WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

Worksheet author(s)
Jack Billi, MD, R. Van Harrison, PhD
(includes citations from EIT 022B in Evidence Tables)

Date Submitted for review: 1.26.2010

Clinical question.
EIT-022A - In communities where processes/guidelines are being implemented (P), does the use of any specific factors (I), compared with no such use (C), improve outcomes (eg. success of implementation) (O)?
“Applied to therapeutic hypothermia after adult out-of-hospital cardiac arrest”. Includes references from EIT 022B by Ko.

Is this question addressing an intervention/therapy, prognosis or diagnosis? Intervention.

State if this is a proposed new topic or revision of existing worksheet: New topic.

Conflict of interest specific to this question
Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No.

Search strategy (including electronic databases searched).

Search Summary – Post-resuscitation Hypothermia
With agreement of the EIT CoChair and E3, we modified this question to focus on successful implementation of a single guideline. After review of 4 possible clinical guidelines, we selected use of “therapeutic hypothermia after adult out-of-hospital cardiac arrest” as the treatment recommendation, based on time since recommendation published and complexity: First, this recommendation has been endorsed internationally since 2003, so there should be time for reports of attempted implementation to reach the literature. Second, the complexity of following the therapeutic hypothermia (TH) recommendation requires that people attempting implementation consider diverse factors at the organizational, group, and individual clinician level including goals and priorities; benefits and costs; structure, resources, personnel, and roles; and introducing and monitoring changes. Studies of implementation of this recommendation should include this diversity of implementation barriers and factors.

Databases searched:
The literature search was developed in conjunction with a medical librarian (Gurpreet Rana, University of Michigan) and conducted in August 2009, then updated in December 2009. In order to insure a comprehensive search, six databases were searched:
- MEDLINE (Ovid interface; 1950 to August 2009)
- MEDLINE In-process & Non-Indexed Citations (Ovid interface; citations requiring indexing as of August 2009 and updated through December 8, 2009)
- Science Citation Index (also known as Web of Science; 1900 to August 2009)
- EMBASE (including EMBASE and EMBASE Classic, 1947 to August 2009 and updated through December 18, 2009)
- Cochrane Central Register of Controlled Trials (1991 to August 2009)
- Cochrane Database of Systematic Reviews (2nd quarter of 2009)

The overall sensitivity of the search strategy appeared good since hand searching of bibliographies of relevant recent literature only produced 2 possibly relevant citations missed by the search. After reviewing the full text, we excluded these papers as not relevant.

Due to the low number of relevant citations retrieved in the Cochrane Database of Systematic Reviews at the time the search was conducted, results from this database were not included in the final search results. The full search strategy was submitted and approved by the E3. We can provide further details of the search strategies if requested.

- State inclusion and exclusion criteria
The initial search was developed in MEDLINE. The subsequent search strategies in other databases used variation on the same search terms in order to maintain consistency. All searches were made up of the intersection of 4 concept elements:
For Medline, we took the union of:
- [human] and
- [hypothermia (expanded)] and
- [cardiac arrest or resuscitation (expanded)] and
- [implementation, exploded to include MeSH terms related to community or institutional implementation, program evaluation, protocol…].
We included all languages. We merged the results of the searches in the different databases into one reference list. Duplicates were excluded.

Through manual review we excluded references for the following reasons:
- **Wrong Population (P):** Hypothermia as cause of arrest, therapeutic hypothermia during cardiac arrest, non-arrest clinical conditions (AMI, stroke…), pediatric patients, animals.
- **Wrong Intervention (I):** cardiac bypass, ECMO, no implementation factors mentioned.
- **No or Wrong Controls (C)** [Note: we included in the review 2 papers with poor/no controls because they described interesting interventions (Sunde 2008 and Storm 2006)].
- **Wrong Outcome (O):**
  - Primary research on efficacy of TH reporting clinical outcomes.
  - Reports of efficacy of various mechanisms of cooling, such as saline, blankets, or intravascular devices.
  - Studies of effectiveness reporting clinical outcomes of non-trial patients treated with hypothermia. Though called “Implementation Studies” these were often registry reviews to demonstrate that real world clinical endpoint results of TH mirrored the results of the RCTs. They did not describe specific implementation factors or strategies. They reported neither percent of institutions using TH nor percent of eligible patients receiving TH.
- **Review articles**, editorials, comments, letters. These often suggested implementation factors or strategies for addressing barriers, but did not study these factors. Two conceptual articles were included as Level 5 (Brooks 2008, Brach/AHRQ 2008) because they used social science literature and concepts to discuss the diverse elements needed for a successful, robust implementation plan.

*Note:* Many of the studies we eliminated contain insights into factors that might be useful to those actually planning implementation of TH. These included primary research, reviews, and even articles on mechanisms of cooling (easier techniques for cooling could facilitate feasibility and overcome resource barriers). We eliminated such studies for this worksheet because they did not provide direct evidence on factors leading to successful implementation across institutions or communities.

*To view the search strategy for EIT 022B, see that worksheet.*

• **Number of articles/sources meeting criteria for further review:**
  - 480 references reviewed.
  - 13 studies were considered relevant to the question and entered onto the grid, below.
# Summary of evidence

## Evidence Supporting Clinical Question

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<tr>
<th>E1 Rittenberger 2008;198 *</th>
<th>E1 Sunde 2007:29 *</th>
<th>E3 Brooks 2008;286 *</th>
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<td>E3 Brach-AHRQ 2008 *</td>
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<td>E4 Ornstein 2004;523</td>
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| E2 Abella 2005;186          | E1 Hay 2008;15    | E1 Storm 2006;425    |
| E2 Merchant 2006;1935       |                   |                     |
| E2 Laver 2006;873           |                   |                     |
| E2 Kennedy 2008;125 *       |                   |                     |
| E2 Bianchin 2009;357        |                   |                     |
| E2 Suffoletto 2008;52       |                   |                     |

**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
* = Key Studies in yellow  
**Italics** = Animal studies  
E = Other endpoints:  
E1 = Sustained, measured use of TH  
E2 = Survey, reported use of TH  
E3 = Theory, opinion  
E4 = Extrapolation from non-arrest studies  
(E4 – see Ko, EIT 022B for details)
### Evidence Neutral to Clinical question

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**Level of evidence**

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*Italics* = Animal studies

### Evidence Opposing Clinical Question

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**Level of evidence**

A = Return of spontaneous circulation  
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D = Intact neurological survival  
E = Other endpoint  
*Italics* = Animal studies
**General Comments on Five Types of Literature:**

**Reports of implementation:** Since the PICO question refers to factors affecting the success of *implementation in communities*, we originally planned to include only multi-site interventions (multi-hospital studies, multi-EMS-system interventions, community, national...). This would lessen the chance that unnamed co-interventions might have contributed to successful implementation, but be missing from the report. Such co-interventions could include personal or institutional factors in the study setting, such as a strong clinical champion or a track record implementing guidelines. We found no studies that included whole communities or multiple institutions. We therefore decided to include single site implementation studies. We downgraded the quality of these studies for the PICO question, since single site implementation reports included only historical controls (pre-post) with no control for contemporaneous events. These single institution studies are the implementation science equivalent of a case report.

Key questions for quality of study (from Instructions for Worksheet Completion) with our assessment:
- Were comparison groups clearly defined? **Yes**
- Were outcomes measured in the same (preferably blinded), objective way in both groups? **Yes, but not blinded**
- Were known confounders identified and appropriately controlled for? **No**
- Was follow-up of patients sufficiently long and complete? **Yes**

Some intervention studies did not list specific factors that led to success or failure. They varied greatly in their description of the context of implementation. Some reports only described one factor or element to which they attributed the success or failure of the implementation (e.g., Storm 2006 only listed written standard operating procedures).

**Surveys:** Much of the information on implementing TH in communities comes from surveys. The surveys were cross-sectional, observational, non-randomized studies of self-reported use of TH. **TH users** were compared to **TH non-users** as controls, and a variety of questions were asked. Since responders who reported not using TH were the “concurrent, non-randomized controls”, all survey data were considered level 2 studies.

Key questions for quality of study (from Instructions for Worksheet Completion) with our assessment:
- Were comparison groups clearly defined? **Yes**
- Were outcomes measured in the same (preferably blinded), objective way in both groups? **No**
- Were known confounders identified and appropriately controlled for? **No**
- Was follow-up of patients sufficiently long and complete? **No**

Problems with survey studies for this PICO question:
- Questions were often asymmetric: most surveys did not ask both users and non-users the same questions. For example, several surveys asked only TH users about presence of written protocols or standard operating procedures, and only TH non-users about the barriers to using TH. Users were not asked about barriers and non-users were not asked about written protocols.
- Self-reported results were not validated; there was no other measurement of any of the variables reported, e.g., actual use, presence of protocols, or reasons given for non-use.
- Even among self-reported users of TH, the actual percent of cases eligible for TH who got TH was not reported.
- Surveys were either of a broad variety of institutions with low response rates and unknown self-selection factors likely not to produce generally representative results, or of a narrow type of institution with high response rates but limited generalizability to other types of institutions. However, results from both types of surveys are still useful for generating hypotheses regarding relevant factors for further study. The survey
studies might contain selection bias overstating use, since it is possible that users of TH would be more likely than non-users to respond.  
- Self reported reasons for non-use may be inaccurate for several reasons: the survey completer may not be aware of implementation factors, such as presence of a protocol available in his/her ICU; non-users may feel more comfortable stating a lack of evidence or consensus instead of logistic or political barriers.

All survey study design reports were considered poor for this PICO question due to lack of validation, potential for selection bias, and asymmetry of questions.

**Reviews:** Many studies hypothesized on barriers to implementation of TH, or strategies to overcome them. All except one was excluded. We included Brooks 2008, which provided a comprehensive framework for implementation drawing from social sciences literature. This was considered level 5. We also included the white paper by Brach 2008 funded by the US AHRQ in this category as well.

**Nursing Literature:** Nursing journal studies often had protocols and practical hints for implementation, but did not report results of interventions in terms of percent of appropriate patients in which TH was attempted. One paper was included (Koran 2009) but result were obtained by personal communication with the author.

**EMS Literature:** EMS literature (such as JEMS) often had rich commentary on the logistical, social, and political journey to implementation of TH, but in general did not include any data on percent of appropriate cases in which TH was attempted before or after the journey.

**Extrapolation from non-arrest literature:** See Worksheet EIT 022B by Ko for details. Citations listed at end of this worksheet.

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<th>REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:</th>
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<td>Social science literature on diffusion of innovations and implementing change demonstrates the importance of factors at the levels of the individual, the work group and unit, the organization, and the country. These factors can be important individually and in interaction with each other in affecting the success of implementing a desired change. A caution is that factors facilitating the successful implementation of TH in one country or institution (like protocols) may not be effective on another (due to differences in familiarity with and acceptance of protocol medicine). Generalizability of successful factors needs to be tied to the (P) population. And for implementing guidelines, the (P) population is the institutions (or institutional units) responsible for implementation. Their description includes the environments in which they function and the structure, resources, and personnel through which they function.</td>
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<td>Extrapolation from social sciences suggests that a team planning to tackle implementation of a complex guideline or treatment recommendation such as TH may benefit from a standard diagnostic approach, assessing the status and barriers to success at multiple levels: country, community, institution, unit and individual person. This assessment can be used to guide development and deployment of the plan for implementing the change. Several successful studies described this multifaceted approach. One key study (Rittenberger 2008;198) described use of a TH order sheet (available in their electronic medical record), a TH kit (order sheet, blanket, IV fluids), cool fluids stocked in units, an education program, email reminders, written and verbal feedback to individual physicians, a dedicated on-call post arrest consult team, and an explicit rapid cycle improvement process (PDSA). They began in ED, and then spread to multiple ICUs managing post arrest. For OHCAs, TH use increased by year (8% to 81% to 85%, p&lt;0.001). For IHCAs TH use increased by year (0% to 36% to 53%, p&lt;0.02).</td>
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A second key study (Koran 2009;48) included a very well designed and described intervention using a comprehensive, holistic approach. They describe building consensus through review of literature, using clinical champions as sponsors (CNS and ED Med Dir), seeking broad input on “whether and how” (physicians, nurses, transporters, pharmacy, critical care medical director), and local adaptation based on current practice (normal saline v LR) and simplicity (bladder temp). They built consensus on inclusion and exclusion criteria, when to start, cooling method, target temp, monitoring technique. They created a simple protocol and a written process for implementation with explicit roles. They did role-specific education through formal and informal sessions and demonstrations, as well as emails. They monitored implementation for problems and used rapid cycle improvement (PDSA) to solve them quickly (e.g., chilled saline bag rotation – First In First Out). They also monitored progress and intervened based on the results (rapid cycle improvement or PDSA – Plan-Do-Study-Adjust – or Plan-Do-Check-Adjust), including feedback to their target group. Although no results were reported in article their detailed description provides a guide for comprehensive implementation consistent with the social science models. (The author reports that TH rose from 25% in Jan 2008 to 67% in Nov 2008 to 90% in Oct 2009 – but this is an unpublished personal communication with author.)

A third key study (Sunde 2007;29) measured use of a comprehensive bundle of hospital care elements (including TH) in an Oslo hospital 2003-2005. Factors reported included a data collection sheet and a goal-directed one page protocol for the bundle. 77% were treated with TH after introduction of the bundle compared to historical controls from the same hospital before ILCOR TH recommendation (1996-8), in which no patients were given TH.

The value of written protocols deserves special comment. Implementation of TH involved written protocols in all five of the included implementation studies (Rittenberger 2008;198; Koran 2009;48; Sunde 2007;29; Hay 2008;15; Storm 2006;425) and in two survey reports (Kennedy 2008;125 and Bianchin 2009;357). While the evolution and use of written protocols was not detailed in the reports, they can contribute to the success of several aspects of implementation. Protocols define the “standard work” to be performed by everyone involved, facilitating multidisciplinary discussion and consensus-building. They identify the resources that need to be easily accessible. They provide a basis for educating the involved personnel and for identifying measures for monitoring the ongoing provision of appropriate care. The protocol provides a standard, which allows rapid detection of deviation from that standard. When problems are then identified, improvements can be incorporated into modified protocols (PDSA).

For details on the extrapolation from non-arrest literature, see Worksheet EIT 022B by Ko, and Citation List at end of this worksheet.

As a side note (perhaps of use to future reviewers of implementation questions), the TH literature went through interesting evolution over time from the 1990s to present. The trend over time roughly was:
- case reports of efficacy of TH,
- non-randomized trials of TH,
- multicenter RCTs that formed the basis of the ILCOR Statement,
- the ILCOR Statement in 2003,
- echo literature repeating the conclusions of the ILCOR statement in different specialties (neurology, trauma), countries, languages, professions (nurses, paramedics), etc.,
- feasibility of TH in real communities,
- effectiveness of TH real communities (reporting approximately the same clinical outcome results in different communities based on secondary/registry data),
- surveys of the use (or lack of use) of TH in various geographic areas
- single institution implementation studies

**KNOWLEDGE GAPS:**

1. **Intervention studies:**
   - More multi-institution or multi-site intervention studies.
   - More thorough descriptions of all co-interventions (such as factors listed in Treatment Recommendations).

2. **Repeat surveys with same population to assess progress:**
   - Ask both users and non-users about facilitating factors and barriers.
   - Ask if respondents used any of the specific factors reported in the intervention studies (such as consensus-building, logistic support, PDSA) to assess which of these factors may be most critical.

3. **Assess the effect of a multi-level diagnostic approach (country, community, organization, unit, individual) when designing implementation to guide which of the elements of a comprehensive multifaceted intervention should be used.**

4. **Asses EMS implementations separately – they may be quite different due to the central command and control, and strict use of protocols.**

**Acknowledgements:**
Gurpreet Rana, Medical Librarian, University of Michigan

Attachments: Tables 1 and 2.
Citation List

(see Tables 1 and 2, attached, for summary of studies reviewed)

Studies included in the worksheet:

Title: Induced hypothermia is underused after resuscitation from cardiac arrest: a current practice survey.
Authors: Abella, B.S.; Rhee, J.W.; Huang, K.N.; Vanden Hoek, T.L.; Becker, L.B.
Source: Resuscitation, 2005, 64, 2, 181-186
Abella 2005;186. LOE 2; quality poor; direction supportive. Nov 2003 Internet Survey of random sample of members of SAEM, ATS, AHA. 19% response rate. 13% had used TH. Reasons for not using TH: 49% not enough data, 32% had not considered it, 28% technically too difficult.

Title: Therapeutic hypothermia in Italian intensive care units: a national survey.
Authors: Bianchin, A.; Pellizzato, N.; Martano, L.; Castioni, C.A.
Source: Minerva Anestesiolo., 2009, 75, 6, 357-362
Bianchin 2009;357. LOE 2; quality poor; direction supportive. Survey of Italian ICUs (July-Oct 2007) with 90% response rate (404 ICUs) and 82% of Italian ICU beds. Asked self-reported TH use after VF cardiac arrest and other events (an unverified point estimate). TH users were asked indications, method, duration, target temp and if they had a written operating procedure for TH. Authors did not ask TH users what percent of cases received TH. Non users were asked why they did not use TH. (TH non-users were not asked about written operating procedure). Results: 16% of Italian ICUs reported using TH for cardiac arrest, though type of arrest (VF, OOH…), method, target temp, and duration of TH all varied. 60% (49/81) of TH users reported using a written operating procedure. TH non-users reported reasons: no experience/need more info, never thought about it, planned not used yet, not effective on clinical study basis, technically too difficult, and “other”.

Title: Therapeutic hypothermia after cardiac arrest – implementation in UK intensive care units.
Authors: Binks, A.C.; Murphy, R.E.; Prout, R.E.; Bhayani, S; Griffiths, C.A.; Mitchell, T.; Padkin, A.; Nolan, J.P.
Source: Anaesthesia, 2010, Published on line. Not in print yet.
Binks 2010; on line. LOE 2; quality poor for this PICO question. Phone Survey of directors of ICUs in UK (March-August 2009) with 98% response rate (243 ICUs). Asked self-reported TH use after cardiac arrest. TH users were asked indications, method, duration, target temp. Authors did not ask TH users about implementation factors such as protocols or what percent of cases received TH. Non users were asked why they did not use TH. Results: 86% of UK ICUs reported ever using TH for cardiac arrest. By asking the year the respondent recalled the ICU began using TH, the authors estimated what the rates of use were across the UK by year between 2002 and 2009. Rates rise steadily from under 20% in 2005 to over 80% in 2008. TH non-users reported reasons based on choices read to them: 26% no local consensus/not enough evidence, 3% unaware of evidence, 31% discussed but not yet implemented, 9% no reason, 29% logistics/resource issues.

Title: Will it work here? A decision-maker’s guide to adopting innovations.
Authors: Brach, C.; Lenfestey, N.; Roussel, A.; Amoozegar, J.; Sorensen, A.
Source: Agency for Healthcare Research and Quality, 2008, Publication No. 08-0051 (Rockville, MD)
Brach AHRQ 2008. LOE 5; quality fair; direction supportive. Review. Comprehensive guide to planning and implementing innovations in health care delivery (e.g., implementing guidelines), prepared under contract by RTI International funded by the US Agency for Healthcare Research and Quality. Drawing from Rogers’ Diffusion of Innovations (5th ed. New York: Free Press, 2003) and other literature, the framework regards
adoption as a process involving a series of interrelated considerations, decisions, and actions at the community, institutional, unit, and individual levels. The information is organized into four primary areas for consideration:

1. **Does the innovation fit?** Is the evidence sound that it works? Does it fit with organization’s mission?
2. **Should we do it here?** Is the benefit worth the costs for this organization? What is the business case?
3. **Can we do it here?** Is it feasible for our local units? What changes are needed in structure, process?
4. **How will we do it here?** After deciding to do it: How will we introduce, implement, and monitor?

   Detailed implementation plan.

These four conceptual areas are used to organize reported barriers and facilitating factors in Table 2 of worksheet.

Title: Implementation of therapeutic hypothermia guidelines for post-cardiac arrest syndrome at a glacial pace: seeking guidance from the knowledge translation literature.

Authors: Brooks, S.C.; Morrison, L.J.

Source: Resuscitation, 2008, 77, 3, 286-292

Brooks 2008;286. LOE 5; quality fair; direction supportive. Review. Good theoretical analysis of barriers to implementing TH, drawing on implementation literature, citing work of Grol (BMJ 1997;315:418) and Cabana (JAMA 1999;282:1458). Implementation approaches include educational, epidemiological, marketing, behavioral, social interaction, organizational, and coercive. Barriers cited include lack of awareness, lack of agreement, lack of self-efficacy, lack of outcome expectancy, inertia of previous practice, guideline-related barriers and inter-professional barriers. Authors offer suggestions for implementing TH using this model. The primary focus of their analysis is on factors at the individual level, with less attention to factors at the unit, institutional and environmental levels.

Title: Therapeutic hypothermia in comatose patients after out-of-hospital cardiac arrest

Authors: Hay, A.W.; Swann, D.G.; Bell, K.; Walsh, T.S.; Cook, B.

Source: Anaesthesia, 2008, 63, 1, 15-19

Hay 2008;15. LOE 3; quality poor; direction supportive. Single institution implementation - one ICU assessment of effect of a written clinical pathway (a “Hypothermia Package”) on TH use, v. historical controls. TH use rose from 44% (20/45) to 75% (41/55) p = 0.04. Authors claim all 14 cases not cooled were for reason (CV instability, treatment withdrawn, bleeding, sepsis, rise in consciousness), which means 100% of appropriate patients were cooled. The percent < 34C within 4 h of ROSC rose from 15% (3/20) to 51% (21/41) p = 0.001, and percent within therapeutic range (32–34C) for > 12 h also increased from 30% (6/20) to 83% (34/41) p < 0.001. Rated poor for this PICO question due to being single institution and because authors only briefly report other environmental factors or co-interventions that might have contributed to success. They mention: “close working relationship with the emergency department and education and support of nursing staff”.

Title: The use of induced hypothermia after cardiac arrest: a survey of Canadian emergency physicians.

Authors: Kennedy, J.; Green, R.S.; Stenstrom, R.; CAEP Critical Care Committee

Source: CJEM Canadian Journal of Emergency Medical Care, 2008, 10, 2, 125-130

Kennedy 2008;125. LOE 2; quality poor; direction supportive. A 2006 Survey of Canadian Emergency Physicians. Cross sectional, observational, self report of TH use. 19% response rate (247). 47% had ever used HT, strongly associated with dept policy/protocol 77% of those working in institutions with protocols reported using TH compared with 24% of those working in institutions without protocols (OR 10.5, CI 5.3-20.8). Other factors not statistically significant in multivariate analysis. TH protocols used in 59% of academic centers v. 28% of non-academic centers. Barriers reported by respondents: lack of policy/protocol (39%), lack of resources (29%), lack of consultant support (9%), disagreement among specialties (9%), lack of evidence (8%), difficult to initiate (6%), administrative hurdles (3%), nursing issues (2%). Of course, surveys assume
that individuals providing the information is aware of current procedures and bases for decisions at their institutions.

Title: Therapeutic hypothermia in the postresuscitation patient: the development and implementation of an evidence-based protocol for the emergency department
Authors: Koran, Z.
Source: Journal of Trauma Nursing, 2009, 16, 1, 48-57
Koran 2009;48. LOE 5; quality fair; direction supportive. Single institution implementation. Detailed description of thorough implementation process at one institution 2008-2009. They describe building consensus through review of literature, clinical champions as sponsors (CNS and ED Med Dir), seeking broad input on “whether and how” (physicians, nurses, transporters, pharmacy, critical care medical director), and local adaptation based on current practice (normal saline v LR) and simplicity (bladder temp). They built consensus on inclusion, exclusion criteria, when to start, cooling method, target temp, monitoring technique. They created a simple protocol and a written process for implementation with explicit roles. They role-specific education through formal and informal sessions and demonstrations, as well as emails. They monitored implementation for problems and used rapid cycle improvement (PDSA) to solve them quickly (e.g., chilled saline bag rotation – First In First Out). Rated LOE 5 due to not reporting any results in the article, but kept in the worksheet due to detailed, practical, multifaceted implementation approach. By personal communication with author, they report that TH rose from 25% in Jan 2008 to 67% in Nov 2008 to 90% in Oct 2009.

Title: Therapeutic hypothermia after cardiac arrest: a survey of practice in intensive care units in the United Kingdom.
Authors: Laver, S.R.; Padkin, A.; Atalla, A.; Nolan, J.P.
Source: Anaesthesia, 2006, 61, 9, 873-877
Laver 2006;873. LOE 2; quality poor; direction supportive. A 2005 Survey of UK ICUs. 98% response rate, 246 ICUs. 73% never used TH. 3 of these had a protocol and were waiting for their first patient. Reasons not using: 26% logistic/resources, 23% evidence not strong enough or no local consensus, 14% did not know evidence, 19% discussed it but not implemented it yet, 29% no reason. 3 ICUs stopped using TH, one after discussion with a neurosurgical center and 2 found it too difficult. No discussion of factors or protocols associated with use. Did not report percent of patients treated with TH.

Title: Therapeutic hypothermia utilization among physicians after resuscitation from cardiac arrest.
Merchant 2006;1935. LOE 2; quality poor; direction supportive. A 2005 internet Survey of US, UK, Australian and Finland physicians. 17% response rate. 26% of US and 36% of non-US had used TH. Reasons for not using TH: 48% not enough data, 41% not part of ACLS, 34% had not considered it, 3% initial results unsatisfactory, 35% technically too difficult, 9% cooling method too slow, 5% concern about consent, 16% other. Using a logistical regression analysis of physician factors independently associated with implementing vs. not implementing TH, factors were non-US vs US physicians (61% Finland, 42% Australia, 31% Great Britain vs. 26% US; OR 1.85), medical specialty (US responses: 34 % critical care vs. 24% cardiology,16 % emergency medicine; OR 1.7), more than 10 arrest patients treated per year (OR 1.2), and larger size hospital (OR 1.1).

Title: Outcomes of a hospital-wide plan to improve care of comatose survivors of cardiac arrest.
Authors: Rittenberger, J.C.; Guyette, F.X.; Tisherman, S.A.; DeVita, M.A.; Alvarez, R.J.; Callaway, C.W.
Rittenberger 2008;198. LOE 3; quality fair; direction supportive. **Single institution implementation** (UPMC) well described multi-element intervention with historical controls. (“A quality improvement program with multiple interventions of escalating intensity”). Jan 2005-Dec 2007. Used TH order sheet (available in EMR), TH kit (order sheet, blanket, IV fluids), cool fluids stocked in units, education program, email reminders, written and verbal feedback to individual physicians, a dedicated on-call post arrest consult team, and an explicit rapid cycle improvement process (PDSA). Began in ED, spread to multiple ICUs managing post arrest. For OHCAs, TH use increased by year (8% to 81% to 85%, p<0.001). For IHCA TH use increased by year (0% to 36% to 53%, p<0.02). Rated fair for this PICO question due to being single institution.

Title: Therapeutic hypothermia after cardiac arrest--the implementation of the ILCOR guidelines in clinical routine is possible!
Source: **Crit.Care**, 2006, 10, 6, 425
Storm 2006;425. LOE 4; quality poor; direction supportive. **Single institution implementation.** Letter report of the effect of a written standard operating procedure for TH in one medical ICU in 2006. Results: 28 of 32 eligible patients received TH after the SOP was implemented. Authors do not report the rate of TH use before the SOP (but presumably it is lower), so this is essentially an uncontrolled case series.

Title: Use of prehospital-induced hypothermia after out-of-hospital cardiac arrest: A survey of the National Association of Emergency Medical Services Physicians
Authors: Suffoletto,B.P.; Salcido,D.D.; Menegazzi,J.J.
Source: **Prehosp.Emerg.Care**, 2008, 12, 1, 52
Suffaletto 2008;52. LOE 2; quality poor; direction supportive. A 2007 Survey of EMS directors at NAEMS D meeting re **pre-hospital cooling. 59% response rate** (145), mostly US. 6.2% reported their systems had protocols. Barriers: overburden 62%, short transport times 61%, lack refrigeration 60%, receiving hosp did not continue TH 57% , lack of guideline for prehospital cooling 22%.

Title: Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest.
Source: **Resuscitation**, 2007, 73, 1, 29-39
Sunde 2007;29. LOE 3; quality fair; direction supportive. **Single institution implementation.** Measured use of a comprehensive bundle of hospital care elements (including TH) in an Oslo hospital 2003-2005. Although clinical outcomes were compared to historical controls from same hospital 1996-8, the control period was before ILCOR recommendation so it is not possible to tell the effect of the intervention, compared to the effect of usual diffusion. 77% treated with TH after the bundle was implemented, compared with none before TH was recommended by ILCOR. Factors reported included a data collection sheet and a goal-directed one page protocol for the bundle. Although the target was better post arrest care in multiple dimensions, not just use of TH, they did report high rate of TH use associated with the bundle.

**Appendix: Interesting, Related Literature Not Meeting Inclusion Criteria:**

Title: Therapeutic hypothermia in cardiac arrest: Feasible? Case series in a community hospital.
Authors: Aghenta,A.; Osowo,A.; Das,V.; Palacio,C.
Source: **Journal of Hospital Medicine (Online)**, 2008, 3, 6, 489-492
Aghenta 2008. A case report of one hospital who made the decision and then “implemented” it with a protocol in 8 cases. No discussion of factors, or percent of cases TH attempted.

Title: Hypothermic resuscitation. Seattle pioneers research & implementation.
Authors: Copass, M.K.
Source: *Journal of Emergency Medical Services*, 2007, 32, 10, S9-11
Copass 2007. Description of several steps used to bring pre hospital TH to Medic 1, Seattle EMS, including clinical results of a trial use v. non-use of TH.

Title: Bringing research to the bedside: the role of induced hypothermia in cardiac arrest
Authors: Cushman, L.; Warren, M.L.; Livesay, S.
Source: *Crit. Care Nurs.Q.*, 2007, 30, 2, 143-153
Cushman 2007. Detailed description of one hospital implementation. No outcomes (cooled 25 patients, but did not state how many were eligible to cool, nor percent in prior period). Begun in 2005, factors include: multidisciplinary team oversaw whole process. Team included nurses, nurse managers, CNS, pharmacists and physicians (neurointensivist experienced in TH, cardiology, pulmonary, neuro, ED). Team reviewed literature, developed protocol, assigned roles, educated staff, supported process (24x7), monitored outcomes. They limited to one unit (CCU) and one clinician (neurointensivist). Revised protocol after first 4 cases (PDSA). Used cooling vendor staff to help. Communication plan included off-shifts.

Title: Use of a standardized order set for achieving target temperature in the implementation of therapeutic hypothermia after cardiac arrest: a feasibility study
Authors: Kilgannon, J.H.; Roberts, B.W.; Stass, M.; Cimino, M.J.; Ferchau, L.; Chansky, M.E.; Dellinger, R.P.; Parrillo, J.E.; Trzeciak, S.
Kilgannon 2008. Single institution use of multidisciplinary education program, standard order set through CPOE, on-call CNS or Nurse Manager available for advice. Improved TH use. July 2006-July 2007. No controls (not even historical controls – no rate of TH given before intervention). TH only attempted in 33% of potentially eligible patients. 96% achieved target temp and only took 4.4 hours.

Title: Use of therapeutic hypothermia after cardiac arrest: A survey of the Society of Critical Care Medicine in South Korea
Authors: Kim, Y-M; Kim, J-H; Park, K-N.
Kim 2009.,836. Letter. Internet survey of members of Korean Society of Critical Car Medicine. Jan-Feb 2008. 19% response. 37% tried TH, 56% fewer than 10 pts. No factors assessed. Barriers stated: Not considered 61%, technically too difficult 29%, not enough evidence 2.5%, not taught in class 2.5% (1).

Title: Induced cooling by EMS (ICE). Year one in Raleigh/Wake County.
Authors: Myers, J.B.; Lewis, R.
Source: *Journal of Emergency Medical Services*, 2007, 32, 10, S13-15
Myers 2007. Description of the multifaceted approach to implementation of pre-hospital TH is a single EMS system (Raleigh/Wake County EMS). Includes description of factors they believed facilitated adoption: discussion among EMS leaders leading to the decision to try pre-hospital TH, discussion with physicians and nurses in receiving EDs, selection of only 2 EDs who did PCI (agree to bypass other hospitals), creation of written real-time Job Aids (weight base doses and checklist for patient selection), reliable and simple process in the field, written protocol overseen by 1 of 5 supervisors dispatched with cold fluids. No data on percent cooled.
Title: Cooling in Pittsburgh: research and implementation of prehospital post cardiac arrest hypothermia by city of Pittsburgh.
Authors: Pinchalk,M.E.; Roth,R.
Source: Journal of Emergency Medical Services, 2009, 34, 1, 25-27
Pinchalk 2009 Pilot guideline in field TH use by EMS. Factors included rapid cycle improvement (revision of protocol), feasibility testing with 2 units followed by expansion, purchase and distribution of equipment, protocols spread throughout a structured delivery system (city EMS). No results reported.

Title: Implementing the International Liaison Committee on Resuscitation guidelines on hypothermia after cardiac arrest. The German Experience: still a long way to go?
Authors: Sander,M.; von Heymann,C.; Spies,C.
Source: Crit.Care, 2006, 10, 2, 407-408.
Sander 2006.407. Letter survey of University Anesthesiological ICUs in Germany (Spring 2005). Cross sectional, observational, self report of TH after CA, and if they used written standard operating procedures (WSOP). Response, 28/39 (72%). Results: 38.5% (10/26) ICUs treating arrest patients reported using TH. 30.8% (8/26) had WSOP, but authors did not mention if those 8 were among the 10 users of TH. Therefore an association of use of WSOP with actual use of TH cannot be assessed. Authors speculate on possible reasons for non-use, but did not ask why.

Title: Uptake of therapeutic hypothermia following out-of-hospital cardiac arrest in Scottish Intensive Care Units
Authors: Sim,M.; Dean,P.; Booth,M.; Kinsella,J.
Source: Anaesthesia, 2008, 63, 8, 886-887
Sim 2008. Letter survey of 24 Scottish ICUs, 1 did not receive arrest patients, 20 used TH, 16 had protocol. Reply to Hay 2008 (169).

Title: Therapeutic hypothermia use among health care providers in 2 developing countries.
Authors: Varon,J.; Acosta,P.
Source: Am.J.Emerg.Med., 2008, 26, 2, 244
Varon 2008. Survey at 2 Emergency Medicine/Critical Care meetings in Mexico and Indonesia, no dates given. 266 (87% response rate). 15% had used TH, 8% had protocols, 80% of those reporting protocols were nurses.

Title: Mild therapeutic hypothermia after cardiac arrest - a nationwide survey on the implementation of the ILCOR guidelines in German intensive care units.
Authors: Wolfrum,S.; Radke,P.W.; Pischon,T.; Willich,S.N.; Schunkert,H.; Kurowski,V.
Source: Resuscitation, 2007, 72, 2, 207-213
Wolfrum 2007. A 2005 survey of German ICUs, 58% response rate. Did not ask about implementation factors, just characteristics of ICU and reasons for not using TH. 23% used TH, more likely in academic hospitals, size of ICU, specialty (IM>Anes), presence of PCI. Reported reasons for not using TH included planned to do it 10, no experience or need more info 20%, technically too difficult 19%, not yet evidence based 11%, no reason 32%.
Table 1. Intervention Studies: Factors Facilitating Implementation

<table>
<thead>
<tr>
<th>INTERVENTION STUDIES</th>
<th>FACTORS FACILITATING IMPLEMENTATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author/yr</td>
<td>Clinical Champion, Consensus Discussion</td>
</tr>
<tr>
<td>Rittenberger 2008 🌸 UPMC (Pittsburgh) OHCA: 6% to 65% to 76% IHCA: 0% to 36% to 53%</td>
<td>MD, RN, HO Spread from ED to CICU (patient flow)</td>
</tr>
<tr>
<td>Sunde 2007 🌸 Ulleval Hospital Oslo 0% (Pre TH 1996) to 75%</td>
<td>Strategic plan Barriers Critical factors</td>
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<tr>
<td>Hay 2008 Royal Infirmary Edinburgh 44% to 75% (100% of eligible)</td>
<td>“Close working relationship ED &amp; RN” mentioned</td>
</tr>
<tr>
<td>Storm 2006 MICU Charite U Berlin 5% to 87%</td>
<td>Written SOP: (std. operating procedure)</td>
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<tr>
<td>Koran 2009 🌸 NW Community Hospital Virginia (no results published; see Citations for personal communication with author)</td>
<td>Clinical Champions Literature review Broad input</td>
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<td>---------------------------------------------------</td>
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<tr>
<td>Abella-2005 (2003) SAEM MDs 19%</td>
<td>13%</td>
</tr>
<tr>
<td>Merchant-2006 (2005) US,UK,Fin MDs 17% (91% are US)</td>
<td>26% US 36% non-US</td>
</tr>
<tr>
<td>Laver-2006 (2005) UK ICU MDs 98%</td>
<td>27%</td>
</tr>
<tr>
<td>Kennedy-2008 (2006) Canada ED MDs 19%  #= Key Study</td>
<td>47%</td>
</tr>
<tr>
<td>Bianchin-2009 (2007) Italian ICU 90%</td>
<td>16%</td>
</tr>
<tr>
<td>Binks – 2010 (2009) UK ICUs 98%</td>
<td>86%</td>
</tr>
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</table>
Citation List from EIT022B, Ko

1. de Villiers JS 2007


Level of evidence: 5
Quality: Poor, supporting
Comments: a study in community, but no control groups (no comparison), showing that an intervention of a multidisciplinary prehospital diagnosis and transfer pathway resulted in D2B time within the recommended period of 90 minutes.

2. Ellrodt G 2007


Level of evidence: 5
Quality: Fair, supporting
Comments: a single-hospital based study, using retrospective controls. It showed multidisciplinary rounds (MDR), a patient-focused communication system integrating care delivered by multiple providers using concurrent feedback, redundancy, and rapid cycle improvement at Berkshire Medical Center, is a clinical quality-improvement implementation system that has driven sustained high-level performance in the American Heart Association's GWTGs (Get With The Guidelines). MDR has improved coordination of care, been flexible, and facilitated rapid and sustained process improvement. Improvement in evidence-based cardiovascular processes for CAD, stroke and heart failure have been associated with improved in hospital AMI mortality and decreased overall community cardiovascular, AMI, stroke and heart failure mortality. MDR can be used by multiple organizations to drive care improvement.

3. Han YY 2003


Level of evidence: 5
Quality: Poor, supporting
Comments: retrospective case series analysis. It indicated early and aggressive resuscitation of pediatric-neonatal septic shock guideline by community physicians is associated with improved outcome.

4. Jackson SL 2004


Level of evidence: 5
Quality: Fair, supporting
Comments: Case-Control study, using concurrent controls without randomization. It indicated educational program increase prescriptions of warfarin for stoke prevention in patients with AF.

5. Khot UN 2007


Level of evidence: 5
Quality: Fair, supporting
Comments: retrospective controls (before-and-after study). Only measure the improvement in a hospital, not really in communities. However, it indicated the potential to facilitate and enhance the outcome (better D2B time) of implementation (emergency department physician activation of the catheterization laboratory) while extending this into the suitable hospitals in communities.

6. Ornstein S 2004

Level of evidence: 5
Quality: Fair, supporting
Comments: a community RCT study, with small number of practices. It indicated primary care practices that use electronic medical records and receive regular performance reports can improve their adherence to clinical practice guidelines for cardiovascular disease and stroke prevention (diagnoses of hypertension and blood pressure control).

7. Read SJ 2006

Level of evidence: 5
Quality: Fair, supporting
Comments: a hospital-based study in four regional hospitals, using before and after comparison, with small number of cases. It indicated stroke care pathways appear to improve the process of care.

8. Soumerai SB 1998

Level of evidence: 5
Quality: Fair, supporting
Comments: a community RCT study. It indicated working with opinion leaders and providing performance feedback can accelerate adoption of some beneficial AMI therapies. Secular changes in knowledge and hospital protocols may extinguish outdated practices. However, it is more difficult to increase use of effective but riskier treatments for frail elderly patients.

9. Wojner-Alexandrov AW 2005

Level of evidence: 5
Quality: Fair, supporting
Comments: a community study using retrospective controls (before-and-after study). It indicated a multiple level educational program including paramedic, hospital, and community education would improve the implementation of stroke guideline.

10. Wright SW 2008

Level of evidence: 5
Quality: Fair, supporting
Comments: only measure the initial impact in a hospital, using asthma as an example, not really in communities. Using concurrent controls for asthma example. High-level departmental support with dedicated personnel is necessary for the success of such a system. Internet site development for product storage has proven valuable.