

# Survey of the use of therapeutic hypothermia after cardiac arrest in UK paediatric emergency departments

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## ABSTRACT

**Objectives** To ascertain current use of therapeutic hypothermia (TH) after paediatric cardiac arrest in UK emergency departments (EDs), and views on participating in a UK randomised controlled trial (RCT) incorporating early induction of TH in ED.

**Design** Anonymous web-based survey of 77 UK Emergency Medicine (EM) consultants from 28 UK EDs that see children during the period April–June 2010.

**Results** 62% (48/77) of surveyed consultants responded from 21/28 (75%) EDs. All managed children post cardiac arrest. 90% (43/48) were aware of the literature concerning TH after cardiac arrest in adults. However, 63% (30/48) had never used TH in paediatric practice. All departments had at least one method of inducing TH (surface cooling; air/water blankets; intravenous cold fluid or catheters). Reasons stated for not inducing TH included no equipment available (26%; 11/42), TH not advocated by the local PICU (24%; 10/42) and not enough evidence for its use (24%; 10/42). TH was considered based on advice from the local Paediatric Intensive Care Units (68%; 17/25) or likelihood of recovery after arrest (32%; 8/25). There was strong support for a UK RCT of TH versus normothermia (85%; 40/47). The proposed RCT was felt to be ethical (87%; 40/48) with use of deferred consent acceptable (74%; 34/46).

**Conclusion** UK EM consultants are aware of TH but infrequently initiate the therapy in children for a number of reasons. Their involvement would enable early induction of TH in EDs after paediatric cardiac arrest during a UK RCT. The authors have demonstrated the availability of suitable equipment and EM consultant support for participation in such a RCT.

## INTRODUCTION

Therapeutic hypothermia (TH) induced to  $33\pm 1^{\circ}\text{C}$  has been shown to significantly improve neurological outcomes after ventricular fibrillation cardiac arrest in adults and hypoxic-ischaemic encephalopathy in neonates.<sup>1–5</sup> Whether the same benefit would be achieved after paediatric cardiac arrest is not yet known, although the International Liaison Committee for Resuscitation (ILCOR) recommend 'considering the use of TH for 12–24 hours in infants and children who remain comatose after resuscitation'.<sup>6</sup>

Animal studies indicate that there is a narrow therapeutic window for TH, and early treatment appears more efficacious, especially in preventing more severe hypoxic-ischaemic injury after cardiac

arrest.<sup>7–10</sup> Adult and neonatal studies showing neurological benefit have recruited patients to receive TH within 6 h of cardiac arrest or hypoxic injury.<sup>1–5</sup> Whether the same therapeutic window applies to paediatric patients following cardiac arrest is as yet unknown.

Children who suffer out of hospital cardiac arrest are brought to their nearest emergency department (ED) for resuscitation. Following successful resuscitation, these patients are cared for in Paediatric Intensive Care Units (PICUs). With the centralisation of PICUs, these children often require transfer from the presenting ED to a regional PICU, often in a different hospital.<sup>11</sup> Due to logistical delays in transportation, it may be necessary for TH to be commenced in the referring ED in order to effectively deliver treatment in the postulated narrow therapeutic window.

The Cold-PACK (Post Arrest Cooling in Kids) study is a multi-centre randomised controlled trial (RCT) comparing TH with normothermia after paediatric cardiac arrest. It is currently in the protocol design stage, and its feasibility is being assessed in the UK. An important element of design is the ability to recruit patients and initiate treatment early after paediatric cardiac arrest. To achieve this, involvement of Emergency Medicine (EM) consultants working in EDs where children are resuscitated would be essential.

A previous survey of consultants in Paediatric Intensive Care in the UK identified a wide variation in uptake and use of TH at that time, but demonstrated support for a RCT of TH after paediatric cardiac arrest.<sup>12</sup> This survey of EM consultants aims to ascertain current practice regarding TH in UK EDs. In addition, it seeks to explore their attitudes and opinions, and assesses potential support from this group of physicians for the Cold-PACK study.

## METHODS

### Survey development

Relevant questions were generated by the study group and piloted on a group of eight EM consultants from three UK hospitals for further feedback and hyperlink access testing (see online supplementary material).

### Survey execution

Seventy-seven EM consultants from 28 UK EDs were invited to participate. Half were from tertiary children's hospitals which have PICU on-site and see only children. The remainder were from secondary general hospitals which have no PICU on-site and

see a mix of adults and children. For the purposes of this paper, we use the term EM consultants to refer to all consultants who participated in the survey. An invitation to participate was sent on the 1 April 2010. Invitations were sent three further times and the internet link was closed on the 30 June 2010.

### Survey template

This was created using Microsoft ASP.NET 2008 (Microsoft, Seattle, Washington, USA). Microsoft Excel (Microsoft) was used for data analysis and results are presented as a per cent of survey responders.

### RESULTS

Of 77 EM consultants surveyed, 48 (62%) responded. Thirty-six (75%) were consultants solely in paediatric EM, and 12 (25%) held dual accreditation in adult and paediatric EM. Responses were from 21/28 (75%) EDs. Ten EDs were located in tertiary children's hospitals which only see children. Eleven were located in secondary general hospitals where consultants manage both adult and paediatric patients.

Consultants responded to questions about their current use of TH (table 1), how they select patients (table 2), methods of cooling available (table 3) and their views on further research (table 4).

### Knowledge of the use of TH

In all, 90% (43/48) of consultants were aware of the literature regarding the use of TH in adults post cardiac arrest.

Very few used TH after paediatric cardiac arrest; 65% (30/46) reported use as 'never' and 30% (14/46) 'seldom'. No responder had a paediatric-specific TH protocol in his or her ED.

A larger proportion used TH after adult cardiac arrest; 27% (13/48) reported 'always' or 'often'. However, half answered 'not applicable' as they did not manage postcardiac arrest adults. Around 17% (8/46) reported being aware of an adult TH protocol in their ED.

The majority (89%; 42/47) did not know if TH improved outcome after paediatric cardiac arrest.

### Patient selection

A number of variables were involved when deciding which patients should receive TH. There were also a number of reasons reported by clinicians for not using TH after cardiac arrest (table 2). Around 52% (25/48) responded to the 'reasons stated for selecting patients for TH post cardiac arrest in children'

**Table 1** Use of TH

	n	Yes n (%)	No n (%)	Unknown n (%)		
Do you look after children post-cardiac arrest in ED?	48	48 (100)	0	0		
Are you aware of published research regarding TH in adults post-cardiac arrest?	48	43 (90)	5 (10)	0		
Do you have a TH protocol for adults?	46	8 (17)	25 (52)	13 (27)		
Do you have a TH protocol for children?	47	0	46 (98)	1 (2)		
Do you believe TH improves outcome after paediatric cardiac arrest?	47	5 (11)	0	42 (89)		
	n	Always	Often	Seldom	Never	NA
Do you use TH after adult cardiac arrest?	48	2 (4)	11 (23)	6 (13)	5 (10)	24 (50)
Do you use TH after paediatric cardiac arrest?	46	0	2 (4)	14 (30)	30 (65)	0

ED, emergency department; TH, therapeutic hypothermia.

**Table 2** Selection of patients for TH

Factors stated in selecting patients for TH post paediatric cardiac arrest (n=25)	n (%)
On advice from PICU	17 (68)
Likelihood of patient recovery after the arrest	8 (32)
Absence of life limiting condition	6 (24)
Availability of equipment	6 (24)
Reasons stated for not using TH post paediatric cardiac arrest (n=42)	n (%)
No equipment available	11 (26)
Not enough research evidence	10 (24)
Not advocated by regional PICU	10 (24)
Not in the advanced paediatric life support guidelines	9 (21)
Rapid transfer to PICU where TH is usually started	6 (14)
Technically too difficult	6 (14)
Not considered for children	3 (7)
Not an emergency department priority or too infrequent	3 (7)
The cooling method available is too slow	2 (5)

PICU, Paediatric Intensive Care Unit; TH, therapeutic hypothermia.

question. The most frequent reason was 'on advice from the regional PICU'. Similarly, 24% (10/42) would not use TH as it was not advocated by the regional PICU and 14% (6/42) would transfer patients quickly to PICU and felt therapy could be commenced there with minimal delay rather than in the ED. The likelihood of patient recovery was also important for 32% (8/25) in choosing which patients should receive TH.

### Methods of inducing hypothermia

Availability of equipment was reported as a factor in patient selection for TH and, conversely, lack of equipment was reported as a reason for not using TH (table 2).

A wide variety of equipment was available in EDs (table 3). ED availability was accepted if *any* consultant from an ED reported it available. Notably, there were discrepancies between responses from within the same ED regarding available equipment (mean inter-responder agreement score within each ED was 0.37; SD 0.06). About 86% of EDs had access to wet linen and 81% to ice packs. Cold air circulating blankets were reported to be present in 62% (13/21) of EDs although only 36% (15/42) of individuals reported it being available. There was a median of three methods of cooling (range 1–6) at each ED.

### Opinions regarding future research into TH after paediatric cardiac arrest

A position of clinical equipoise is defined as the existence of an honest, professional disagreement among expert clinicians about the preferred treatment.<sup>13</sup> Around 52% (24/46) of EM consultants agreed or strongly agreed that this exists regarding the use of TH after paediatric cardiac arrest. Only 7% (3/46) 'disagreed' and the remainder were neutral (table 4).

**Table 3** Availability of methods for inducing therapeutic hypothermia reported by individuals and per emergency departments

Methods	Consultant response (n=42) n (%)*	Emergency department availability (n=21) n (%)*
Wet linen	35 (83)	18 (86)
Ice-pack to skin	24 (57)	17 (81)
Cold air blanket	15 (36)	13 (62)
Iced cold (4°C) intravenous saline	9 (21)	5 (24)
Cold water blanket	2 (5)	2 (10)
Intravascular cooling catheter	1 (2)	1 (5)

\*Percentage total >100 as there was an option to select multiple methods.

**Table 4** Opinions regarding therapeutic hypothermia randomised controlled trial

Please state your strength of agreement with the following:	n	Agreement* n (%)	Mean†	SD
There is clinical equipoise	46	24 (52)	3.5	0.69
It is ethical to perform a RCT	46	40 (87)	4.2	0.72
I approve of the use of deferred consent	46	34 (74)	3.8	1.10
Would you:	n	Yes n (%)	No n (%)	Don't know n (%)
Support a comparative intervention trial?	47	40 (85)	2 (4)	5 (11)
Support a method of cooling study?	45	34 (76)	5 (11)	6 (13)
Allow your patients to be recruited?	47	43 (91)	1 (2)	3 (6)
Use a trial protocol in your ED?	48	41 (85)	1 (2)	6 (13)

\*Agreement = percentage responding 'agree' or 'strongly agree'.

†Mean score on a Likert scale: 5 (strongly agree), 4 (agree), 3 (neutral), 2 (disagree) and 1 (strongly disagree).

Ninety one per cent would agree to their patients being recruited into a RCT of TH after paediatric cardiac arrest. There was greater support for a trial of TH versus normothermia than there was for a method of cooling trial. There was strong support that a RCT of TH is ethical (87%) and that deferred consent is appropriate (74%).

## DISCUSSION

The results of this survey suggest that very few UK EM consultants currently initiate TH after paediatric cardiac arrest in their ED. Various reasons for this emerge from the survey.

EM consultants are unsure whether TH improves outcome after paediatric cardiac arrest. There is an awareness of adult postventricular fibrillation cardiac arrest TH studies which have demonstrated a reduction in bad neurological outcome when treated with TH rather than normothermia.<sup>1 2 14</sup> However, the vast majority of responding consultants in this survey did not know if TH improved neurological outcome after paediatric cardiac arrest.

The 2006 ILCOR guideline recommended the consideration of hypothermia therapy after paediatric cardiac arrest.<sup>6</sup> A more recent edition of the ILCOR guideline has been published since this survey was carried out. However, the recommendations have changed only for adolescents, suggesting that TH is beneficial after ventricular fibrillation cardiac arrest in this group.<sup>15</sup> The evidence to support the ILCOR recommendation is from animal, neonatal and the adult studies described above. There has been no paediatric-specific RCT. Only two retrospective observational cohort studies<sup>16 17</sup> have been published in this area, but they use unbalanced groups and show no difference in outcomes of patients receiving TH compared with normothermia. This lack of evidence may explain the demonstrated lack of uptake of this recommendation. The ongoing Therapeutic Hypothermia After Paediatric Cardiac Arrest multi-centre RCT (clinical trial.gov ID: NCT00880087 and NCT00878644) in the USA may gather important data on safety and efficacy to strengthen any future guidance.

The role of the regional paediatric intensive care team appears to influence the management of paediatric postcardiac arrest patients in the ED. Of EM consultants who would consider using the therapy, 68% reported that they would only commence it if their regional PICU requested and advocated it. If the time taken to admit to PICU was anticipated to be short, then therapy would be delayed until then.

A number of methods of cooling appear to be accessible in most EDs. However, between consultants from the same ED, there is discrepancy in the perception of what equipment is available. There was a belief that the PICU would have access to more sophisticated cooling equipment and be able to

administer the therapy more safely. This may be due to lack of personal experience and infrequent use of the equipment. Three members of this group have previously reported the results of a survey of UK Paediatric Intensive Care consultants conducted in 2009.<sup>12</sup> In this survey, 48% (66/113) of responders 'always' or 'often' used TH after paediatric cardiac arrest. Of those who had used TH, only 30% (24/73) would actively induce TH in an ED. The regional variation of paediatric intensive care practice and the low proportion who would consider starting the therapy in the ED mirror the findings in this present study.

## Further points

This survey highlights the lack of existing protocols for the management of paediatric postcardiac arrest temperature. The temperature of paediatric patients transferred to PICU after cardiac arrest tends already to be low. The US study by Fink *et al* reported a mean postcardiac arrest PICU admission temperature of 34.6°C (±2.2). This included all patients admitted irrespective of whether they were subsequently treated with TH or normothermia.<sup>16</sup> Data for postcardiac arrest temperature of UK children in the ED or PICU are not yet available. However, we hypothesise that young infants and toddlers would generally reduce their core temperature or become frankly hypothermic during or after a cardiac arrest due to the exposure necessary for effective resuscitation despite all efforts to maintain normothermia. Complex methods of inducing TH may therefore not be required in the initial stages. Larger children and adolescents may require more active therapies to initiate and maintain hypothermia or normothermia. Simple methods such as intravenous iced cold (4°C) saline have been used successfully in adults<sup>18–20</sup> and children<sup>21 22</sup> and should be easily accessible with minimal resource implications. Alternatively, if available, more complex methods such as servo-controlled surface cooling air or water blankets could be used.<sup>23</sup> However, continuous monitoring of core temperature (rectal, oesophageal or bladder) would be essential in all cases. Further research is needed to enable the development of consensus guidelines on appropriate paediatric temperature monitoring and management.<sup>24 25</sup>

Only 52% of EM consultants agreed that there is clinical equipoise regarding the use of TH after paediatric cardiac arrest, although another 41% were 'neutral'. The presence of clinical equipoise remains a fundamental prerequisite to undertaking a RCT.<sup>13</sup> There is strong support among EM consultants (85%) for a comparative trial of TH versus normothermia in paediatric patients post cardiac arrest. A large proportion (91%) of these consultants would allow their patients to be recruited into such a study.

The use of deferred consent is still a relatively new process in paediatric resuscitation research in the UK. Changes were made to the Medicines for Human Use (clinical trials) regulations UK in 2008, allowing deferred consent to be used (with ethics committee approval) in emergency resuscitation research.<sup>26</sup> Approval for the use of deferred consent as demonstrated in this survey (74%) would allow very early patient recruitment and initiation of temperature control. This would maximise the potential benefits of TH by ensuring the desired temperature is reached within the postulated narrow therapeutic window.

### Limitations

This survey targeted EM consultants with direct clinical involvement and decision-making responsibility for paediatric patients. We achieved a credible 62% response rate, but not all UK EM consultants, some of whom may occasionally manage paediatric cardiac arrest patients, were surveyed. In addition, as with all surveys, the findings only represent self-reported behaviour and do not necessarily equate to actual clinical behaviour. However, the findings of this survey add strength to the case for further investigative research into the use of TH after paediatric cardiac arrest. We have demonstrated both additional support for, and willingness to participate, in such a RCT, which would incorporate early use of TH in the ED.

### CONCLUSION

This survey of practice and opinions finds that very few UK EM consultants initiate TH in their EDs after paediatric cardiac arrest. Regional PICUs play significant roles in influencing the management of paediatric cardiac arrest patients. With their support, EM consultants would consider using TH. Although simple methods of cooling patients are already available in most EDs, their use is limited due to clinician concerns regarding safety, lack of protocols and lack of evidence of improved outcomes. There is support among UK paediatric intensive care and EM consultants for further research into the safety and efficacy of TH. This research would require involvement of EM consultants and their departments in order to be able to initiate TH early. This survey supports the proposal that the feasibility of the Cold-PACK Study of TH versus normothermia commenced in the ED after paediatric cardiac arrest should be explored further.

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**Contributors** BS and ML designed data collection tools, monitored data collection and analysed the data. BS drafted and revised the paper. BS is guarantor. ML revised the paper. KB, HD and KM piloted data collection tool, analysed the data and revised the paper. DS adapted the data collection tool for internet use.

**Competing interests** None.

**Ethics approval** This study was a service evaluation via a survey of medical practitioners working in emergency medicine in the UK; we, therefore, were satisfied that ethics committee approval was not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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## Appendix One: Supplementary Material

Top of Form

/w EPDw UKMTEx

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### **Survey of the use of therapeutic hypothermia after cardiac arrest in UK paediatric emergency departments.**

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#### **Demographics**

1) Which of the following best describes your current role?

- a) Consultant in Emergency Medicine
- b) Consultant in Paediatric Emergency Medicine
- c) Consultant in Emergency Medicine with dual accreditation in Paediatrics

2) Which of the following best describes your Emergency Department?

- a) Paediatric Emergency Department within a Tertiary Children's Hospital
- b) Emergency Department with Audio-Visual separation of children and adults
- c) Emergency Department with no Audio-Visual separation of children and adults

Other (please specify)

3) On average how many children are seen in your Emergency Department per year?

4) Are children who have suffered a cardiac arrest managed in your Emergency Department?

- a) Yes
- b) No

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#### **Current practice in Therapeutic Hypothermia**

5) Are you aware of the published research regarding the use of therapeutic hypothermia in adults (18 yrs) who have a return of spontaneous circulation (ROSC) following out-of-hospital cardiac arrest?

- a) Yes
- b) No

6) Do you use therapeutic hypothermia as a therapy for adults (>18 yrs) who have a return of spontaneous circulation (ROSC) following out-of-hospital cardiac arrest?

- a) Never
- b) Seldom
- c) Often
- d) Always

e) N/A

7) Does your Emergency Department have a specific protocol for implementing hypothermia therapy in adults >18 yrs?

- a) Yes
- b) No
- c) Don't know

8) Does your Emergency Department have a specific protocol for implementing hypothermia therapy in children <16 yrs?

- a) Yes
- b) No
- c) Don't know

9) Do you currently have access to any of the equipment listed below in your Emergency Department which could be used to induce therapeutic hypothermia in a child? (you can select more than one)

- a) Cold air circulating blanket
- b) Ice Cold (4°Celsius) intravenous fluid
- c) Ice packs to be applied to skin
- d) Wet linen
- e) Cold water circulating Blanket
- f) Intravascular cooling device

Other (please specify)

10) Do you believe that the use of therapeutic hypothermia after cardiac arrest in children (<16 yrs) improves clinical outcome?

- a) Yes
- b) No
- c) Don't know

11) In the management of children (<16yrs) who have had or shown a return of spontaneous circulation (ROSC) following resuscitation from cardiac arrest, how often do you use therapeutic hypothermia in your Emergency Department?

- a) Never
- b) Seldom
- c) Often
- d) Always

*If you answered 'Often' or 'Always' proceed directly to question 13.*

12) Which of the following describes your reason(s) for not using therapeutic hypothermia after resuscitation from paediatric cardiac arrest? (you can select more than one)

- a) I do not look after patients post cardiac arrest
- b) There is not enough research evidence to support its use
- c) Therapeutic hypothermia is not in the APLS guidelines
- d) Therapeutic hypothermia is technically too difficult to initiate
- e) I have concerns that patients are unable to give informed consent
- f) The cooling method to which I have access is too slow
- g) I have never considered hypothermia as a therapy in post arrest children
- h) Hypothermia is not advocated by my local Paediatric Intensive Care Unit
- i) I do not have any equipment available to initiate cooling

Other (please specify)

13) Which method(s) of cooling do you commonly use to induce hypothermia (all age groups)? (you can select more than one)

- a) Cold air circulating blanket
- b) Ice Cold (4°Celsius) intravenous fluid
- c) Ice packs applied to skin
- d) Wet linen
- e) Cold water circulating Blanket
- f) Intravascular cooling device

Other (please specify)

14) What temperature (degrees celcius) do you aim to cool to?

- a) 36-36.9
- b) 35-35.9
- c) 34-34.9
- d) 33-33.9
- e) 32-32.9
- f) 31-31.9
- g) 30-30.9
- h) Don't know

15) On what basis do you select patients to induce therapeutic hypothermia? (you can select more than one)

- a) Likelihood of patient recovery after the arrest
- b) Absence of life limiting condition

- c) Absence of need for vasoactive drug support
- d) Presence of coma for >1hr post successful resuscitation
- e) Availability of equipment
- f) On advice from PICU
- g) Don't know

Other (please specify)

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### Research Opinion/Support

*Regarding the following statements, please select whether you: Strongly agree, Agree, No opinion or Neutral, Disagree, Strongly disagree*

16) There is clinical equipoise regarding the use of therapeutic hypothermia versus normothermia after cardiac arrest in children?

*(Clinical Equipoise: defined as "the existence of an honest, professional disagreement among expert clinicians about the preferred treatment") Freedman B: Equipoise and the ethics of clinical research. N Engl J Med 1987 Jul 16;317(3): 414-5*

- a) Strongly agree
- b) Agree
- c) No opinion or Neutral
- d) Disagree
- e) Strongly disagree

17) It is ethical to perform a randomized controlled trial of hypothermia in children after cardiac arrest

- a) Strongly agree
- b) Agree
- c) No opinion or Neutral
- d) Disagree
- e) Strongly disagree

18) It is ethical to use deferred consent in clinical trials investigating therapies commenced immediately after cardiac arrest

*(Deferred consent: defined as "Obtaining informed consent (from parent or guardian) as soon as is reasonably practicable after the initial emergency. This would be a requirement of continued participation in the trial; but its absence would not preclude initial entry into a trial. The use of deferred consent would only be used after specific approval by an ethics committee")*

- a) Strongly agree
- b) Agree
- c) No opinion or Neutral
- d) Disagree

e) Strongly disagree

19) Would you support a randomized controlled trial in the UK investigating the use of hypothermia after cardiac arrest in children

comparing:

a. Hypothermia versus Normothermia

a) Yes

b) No

c) Don't know

b. Variation in the method of inducing and maintaining hypothermia

a) Yes

b) No

c) Don't know

20) Would you, in principle, allow your patients in the Emergency Department to be included into a multi-centre randomized UK study

of hypothermia after cardiac arrest in children?

a) Yes

b) No

c) Don't know

If you answered 'No' could you briefly explain your answer?

21) Would you be willing to commence therapeutic hypothermia in your Emergency Department as part of a research protocol?

a) Yes

b) No

c) Don't know

If you answered 'No' or 'Don't know' could you briefly explain your answer?

Please write any further comments you have regarding the use of hypothermia after cardiac arrest in children and the prospect of future UK research and your involvement in this area:

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