Therapeutic hypothermia initiated in the pre-hospital setting: a meta-analysis
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CRD summary
The review concluded that induced therapeutic hypothermia in the pre-hospital setting was safe and effective after cardiac arrest. Potential for bias and a limited evidence base of unknown quality mean that the authors' conclusions cannot be considered reliable.

Authors' objectives
To examine the feasibility and safety of pre-hospital hypothermia after cardiac arrest.

Searching
CINAHL, MEDLINE, EMBASE, The Cochrane Library and Web of Science were searched from 2007 to 2010 for relevant studies published in English; search terms were not reported. Reference lists of retrieved studies were searched.

Study selection
Randomised controlled trials (RCTs) of patients 15 years or older who received therapeutic hypothermia after cardiac arrest in the pre-hospital setting were eligible for the review. Therapeutic hypothermia was defined as a body temperature between 32°C and 34°C. Interventions for hypothermia included intravenous infusion of cooled lactated ringers, infusion of cooled intravenous saline or a transnasal-cooling device in addition to the normal standard of care by emergency systems. Control groups received the standard of care used by each emergency system. Participants were required to be comatose after successful return of spontaneous circulation during transportation to the receiving facility. Studies were excluded if they were of people who experienced traumatic arrest, obviously pregnant women (>20 weeks gestation), paediatric patients, patients who were awake and followed commands after resuscitation, patients who had a non resuscitation order and patients with body temperature less than 34°C after return of spontaneous circulation.

One study used an intranasal cooling device, one used infusion of 4°C normal saline with a goal of two litres by arrival to hospital and two studies used infusion of two litres of Ringer’s solution.

The authors did not state how many reviewers selected studies for the review.

Assessment of study quality
Studies were assessed for quality using the critical appraisal skills program (CASP) tool; criteria were not reported.

Two reviewers independently assessed studies for quality. Disagreements resolved through discussion or consultation with a third reviewer.

Data extraction
Data were extracted on mean decrease in core temperature and mean differences between groups and corresponding 95% confidence intervals (CIs) were calculated. The authors extracted data on the adverse effects of haemodynamic instability and pulmonary oedema on chest radiography and discharge outcomes but did not report how these were calculated.

Two reviewers independently extracted data and performed double data entry. Disagreements were resolved through discussion or consultation with a third reviewer.

Methods of synthesis
Where possible, data were pooled in meta-analyses and summary weighted mean differences (WMDs) and their 95% CIs were calculated using the Cohen fixed-effect method. Heterogeneity was assessed with $X^2$.

Results of the review
Four RCTs (511 participants) were included in the review.
Compared to standard post cardiac arrest care, pre-hospital therapeutic hypothermia was significantly associated with a decrease in mean core temperature (WMD -0.89°C, 95% CI -1.06 to -0.72; four studies). There was no evidence of significant heterogeneity between studies.

**Authors' conclusions**
Induced therapeutic hypothermia in the pre-hospital setting was feasible, safe and effective after cardiac arrest.

**CRD commentary**
The review addressed a clear research question: to evaluate the safety and feasibility of induced hypothermia. The authors stated that they assessed adverse events but the results were not analysed and were discussed only in narrative format. Inclusion criteria were appropriate. Various sources were searched for relevant studies published in English. No specific attempts were made to find unpublished studies so language and publication biases could not be ruled out. The time scale of the search was very narrow and so relevant studies may have been missed. Appropriate methods were used to assess study quality and extract data; the authors did not state how many reviewers selected studies so reviewer error and bias could not be ruled out. A valid tool was used for quality assessment, but neither criteria nor the quality of the included studies were reported and this made it difficult to interpret the reliability of the results. The synthesis of studies assessed only feasibility and not safety so the conclusions on safety were not supported by the evidence presented. Assessment of heterogeneity was appropriate.

Potential for bias and a limited evidence base of unknown quality mean that the authors' conclusions cannot be considered reliable.

**Implications of the review for practice and research**
**Practice:** The authors stated that it was safe and feasible to initiate therapeutic hypothermia in the pre-hospital setting after return of spontaneous circulation from cardiac arrest. Development of systems to support therapeutic hypothermia protocols in local and rural emergency medical services systems should be encouraged. Supportive therapy should be continued in the hospital setting.

**Research:** The authors stated that further RCTs of adequate power were needed to assess long-term outcomes, in particular neurologic outcomes, discharge outcomes and survival. Research should also focus on the method and duration of cooling and how low to cool patients.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.