WHO Surgical Site Infection Prevention Guidelines

Web Appendix 14

Summary of a systematic review on maintaining normal body temperature (normothermia)

1. Introduction

Hypothermia is defined as a core temperature below 36°C and is common during and after major surgical procedures lasting more than 2 hours. The human body has a central compartment comprising the major organs where temperature is tightly regulated, and a peripheral compartment where temperature varies widely. Heat loss is compensated by reducing blood flow through the skin and increasing heat production, mainly by inducing muscular activity (shivering) and increasing the basal metabolic rate. Typically, the periphery compartment may be 2°C to 4°C cooler than the core compartment.

Exposure to a cold operating room environment and anaesthetic-induced impairment of thermoregulatory control are the most common events leading to hypothermia. Skin surface exposure during the perioperative period can increase heat loss. In addition, cool intravenous and irrigation fluids directly cool patients. Sedatives and anaesthetic agents inhibit the normal response to cold, resulting in an improved blood flow to the periphery and increased heat loss. During the early period of anaesthesia, these effects are seen as a rapid decrease in core temperature caused by redistribution of heat from the central to the peripheral compartment. This early decrease is followed by a more gradual decline, reflecting ongoing heat loss. With epidural or spinal analgesia, the peripheral blockade of vasoconstriction below the level of the nerve block results in vasodilatation and greater ongoing heat loss. Inadvertent non-therapeutic hypothermia is considered to be an adverse effect of general and regional anaesthesia.

Cardiac complications are the principal cause of morbidity during the postoperative phase. Hypothermia stimulates the release of noradrenaline and causes peripheral vasoconstriction and hypertension, which are factors that favour or increase the chances of myocardial ischaemia (with reduced blood supply to the heart muscle). It appears that this increased risk can be reversed by the maintenance of normothermia. Other problems associated with hypothermia are prolonged recovery from anaesthesia and a longer length of hospital stay. Furthermore, even moderate hypothermia (35°C) can alter physiological coagulation mechanisms by affecting platelet function and modifying enzymatic reactions. Decreased platelet activity results in increased bleeding and a greater need for transfusion. Moderate hypothermia can also reduce the metabolic rate, manifesting as a prolonged effect of certain drugs used during anaesthesia and some uncertainty about their effects. This is particularly significant for elderly patients.

It is unclear how the maintenance of normothermia might reduce the incidence of surgical site infection (SSI). All available studies in this field measure core and not peripheral temperature.
However, it is highly likely that the reported lower core temperatures result in a reduced cutaneous temperature at the operative site. Nonetheless, incisional warming has not been shown to decrease SSI rates\(^\text{10}\). A recent Cochrane review of the effect of warmed intravenous fluids found no statistically significant differences in core body temperature or shivering between individuals given warmed or room temperature irrigation fluids\(^\text{11}\), but SSI data was not reported as it was not the primary outcome of the study\(^\text{11}\). It is important to recognize that the extensive body of evidence concerning cardiac and coagulation defects based on the surrogate measure of maintenance of core temperature drives recommendations on the importance of maintaining normothermia, rather than concerns related to SSI reduction. Another Cochrane review of interventions used for treating inadvertent postoperative hypothermia concluded that active warming reduces the time to achieve normothermia. Several warming devices have been studied in this review, including forced-air warming, circulating hot water devices, radiant blankets, radiant warmers and electric blankets, but SSI was not among the primary outcomes\(^\text{12}\).

Recent health care bundles and guidelines for SSI prevention recommend that body temperature should be maintained above 35.5-36°C during the perioperative period\(^\text{13-16}\), but there is no consensus among these recommendations about the lower temperature limit for normothermia or its optimal timing.

### 2. PICO question

In surgical patients, should systemic body warming vs. no warming be used for the prevention of SSI?

- **Population:** inpatients and outpatients of any age undergoing surgical operations (any type of procedure)
- **Intervention:** normothermia (warming)
- **Comparator:** standard procedure (non-warming)
- **Outcomes:** SSI, SSI-attributable mortality

### 3. Methods

The following databases were searched: Medline (PubMed); Excerpta Medica Database (EMBASE); Cumulative Index to Nursing and Allied Health Literature (CINAHL); Cochrane Central Register of Controlled Trials (CENTRAL); and the WHO Global Health Library. The time limit for the review was between 1 January 1990 and 17 August 2015. Language was restricted to English, French and Spanish. A comprehensive list of search terms was used, including Medical Subject Headings (MeSH) (Appendix 1).

Two independent reviewers screened the titles and abstracts of retrieved references for potentially relevant studies. The full text of all potentially eligible articles was obtained. Two
authors independently reviewed the full text articles for eligibility based on inclusion criteria. Duplicate studies were excluded.

Two authors extracted data in a predefined evidence table (Appendix 2) and critically appraised the retrieved studies. Quality was assessed using the Cochrane Collaboration tool to assess the risk of bias of randomized controlled studies (RCTs) \(^{17}\) (Appendix 3). Any disagreements were resolved through discussion or after consultation with the senior author, when necessary.

Meta-analyses of available comparisons were performed using Review Manager v5.3 as appropriate \(^{18}\) (Appendix 4). Adjusted odds ratios (OR) with 95% confidence intervals (CI) were extracted and pooled for each comparison with a random effects model. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology \(^{19}\) (GRADE Pro software) was used to assess the quality of the body of retrieved evidence (Appendix 5).
4. Study selection

Flow chart of the study selection process

Potentially relevant articles  \( n = 1794 \)
- Medline  \( n = 663 \)
- EMBASE  \( n = 773 \)
- CINAHL  \( n = 159 \)
- Cochrane CENTRAL  \( n = 46 \)
- WHO Global Health Library  \( n = 153 \)

Citations identified through other sources  \( n = 1 \)

Total articles after removal of duplicates  \( n = 1268 \)

Total articles screened  \( n = 1268 \)

Excluded after title and abstract screening  \( n = 1251 \)

Full-text articles assessed for eligibility  \( n = 17 \)

Full-text articles excluded  \( n = 15 \)
- Study type (retrospective, review)  \( n = 11 \)
- Duplicate study data  \( n = 2 \)
- Warming in all study arms  \( n = 1 \)
- No SSI outcomes  \( n = 1 \)

Randomized controlled trials included in the analysis  \( n = 2 \)
5. Summary of the findings

Two randomized RCTs\textsuperscript{20,21} that evaluated systemic body warming to achieve normothermia vs. no warming for the prevention of SSI were identified. No relevant observational studies were identified to answer the PICO question. One study\textsuperscript{20} collected data from 3 hospitals. Both studies addressed pre- and intraoperative warming. No studies assessing the effect of postoperative warming on SSI were identified.

One study included adults undergoing elective colorectal surgery and the other concerned patients operated for hernia repair or vascular and breast surgical procedures. Both studies used forced-air warming in the intervention group to maintain patient normothermia during the procedure. In one study\textsuperscript{20}, patients in the control group were actively cooled and intravenous fluids were administered through a fluid warmer to both the intervention and the control groups, but the warmer was activated only in patients assigned to the intervention group. Both studies used a modified version of the ASEPSIS (Additional treatment, Serous discharge, Erythema, Purulent exudate, Separation of deep tissues, Isolation of bacteria and Stay as inpatient prolonged over 14 days) scoring system\textsuperscript{22} for the definition of SSI. A third study\textsuperscript{23} was identified as potentially relevant, but it was excluded after careful appraisal against the PICO question as warming procedures were applied in both the intervention and control groups.

Each of the 2 included studies reported independently that systemic body warming has significant benefit compared to no warming in reducing SSI following surgery and this was confirmed by meta-analysis (OR: 0.33; 95% CI: 0.17-0.62) (Appendix 4). Overall, the quality of evidence was moderate due to serious imprecision (Appendix 5).

In conclusion, the retrieved evidence can be summarized as follows: moderate quality evidence showed that systemic body warming has benefit in reducing the SSI rate when compared to no warming. Of note, there are some limitations to this analysis as it is based only on 2 studies with a relatively small sample size and populations undergoing only clean or clean-contaminated surgical procedures.

6. Other factors considered in the review

The systematic review team identified the following other factors to be considered.

Potential benefits or harms

There is separate evidence that blood loss and critical myocardial events are reduced when active warming strategies are employed\textsuperscript{7,24}. A meta-analysis of interventions aimed at body warming found a 16% increase in blood loss and a 22% increase in the relative risk of requiring a transfusion in patients whose temperature was on average approximately 1°C less than the 36°C threshold\textsuperscript{8}. These are benefits of body warming that go beyond SSI prevention, but they are worth being highlighted. In terms of potential harm, there have been individual case reports of
burn injuries caused by the inappropriate use of forced-air warming devices \textsuperscript{25,26}.

Resource use

Costs of warming systems, including forced-air warming, radiant blankets and other devices, are substantial. The use of these devices increases primarily health care costs, but the cost savings in reduced transfusions, morbid cardiac events and SSI make it cost effective if used in appropriate settings \textsuperscript{27-32}.

Feasibility and equity (if applicable):

In addition to economic concerns regarding the perioperative use of warming devices, the availability of these commercial products may be an added barrier for low- and middle-income countries. Of note, access to a regular electricity supply is required to run these devices, thus adding to costs and resources needed.

7. Key uncertainties and future research priorities

Overall, robust high-quality studies that evaluate the efficacy of systemic body warming vs. standard surgical care are needed. There is little consensus regarding patient populations that should be managed with perioperative warming. There is also no consensus on the duration of pre- and postoperative warming. Future research should address the mechanism of action, target warming temperature, the optimal device and the proper timing and duration of warming.
APPENDICES

Appendix 1: Search terms

MEDLINE (via PubMed)


3) #1 AND #2

4) LIMIT 1990-PRESENT

EMBASE

1) 'body temperature'/exp OR 'thermoregulation'/exp OR 'skin temperature'/exp OR cutaneous AND temperature:de,ab,ti OR 'transition temperature'/exp OR 'thermal regulation':de,ab,ti OR 'thermodynamics'/exp OR 'warming'/exp OR 'hypothermia'/exp OR 'hyperthermia'/exp OR 'heat loss'/exp OR 'hypothermia':de,ab,ti OR 'hyperthermia':de,ab,ti OR 'heat loss':de,ab,ti OR 'non warming':de,ab,ti OR 'nonwarming':de,ab,t

2) 'surgical infection'/exp OR 'surgical infection' OR 'surgical site infection':de,ab,ti OR 'surgical site infections':de,ab,ti OR ssis:de,ab,ti OR ssi:de,ab,ti OR 'surgical infection wound':de,ab,ti OR 'surgical infection wounds':de,ab,ti OR 'surgical infection':de,ab,ti OR 'postoperative wound infection':de,ab,ti OR 'postoperative wound infections':de,ab,ti OR 'post-operative wound infection':de,ab,ti OR 'post-operative wound infections':de,ab,ti OR ('wound infection':de,ab,ti OR 'wound infections':de,ab,ti AND (operation*:de,ab,ti OR surgical:de,ab,ti OR surger*:de,ab,ti OR postoperat*:de,ab,ti OR 'post-operative':de,ab,ti OR 'post-operation':de,ab,ti)) OR 'prosthesis related infections':de,ab,ti OR 'prosthesis related infection':de,ab,ti

3) #1 AND #2
CINAHL
1) (“body temperature” OR “body temperature regulation” OR “body temperature changes” OR “skin temperature” OR “transition temperature” OR “hot temperature” OR “temperature regulation” OR “thermodynamics” OR “rewarming” OR "hypothermia, induced" OR “thermogenesis”[MeSH] OR “hypothermia” OR “heat loss” OR “normothermia” OR “body temperature” OR “warming” OR “non warming”)
2) (“surgical wound infection” OR "surgical site infection" OR "wound infection" OR “prosthesis-related infection” OR “SSI” OR “SSIs”)
3) #1 AND #2

Cochrane CENTRAL
("normothermia" OR "temperature control" OR "thermoregulation" OR "body temperature") AND ("surgical site infection" OR "wound infection" OR "surgical wound infection")

WHO Global Health Library
("normothermia" OR "temperature control" OR "thermoregulation" OR "body temperature") AND ("surgical site infection" OR "wound infection" OR "surgical wound infection")
### Appendix 2: Evidence table

<table>
<thead>
<tr>
<th>Author, year, reference</th>
<th>Design, scope, setting, population</th>
<th>Objective</th>
<th>SSI definition</th>
<th>Type of surgery</th>
<th>Study methods</th>
<th>Intervention</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kurz, 1996 (^{20})</td>
<td>RCT 3 hospitals (1 university, n=155; 1 university, n=30; 1 other hospital, n=15) July 1993 to March 1995 Austria</td>
<td>To test the hypothesis that mild core hypothermia increases both the incidence of surgical wound infection and length of hospitalization in patients undergoing colorectal surgery.</td>
<td><strong>Wound infection (suspected):</strong> if pus could be expressed from the surgical incision or aspirated from a lobulated mass inside the wound. <strong>Wound infection (confirmed):</strong> if pus culture was positive for pathogenic bacteria. ASPESIS score &gt;20.</td>
<td>Elective colorectal surgery for cancer or inflammatory bowel disease. Cancer 182/200 (91%). Inflammatory bowel disease 18/200 (9%). Inclusion criteria: abdominal intra-peritoneal pull-through procedures.</td>
<td>Patients were randomly assigned to either normothermia or hypothermia groups. Apart from temperature management, other perioperative procedures were standardized for the two groups. Standard mechanical bowel preparation with an electrolyte solution. Intravenous cefamandole (2g every 8 hours) and metronidazole (500 mg every 8 hours) treatment was maintained for approximately 4 days postoperatively. Fluids were administered as 15 mL of crystalloid per kg per hour</td>
<td>Normothermia group: patients were actively warmed by using a forced-air cover placed over the upper body and set to deliver air at 40°C. In addition, intravenous fluids were actively warmed through a fluid warmer. Patient core temperatures were maintained close to 36.5°C. Hypothermia group: used the same forced-air cover as the intervention group, but set to deliver air at ambient temperature. Intravenous fluids were administered through the fluid</td>
<td>SSI: 2 weeks Overall: 24/200 (12%) I: 6/104 (6%) C: 18/96 (19%) (P=0.009) Smokers: 14/62 (23%) Non-smokers10/138 (7%) (P=0.004)</td>
</tr>
</tbody>
</table>

### Population: 200 patients undergoing elective colorectal resection
- **Age:** 18-80 years
- **Gender (male/female):** 108/92
- **Operating time:**
  - I: 170±9 minutes
  - C: 169±9 minutes
  - \(P=0.43\) minutes

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| Exclusion criteria: minor colon surgery (for example, polypectomy or colostomy performed as the only procedure), use of corticosteroids or other immuno-suppressants. | | | throughout surgery and replaced the volume of blood lost with either crystalloid in a 4:1 ratio or colloid in a 2:1 ratio. Fluids were administered intravenously at rates of 3.5 mL per kg per hour for the first 24 hours postoperatively and 2 mL per kg per hour for the subsequent 24 hours. warmer, similar to the inter-vention group, but the warmer was set to off for the control group. Core temperature was allowed to decrease to approximately 34.5°C. |
**Melling, 2001**

- **RCT**
  - District general hospital
  - April 1999 to May 2000
  - United Kingdom

**Population:** 416 patients undergoing elective hernia repair (n=155), varicose vein surgery (n=86) or breast surgery with incision >3 cm (n=175)

**Patient characteristics:** similar in all groups, including age, body mass index, gender, fasting >8 hours, hair removal (shaving) >6 hours, type of surgery, surgery in last 3 months, cancer hours, diagnosis, initial core temperature, AMP, length of surgery, seniority

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Method</th>
<th>Criteria</th>
<th>Note</th>
<th>Other DATA</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective hernia repair, varicose vein surgery or breast surgery</td>
<td>Warming device and a warm air blanket before surgery for the reduction of infection within 6 weeks of surgery. Wounds were swabbed for culture if purulent discharge present at the time of review. Note: only 14 wound swabs were obtained because of postoperative antimicrobials: “Patients seen at 2 and 6 weeks had often been prescribed antimicrobial treatment by</td>
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<tr>
<td>Prophylactic antibiotics C: 47 (34%) I: 36 (26%) in systemic warming and 36 (26%) in the incisional warming.</td>
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<tr>
<td>Perioperative care anaesthesia: not described</td>
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<tr>
<td>Hair removal-shaving</td>
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<tr>
<td>No shaving: 110/416 (26.4%). Shaving &lt;7 hours preoperatively: 116/416 (27.9%). Shaving &gt;7 hours preoperatively: 183/416 (20%).</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Data missing: 9/416.</td>
<td></td>
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<tr>
<td>A single trained observer unaware of treatment allocation reviewed patients at 2</td>
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<tr>
<td>Timing of intervention: preoperative. Duration of intervention: a minimum of 30 minutes</td>
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</tbody>
</table>

**SSI:**
- Non-warmed: 19/138 (14%)
- Local: 5/139 (4%)
- Systemic: 8/139 (6%)
- All warmed: 13/277 (5%)

C vs. local: P=0.003

Co vs. systemic: P=0.026
of surgeon. 
**Age**: ≥18 years (mean) 
**Intervention** 1: 49.7 years 
**Intervention 2**: 50 years 

**Inclusion criteria**: Elective hernia repair, varicose vein surgery or breast surgery that would result in a scar longer than 3 cm in length. 

**Exclusion criteria**: Pregnant, taking long-term oral steroids, had received radiotherapy (to the incision site) or chemotherapy in the last 4 weeks, or had an infection at the time of surgery.

<table>
<thead>
<tr>
<th>ASEPSIS (scoring system):</th>
<th>Additional treatment, Serous discharge, Erythema, Purulent exudate, Separation of deep tissues, Isolation of bacteria and Stay as inpatient prolonged over 14 days; SSI: surgical site infection; RCT: randomized controlled trial; AMP: antimicrobial prophylaxis; I: intervention; C: control.</th>
</tr>
</thead>
</table>

minutes until just before surgery. 

**Device**: 
(1) **systemic**: forced-air warming blanket; 
(2) **local**: non-contact, radiant heat dressing.
### Appendix 3: Risk of bias assessment of the included studies

<table>
<thead>
<tr>
<th>RCT Author, year, reference</th>
<th>Sequence generation</th>
<th>Allocation concealment</th>
<th>Participants and personnel blinded</th>
<th>Outcome assessors blinded</th>
<th>Incomplete outcome data</th>
<th>Selective outcome reporting</th>
<th>Other sources of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kurz, 1996&lt;sup&gt;20&lt;/sup&gt;</td>
<td>LOW</td>
<td>LOW</td>
<td>LOW</td>
<td>LOW</td>
<td>LOW</td>
<td>LOW</td>
<td>LOW</td>
</tr>
<tr>
<td>Melling, 2001&lt;sup&gt;21&lt;/sup&gt;</td>
<td>UNCLEAR</td>
<td>UNCLEAR</td>
<td>UNCLEAR</td>
<td>LOW</td>
<td>LOW</td>
<td>LOW</td>
<td>UNCLEAR</td>
</tr>
</tbody>
</table>

RCT: randomized controlled trial
Appendix 4: Comparison

Body warming vs. no warming for SSI prevention

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Warming Events</th>
<th>Total</th>
<th>No Warming Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio M–H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kurz,</td>
<td>6</td>
<td>104</td>
<td>18</td>
<td>96</td>
<td>44.1%</td>
<td>0.27 [0.10, 0.70]</td>
</tr>
<tr>
<td>Melling</td>
<td>8</td>
<td>139</td>
<td>19</td>
<td>139</td>
<td>55.9%</td>
<td>0.39 [0.16, 0.91]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>243</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>235</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>0.33 [0.17, 0.62]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 14 37
Heterogeneity: $\tau^2 = 0.00; \text{Chi}^2 = 0.32, \text{df} = 1 (P = 0.57); I^2 = 0$
Test for overall effect: $Z = 3.40 (P = 0.0007)$

M-H: Mantel-Haenszel (test); CI: confidence interval

**Funnel plot**: Body warming vs. no warming for SSI prevention
### Appendix 5: GRADE Table

<table>
<thead>
<tr>
<th>Quality assessment</th>
<th>№ of patients</th>
<th>Effect</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>№ of studies</td>
<td>Study design</td>
<td>Risk of bias</td>
<td>Inconsistency</td>
</tr>
<tr>
<td>Surgical site infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>RCTs</td>
<td>Not serious</td>
<td>Not serious</td>
</tr>
</tbody>
</table>

1. Optimal information size not met

RCT: randomized controlled trial; CI: confidence interval; OR: odds ratio
References


