5: Comprehensive care		
Clinical governance and quality improvement to support comprehensive care Systems are in place to support clinicians to deliver comprehensive care	**Integrating clinical governance** 5.1 Clinicians use the safety and quality systems from the Clinical Governance Standard when: a. Implementing policies and procedures for comprehensive care b. Managing risks associated with comprehensive care c. Identifying training requirements to deliver comprehensive care **Partnering with consumers** 5.3 Clinicians use organisational processes from the Partnering with Consumers Standard when providing comprehensive care to: a. Actively involve patients in their own care b. Meet the patient's information needs c. Share decision-making	☑ The guideline has accompanying educational resources to support ongoing safety and quality education for identified professional and personal development. The resources are freely available on the internet http://www.health.qld.gov.au/qcg ☑ The guideline provides evidence-based and best practice recommendations for care ☑ Consumer information is developed for the guideline
NSQHS Standard 6: Communicating for safety		
Clinical governance and quality improvement to support effective communication Systems are in place for effective and coordinated communication that supports the delivery of continuous and safe care for patients.	**Integrating clinical governance** 6.1 Clinicians use the safety and quality systems from the Clinical Governance Standard when: a. Implementing policies and procedures to support effective clinical communication b. Managing risks associated with clinical communication c. Identifying training requirements for effective and coordinated clinical communication **Partnering with consumers** 6.3 Clinicians use organisational processes from the Partnering with Consumers Standard to effectively communicate with patients, carers and families during high-risk situations to: a. Actively involve patients in their own care b. Meet the patient's information needs c. Share decision-making **Organisational processes to support effective communication** 6.4 The health service organisation has clinical communications processes to support effective communication when: a. Identification and procedure matching should occur b. All or part of a patient's care is transferred within the organisation, between multidisciplinary teams, between clinicians or between organisations; and on discharge c. Critical information about a patient's care, including information on risks, emerges or changes	☑ Requirements for effective clinical communication by clinicians are identified ☑ The guideline provides evidence-based and best practice recommendations for communication between clinicians ☑ The guideline provides evidence-based and best practice recommendations for communication with patients, carers and families ☑ The guideline provides evidence-based and best practice recommendations for discharge planning and follow –up care

NSQHS/EQuIPNational Criteria	Actions required	☑ Evidence of compliance
NSQHS Standard 6: Communicating for safety (continued)		
Communication of critical information Systems to effectively communicate critical information and risks when they emerge or change are used to ensure safe patient care.	**Communicating critical information** 6.9 Clinicians and multidisciplinary teams use clinical communication processes to effectively communicate critical information, alerts and risks, in a timely way, when they emerge or change to: a. Clinicians who can make decisions about care b. Patients, carers and families, in accordance with the wishes of the patient 6.10 The health service organisation ensures that there are communication processes for patients, carers and families to directly communicate critical information and risks about care to clinicians	☑ Requirements for effective clinical communication of critical information are identified ☑ Requirements for escalation of care are identified
Communicating at clinical handover Processes for structured clinical handover are used to effectively communicate about the health care of patients.	**Clinical handover** 6.7 The health service organisation, in collaboration with clinicians, defines the: a. Minimum information content to be communicated at clinical handover, based on best-practice guidelines b. Risks relevant to the service context and the particular needs of patients, carers and families c. Clinicians who are involved in the clinical handover 6.8 Clinicians use structured clinical handover processes that include: a. Preparing and scheduling clinical handover b. Having the relevant information at clinical handover c. Organising relevant clinicians and others to participate in clinical handover d. Being aware of the patient's goals and preferences e. Supporting patients, carers and families to be involved in clinical handover, in accordance with the wishes of the patient f. Ensuring that clinical handover results in the transfer of responsibility and accountability for care	☑ The guideline acknowledges the need for local protocols to support transfer of information, professional responsibility and accountability for some or all aspects of care

NSQHS/EQuIPNational Criteria	Actions required	☑ Evidence of compliance
NSQHS Standard 8: Recognising and responding to acute deterioration		
Clinical governance and quality improvement to support recognition and response systems Organisation-wide systems are used to support and promote detection and recognition of acute deterioration, and the response to patients whose condition acutely deteriorates.	**Integrating clinical governance** 8.1 Clinicians use the safety and quality systems from the Clinical Governance Standard when: a. Implementing policies and procedures for recognising and responding to acute deterioration b. Managing risks associated with recognising and responding to acute deterioration c. Identifying training requirements for recognising and responding to acute deterioration **Partnering with consumers** 8.3 Clinicians use organisational processes from the Partnering with Consumers Standard when recognising and responding to acute deterioration to: a. Actively involve patients in their own care b. Meet the patient's information needs c. Share decision-making **Recognising acute deterioration** 8.4 The health service organisation has processes for clinicians to detect acute physiological deterioration that require clinicians to: a. Document individualised vital sign monitoring plans b. Monitor patients as required by their individualised monitoring plan c. Graphically document and track changes in agreed observations to detect acute deterioration over time, as appropriate for the patient	☑ The guideline is consistent with National Consensus statements recommendations ☑ The guideline recommends use of tools consistent with the principles of recognising and responding to clinical deterioration ☑ Consumer information is developed for the guideline
EQuIP Standard 12 Provision of care		
Criterion 1: Assessment and care planning 12.1 Ensuring assessment is comprehensive and based upon current professional standards and evidence based practice	12.1.1 Guidelines are available and accessible by staff to assess physical, spiritual, cultural, physiological and social health promotion needs	☑ Assessment and care appropriate to the cohort of patients is identified in the guideline ☑ The guideline is based on the best available evidence

5 Research

5.1 Current research areas

There is ongoing international research in the area of HIE and neuroprotective strategies.

Table 10. HIE research

Queensland facilities involved in:	
NEST[4]	• Neonatal electrographic seizure trial (NEST) • A randomised controlled trial comparing the treatment of electrographic and clinical seizures, to the treatment of clinical seizures alone, in term or near-term encephalopathic infants and measuring the impact on death and neurodevelopment at 2 years
PAEAN[5]	• Erythropoietin for HIE in newborns (PAEAN) • A randomised controlled trial involving newborns who are receiving, or planned to receive therapeutic hypothermia and who are able to be recruited in time to allow study treatment to commence before 24 hours of age. The treatment group will receive human recombinant Epo, 1000 IU/kg IV on days 1, 2, 3, 5 & 7 of life. Families will be followed up every 6 months until the primary assessment of death or disability at 2 years of age
Core body temperature[6]	• Neonatal core body temperature extended investigation • Observational study of 5 body temperature sites on critically ill neonates including HIE babies or critically ill babies requiring initial ventilator support greater than 35 weeks gestational age, and less than 4 weeks postpartum • Hypothesis: that rectal temperature would be slower to respond to changes in environmental temperature than oesophageal temperature
Other Australian facilities are currently researching:	
OCHIE[7]	• Investigation of the optimal cooling period for hypothermic treatment of HIE in term neonates (OCHIE) • A study which will analyse all available clinical parameters of term babies where the clinical decision has been to administer hypothermia treatment following a hypoxic event during cooling and re-warming to determine if there are clinical parameters which aids diagnosis of the severity of the hypoxic insult and outcome prediction and allows analysis and determination of the optimal cooling period based on the severity

5.2 Emerging research areas

Emerging research areas include:

- Stem cell therapy[8-10]
- Hypothermia and xenon[8,11,12]
- Hypothermia and erythropoietin[5,12-18]

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