

**ILCOR SCIENTIFIC ADVISORY STATEMENT PROPOSAL**

**1. Proposed Manuscript Title Therapeutic Hypothermia for Neonatal Hypoxic Ischaemic Encephalopathy**

**2. Environmental Scan**

* *What other papers are already available on same/ similar topic area*

*Parga-Belinkie J, Foglia EE, Flibotte J. Caveats of Cooling: Available*

*Evidence and Ongoing Investigations of Therapeutic Hypothermia. Neoreviews. 2019*

*Sep;20(9):e513-e519.*

 *Wassink G, Davidson JO, Dhillon SK, Zhou K, Bennet L, Thoresen M, Gunn AJ.*

*Therapeutic Hypothermia in Neonatal Hypoxic-Ischemic Encephalopathy. Curr Neurol*

*Neurosci Rep. 2019 Jan 14;19(2):2.*

* Previous systematic reviews:

*Kariholu U, Montaldo P, Markati T, Lally PJ, Pryce R, Teiserskas J, Liow N,*

*Oliveira V, Soe A, Shankaran S, Thayyil S. Therapeutic hypothermia for mild*

*neonatal encephalopathy: a systematic review and meta-analysis. Arch Dis Child*

*Fetal Neonatal Ed. 2018 Dec 19. pii: fetalneonatal-2018-315711*

*Tann CJ, Martinello KA, Sadoo S, Lawn JE, Seale AC, Vega-Poblete M, Russell*

*NJ, Baker CJ, Bartlett L, Cutland C, Gravett MG, Ip M, Le Doare K, Madhi SA,*

*Rubens CE, Saha SK, Schrag S, Sobanjo-Ter Meulen A, Vekemans J, Heath PT; GBS*

*Neonatal Encephalopathy Investigator Group. Neonatal Encephalopathy With Group B*

*Streptococcal Disease Worldwide: Systematic Review, Investigator Group Datasets,*

*and Meta-analysis. Clin Infect Dis. 2017 Nov 6;65(suppl\_2):S173-S189.*

*Rossouw G, Irlam J, Horn AR. Therapeutic hypothermia for hypoxic ischaemic*

*encephalopathy using low-technology methods: a systematic review and*

*meta-analysis. Acta Paediatr. 2015 Dec;104(12):1217-28.*

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*Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for*

*newborns with hypoxic ischaemic encephalopathy. Cochrane Database Syst Rev. 2013*

*Jan 31;(1):CD003311. doi: 10.1002/14651858.CD003311.pub3.*

* *What ILCOR and member council guidelines will be cross-referenced?*  All relevant (neonatal)

**3. Need for the Paper -** Please provide a subject summary (delete yellow text when actioned). How will the paper support ILCOR’s mission, vision and values?

The role of induced hypothermia in management after adult cardiac arrest has been the subject of an advisory statement by ILCOR. Induced hypothermia has a well-established role in management after resuscitation of newborns who have moderate or severe hypoxic ischemic encephalopathy after depression at birth requiring resuscitation. However, there are gaps in knowledge that are the subject of recent and ongoing research. The role of induced hypothermia in settings where other intensive care components cannot be provided is not established (low resource settings). In high resource settings, there has been significant “practice creep”, leading to use of induced hypothermia for infants who did not meet inclusion criteria for randomized trials. Examples are preterm infants, infants with a high likelihood of sepsis, those with only mild encephalopathy, (and those in whom the presence of moderate or severe encephalopathy has not been diagnosed). The balance of benefits and harms in these groups is not yet established. Although animal studies suggest that induced hypothermia should be commenced as soon as possible, very early commencement of hypothermia (during resuscitation) is at odds with other evidence and ILCOR guidelines that support maintaining normothermia to achieve the best outcomes of resuscitation. There is a need for a position statement to clarify when and how to use evidence-based induced hypothermia, and to define situations where there is a need for caution or more evidence.

**4. Audience -** Intended audience (e.g.: healthcare professionals, lay, policy makers, outside societies) Healthcare professionals, relevant members of the basic science and clinical research communities, research funding agencies

**5. Lay Summary** - Write a lay summary of 200 words or less (include clinical relevance)

Neonatal hypoxic ischaemic encephalopathy (abbreviated HIE, caused by low oxygen or blood supply to the brain around the time of birth) affects about 1-3 per 1000 infants in countries with high healthcare resources, and a higher proportion of babies in countries with lower healthcare resources. In higher resourced settings, induced hypothermia (cooling the baby’s whole body or head to a few degrees below normal, in a controlled manner) has been shown to be effective in reducing the rates of death or disability ensuing from HIE and is now standard of care when moderate or severe encephalopathy is present. As with all treatments, there is uncertainty about the risks and benefits in babies who for one reason or another don’t meet the strict criteria that were used for entry into the clinical trials that form the evidence basis for cooling. Some may benefit, but some could be harmed. There is also a potential dilemma in that cooling should be started early to achieve maximal benefit, but this can be at odds with ILCOR recommendations to keep babies’ temperature normal during resuscitation to have the best likelihood of success. There is a need for clear guidance about the best evidence when and how cooling should be provided, and what areas should be the subject of research studies.

Induced hypothermia has been recommended by ILCOR for moderate or severe HIE in neonates since 2010. Meanwhile, the maintenance of normothermia during resuscitation has achieved greater prominence, leading to uncertainty in what to do for individual infants

**6. Implications** – Will there be implications in this guideline/statement for public health and/or are there recommendations that will change the practice of clinicians? If so, please summarize.

Implications for clinical practice

**7. Proposed Writing Group** – 8-10 members in total. Provide full name, institution, and email address for each proposed member. Please consider ILCOR’s values of collaboration and diversity when making nominations. Members of the ILCOR Neonatal Task Force (undergoing transition) and other members of the ILCOR Neonatal Working Group – details to be confirmed at upcoming Task Force meeting in Cape Town, RSA November 2019 and Neonatal Working Group Meeting in Washington DC in December 2019

**Writing Group Chair** (confirm that writing group chair has no relevant COI. 51% of proposed writing group members must be free of COI.)

Helen Liley – No COI

**Writing Group Vice Chair**

TBA

**Writing Group Members**

TBA

**\*Early Career Member**

TBA

**Minority Member**

TBA

\*\*All ILCOR member councils will be invited to nominate a writing group member if proposal is accepted\*\*

**8. Timetable for Completion of Paper** – 6-9 months to time of peer review

**Months 0-1:**

Identification of topic areas of importance for advisory statement

**Months 1-3:**

* Development of protocol, search strategy for relevant evidence

**Months 3-6:**

* Completion of evidence appraisal

**Months 6-9:**

* Manuscript preparation and submission