Clinical practice guideline

The management of inadvertent perioperative hypothermia in adults

National Collaborating Centre for Nursing and Supportive Care
commissioned by
National Institute for Health and Clinical Excellence

DRAFT

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National Collaborating Centre for Nursing and Supportive Care

This guideline was developed by the National Collaborating Centre for Nursing and Supportive Care (NCCNSC) on behalf of the National Institute for Health and Clinical Excellence (NICE). The guideline was commissioned and funded by NICE and developed in accordance with NICE processes and methodologies.

Based at the Royal College of Nursing, the NCCNSC is a partnership of organisations brought together for the purposes of supporting the development of NICE clinical practice guidelines. The partnership is comprised of representatives from the following organisations:

- Centre for Evidence-Based Medicine, University of York
- Clinical Effectiveness Forum for Allied Health Professions
- Healthcare Libraries, University of Oxford
- Health Economics Research Centre, University of Oxford
- Royal College of Nursing
- UK Cochrane Centre.

Disclaimer

As with any clinical practice guideline, the recommendations contained in this guideline may not be appropriate in all circumstances. A limitation of a guideline is that it simplifies clinical decision-making (Shiffman, 1997). Decisions to adopt any particular recommendations must be made by practitioners in the context of:

- Available resources
- Local services, policies and protocols
- The circumstances and wishes of the patient
- Available personnel and devices
- Clinical experience of the practitioner
- Knowledge of more recent research findings

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Appendices A–H are in a separate file

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Abbreviations

ASA: American Society of Anaesthesiologists Physical Status Classification System
BMI: Body mass index
BNF: British National Formulary
CI: confidence interval
CT: core temperature
CWM: circulating water mattress
EHP: electric heating pads
FAW: forced air warming
GA: general anaesthesia
GDG: Guideline Development Group
HDU: High Dependency Unit
HES: Hospital Episode Statistics
HH: heated-humidifer
HME: heat and moisture exchanger
HPA: Health Protection Agency
HRG: Healthcare Resource Group
HRQoL: Health related quality of life
HTA: Health Technology Assessment
ICU: intensive care unit
i.m: intramuscular
INB: incremental net benefit
IPH: inadvertent perioperative hypothermia
IQR: interquartile range
IV: intravenous fluids
MCE: morbid cardiac events
MD: mean difference
MI: myocardial infarction
NB: net benefit
NNT: numbers needed to treat
OR: odds ratio
PACU: post anaesthesia care unit
pca: patient controlled analgesia
p.o.: per ora
prn: as required
PSA: probabilistic sensitivity analysis
QALY: Quality adjusted life-year
RA: regional anaesthesia
RCT: randomised controlled trial
RR: relative risk

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s.c.: sub cutaneous

SEM: Standard error of the mean

SWI: surgical wound infection

TI: thermal insulation

WCB: warmed cotton blankets

WF: warmed IV fluids

WMD: weighted mean difference

UC: usual care

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General glossary

Absolute risk reduction (Risk difference): The difference in event rates between two groups (one subtracted from the other) in a comparative study.

Abstract: Summary of a study, which may be published alone or as an introduction to a full scientific paper.

Adjustment: A statistical procedure in which the effects of differences in composition of the populations being compared (or treatment given at the same time) have been minimised by statistical methods.

Algorithm (in guidelines): A flow chart of the clinical decision pathway described in the guideline, where decision points are represented with boxes, linked with arrows.

Allocation concealment: The process used to prevent advance knowledge of group assignment in a RCT. The allocation process should be impervious to any influence by the individual making the allocation, by being administered by someone who is not responsible for recruiting participants.

Applicability : The degree to which the results of an observation, study or review are likely to hold true in a particular clinical practice setting.

Arm (of a clinical study): Subsection of individuals within a study who receive one particular intervention, for example placebo arm.

Association: Statistical relationship between two or more events, characteristics or other variables. The relationship may or may not be causal.

Baseline: The initial set of measurements at the beginning of a study (after run-in period where applicable), with which subsequent results are compared.

Bias: Systematic (as opposed to random) deviation of the results of a study from the 'true' results that is caused by the way the study is designed or conducted.

Blinding (masking): Keeping the study participants, caregivers, researchers and outcome assessors unaware about the interventions to which the participants have been allocated in a study

Carer (caregiver): Someone other than a health professional who is involved in caring for a person with a medical condition.

Case-control study: A study in which the amount of exposure to a potentially causative factor in a group of patients (cases) who have a particular condition is compared with the exposure in a similar group of people who do not have the clinical condition (the latter is called the control group).

Clinical effectiveness: The extent to which an intervention produces an overall health benefit in routine clinical practice.

Clinical efficacy: The extent to which an intervention is active when studied under controlled research conditions.

Clinical impact: The effect that a guideline recommendation is likely to have on the treatment or treatment outcomes, of the target population.

Clinical question: In guideline development, this term refers to the questions about treatment and care that are formulated to guide the development of evidence-based recommendations.

Clinician: A healthcare professional providing healthcare, for example doctor, nurse or physiotherapist.

Cochrane Library: A regularly updated electronic collection of evidence-based medicine databases, including the Cochrane Database of Systematic Reviews.

Cochrane Review: A systematic review of the evidence from randomised controlled trials relating to a particular health problem or healthcare intervention, produced by the Cochrane Collaboration. Available electronically as part of the Cochrane Library.

Cohort study: A retrospective or prospective follow-up study. Groups of individuals to be followed up are defined on the basis of presence or absence of exposure to a suspected risk factor or intervention. A cohort study can be comparative, in which case two or more groups are selected on the basis of differences in their exposure to the agent of interest.

Co-morbidity: Coexistence of more than one disease or an additional disease (other than that being studied or treated) in an individual.

Comparability: Similarity of the groups in characteristics likely to affect the study results (such as health status or age).

Compliance: The extent to which a person adheres to the health advice agreed with healthcare professionals. May also be referred to as 'adherence'.

Confidence interval (CI): The range of numerical values within which we can be confident that the population value being estimated is found. Confidence intervals indicate the strength of evidence; where confidence intervals are wide they indicate less precise estimates of effects.

Confounding: In a study, confounding occurs when the effect of an intervention on an outcome is distorted as a result of an association between the population or intervention or outcome and another factor (the 'confounding variable') that can influence the outcome independently of the intervention under study.

Consensus methods: Techniques that aim to reach an agreement on a particular issue. Formal consensus methods include Delphi and nominal group techniques, and consensus development conferences. In the development of clinical guidelines, consensus methods may be used where there is a lack of strong research evidence on a particular topic. Expert consensus methods will aim to reach agreement between experts in a particular field.

Consultation: The process that allows stakeholders and individuals to comment on initial versions of NICE guidance and other documents so their views can be taken into account when the final version is being produced.

Cost-benefit analysis: A type of economic evaluation, which estimates the net benefit to society of an intervention as the incremental (difference in) benefit of the intervention minus the incremental (difference in) cost, with all benefits and costs measured in monetary units. If benefits exceed costs, the evaluation would be a basis for recommending the intervention.

Cost-consequences analysis: A type of economic evaluation, whereby both outcomes and costs of alternative interventions are described, without any attempt to combine the results.

Cost effectiveness: The cost per unit of benefit of an intervention. Benefits of different interventions are measured using a single outcome (for example, life-years gained, quality-adjusted life-years gained, deaths avoided, heart attacks avoided, cases detected).

Cost-effectiveness analysis: An economic study design in which alternative interventions are compared in terms of cost per unit of effectiveness.

Cost-effectiveness model: An explicit mathematical framework, which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes.

Cost impact: The total cost to the person, the NHS or to society.

Costing study: The simplest form of economic study, measuring only the costs of given interventions.

Cost-minimisation analysis: A type of economic evaluation used to compare the difference in costs between programs that have the same health outcome.

Cost-of-illness/economic burden studies: An analysis of the total costs incurred by a society due to a specific disease.

Cost-utility analysis: A form of cost-effectiveness analysis in which the units of effectiveness are quality-adjusted life-years (QALYs).

Cross sectional study: Examination of the relationship between disease and other variables of interest as they exist in a defined population assessed at a particular time.

Data extraction tables: Tabulated presentation of data collected from individual studies.

Decision analytic techniques: A way of reaching decisions, based on evidence from research. This evidence is translated into probabilities, and then into diagrams or decision trees that direct the clinician through a succession of possible scenarios, actions and outcomes.

Decision problem: A clear specification of the interventions, patient populations and outcome measures and perspective adopted in an evaluation, with an explicit justification, relating these to the decision which the analysis is to inform.

Deterministic analysis: A deterministic analysis is one in which the best estimate for each parameter has been used to give a single estimate of cost-effectiveness. It is the opposite of a probabilistic sensitivity analysis (See sensitivity analysis)

Discounting: Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present.

Dominance: An intervention is said to be dominated if there is an alternative intervention that is both less costly and more effective.

Dosage: The prescribed amount of a drug to be taken, including the size and timing of the doses.

Drop-out: A participant who withdraws from a clinical trial before the end.

Economic evaluation: Comparative analysis of alternative courses of action in terms of both their costs and consequences.

Effect (as in effect measure, treatment effect, estimate of effect, effect size): The observed association between interventions and outcomes or a statistic to summarise the strength of the observed association.

Effectiveness: See "Clinical effectiveness"

Efficacy: See "Clinical efficacy"

Epidemiological study: A study which looks at how a disease or clinical condition is distributed across populations, e.g. across geographical areas or over time, or between age groups.

Evidence: Information on which a decision or guidance is based. Evidence is obtained from a range of sources including randomised controlled trials, observational studies, expert opinion (of clinical professionals and/or patients).

Evidence table: A table summarising the results of a collection of studies which, taken together, represent the evidence supporting a particular recommendation or series of recommendations in a guideline.

Exclusion criteria (clinical study): Criteria that define who is not eligible to participate in a clinical study.

Exclusion criteria (literature review): Explicit standards used to decide which studies should be excluded from consideration as potential sources of evidence.

Expert consensus: See 'Consensus methods'.

Extrapolation: In data analysis, predicting the value of a parameter outside the range of observed values.

False positive: Positive test diagnostic result in a subject who does not possess the attribute for which the test is conducted. The incorrect labelling of a healthy person following screening.

Follow-up: Observation over a period of time of an individual, group or population whose relevant characteristics have been assessed in order to observe changes in health status or health-related variables.

Generalisability: The extent to which the results of a study based on measurement in a particular patient population and/or a specific context hold true for another population and/or in a different context. In this instance, this is the degree to which the guideline recommendation is applicable across both geographical and contextual settings. For instance, guidelines that suggest substituting one form of labour for another should acknowledge that these costs might vary across the country.

Generic name: The general non-proprietary name of a drug or device.

Gold standard: A method, procedure or measurement that is widely accepted as being the best available, to which a new method is compared.

Good Practice Points: Recommended good practice based on the clinical experience of the Guideline Development Group.

Grey literature: Reports that are unpublished or have limited distribution, and are not included in the common bibliographic retrieval systems.

Harms: Adverse effects of an intervention.

Health economics: The study of the allocation of scarce resources among alternative healthcare treatments. Health economists are concerned with both increasing the average level of health in the population and improving the distribution of health

Health professional: Includes nurses, allied health professionals and doctors.

Health-related quality of life: A combination of an individual's physical, mental and social well-being; not merely the absence of disease.

Health technology assessment: The process by which evidence on the clinical effectiveness and the costs and benefits of using a technology in clinical practice is systematically evaluated.

Hypothesis: A supposition made as a starting point for further investigation.

Implementation: Introducing the use of the guidance recommendations in practice.

Incidence: The number of new cases of illness commencing, or of persons falling ill during a specified time period in a given population.

Inclusion criteria (literature review): Explicit criteria used to decide which studies should be considered as potential sources of evidence.

Incremental analysis: The analysis of additional costs and additional clinical outcomes with different interventions.

Incremental cost: The mean cost per patient associated with an intervention minus the mean cost per patient associated with a comparator intervention

Incremental cost effectiveness ratio (ICER): The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest.

Incremental net benefit (INB): The value (usually in monetary terms) of an intervention net of its cost compared with a comparator intervention. The INB can be calculated for a given cost-effectiveness (willingness to pay) threshold. If the threshold is £20,000 per QALY gained then the INB is calculated as: (£20,000 x QALYs gained) – Incremental cost

Indication (specific): The defined use of a technology as licensed by the Medicines and Healthcare products Regulatory Agency (MHRA).

Intention-to-treat analysis (ITT analysis): An analysis of the results of a clinical study in which the data are analysed for all study participants as if they had remained in the group to which they were randomised, regardless of whether or not they remained in the study until the end, crossed over to another treatment or received an alternative intervention

Internal validity: The degree to which the results of a study are likely to approximate the 'truth' for the participants recruited in a study (that is, are the results free of bias?). It refers to

the integrity of the design and is a prerequisite for applicability (external validity) of a study's findings.

Intervention: Healthcare action intended to benefit the patient, for example, drug treatment, surgical procedure, psychological therapy.

Intrinsic: Factors present within the individual.

Licence: An authorisation from the MHRA to market a medicinal product.

Life-years gained: Average years of life gained per person as a result of the intervention.

Logistic regression model: A data analysis technique to derive an equation to predict the probability of an event given one or more predictor variables. This model assumes that the natural logarithm of the odds for the event (the logit) is a linear sum of weighted values of the predictor variable. The weights are derived from data using the method of maximum likelihood.

Meta-analysis: A statistical technique for combining (pooling) the results of a number of studies that address the same question and report on the same outcomes to produce a summary result. The aim is to derive more precise and clear information from a large data pool. It is generally more reliably likely to confirm or refute a hypothesis than the individual trials.

Multivariate model: A statistical model for analysis of the relationship between two or more predictor (independent) variables and the outcome (dependent) variable.

Multi-way simple sensitivity analysis (scenario analysis): two or more parameters are varied at the same time and the overall effect on the results is evaluated.

Narrative summary: Summary of findings given as a written description.

Negative predictive value: The proportion of individuals with a negative test result who do NOT have the disease.

Number needed to treat (NNT): The number of patients that who on average must be treated to prevent a single occurrence of the outcome of interest.

Observational study: Retrospective or prospective study in which the investigator observes the natural course of events with or without control groups; for example, cohort studies and case–control studies.

Odds ratio: A measure of treatment effectiveness. The odds of an event happening in the treatment group, expressed as a proportion of the odds of it happening in the control group. The 'odds' is the ratio of non-events to events.

Off-label: A drug or device used treat a condition or disease for which it is not specifically licensed.

One-way simple sensitivity analysis (univariate analysis): each parameter is varied individually in order to isolate the consequences of each parameter on the results of the study.

Opportunity cost: The opportunity cost of investing in a healthcare intervention is the other healthcare programmes that are displaced by its introduction. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.

Outcome: Measure of the possible results that may stem from exposure to a preventive or therapeutic intervention. Outcome measures may be intermediate endpoints or they can be final endpoints.

P value: The probability that an observed difference could have occurred by chance, assuming that there is in fact no underlying difference between the means of the observations. If the probability is less than 1 in 20, the P value is less than 0.05; a result with a P value of less than 0.05 is conventionally considered to be ‘statistically significant’.

Peer review: A process where research is scrutinised by experts that have not been involved in the design or execution of the studies.

Placebo: An inactive and physically identical medication or procedure used as a comparator in controlled clinical trials.

Positive predictive value: The proportion of individuals with a positive test result who actually have the disease

Prevalence: The proportion of persons with a particular disease within a given population at a given time.

Probabilistic sensitivity analysis: probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (For example, Monte Carlo simulation).

Prognosis: A probable course or outcome of a disease. Prognostic factors are patient or disease characteristics that influence the course. Good prognosis is associated with low rate of undesirable outcomes; poor prognosis is associated with a high rate of undesirable outcomes.

Proprietary name: The brand name given by the manufacturer to a drug or device it produces.

Qualitative research: Research concerned with subjective outcomes relating to social, emotional and experiential phenomena in health and social care.

Quality adjusted life years (QALYs): An index of survival that is adjusted to account for the patient's quality of life during this time. QALYs have the advantage of incorporating changes in both quantity (longevity/mortality) and quality (morbidity, psychological, functional, social and other factors) of life. Used to measure benefits in cost-utility analysis. The QALYs gained are the mean QALYs associated with one treatment minus the mean QALYs associated with an alternative treatment.

Quality of life: See "Health-related quality of life"

Quick reference guide (for a guideline): An abridged version of NICE guidance, which presents the key priorities for implementation and summarises the recommendations for the core clinical audience.

Randomisation: Allocation of participants in a research study to two or more alternative groups using a chance procedure, such as computer-generated random numbers. This approach is used in an attempt to ensure there is an even distribution of participants with different characteristics between groups and thus reduce sources of bias.

Randomised controlled trial (RCT): A comparative study in which participants are randomly allocated to intervention and control groups and followed up to examine differences in outcomes between the groups. The random allocation eliminates bias in the assignment of treatment to patients and establishes the basis for the statistical analysis.

Reference standard (or gold standard): An agreed standard, for example for a test or treatment, against which other interventions can be compared.

Relative risk: The number of times more likely or less likely an event is to happen in one group compared with another (calculated as the risk of the event in group A/the risk of the event in group B).

Reliability/repeatability: The degree of agreement exhibited when a measurement is repeated under identical conditions. Reliability refers to the degree to which the results obtained by a measurement procedure can be replicated.

Remit: The brief given by the Department of Health and Welsh Assembly Government at the beginning of the guideline development process. This defines core areas of care that the guideline needs to address.

Resource implication: The likely impact in terms of finance, workforce or other NHS resources.

Retrospective cohort study: A study in which a defined group of persons with an exposure that occurred in the past and an appropriate comparison group who were not exposed are identified at a time later than when they were exposed and followed from the time of exposure to the present, and in which the incidence of disease (or mortality) for the exposed and unexposed are assessed.

Review of the literature: An article that summarises the evidence contained in a number of different individual studies and draws conclusions about their findings. It may or may not be systematically researched and developed.

Secondary benefits: Benefits resulting from a treatment in addition to the primary, intended outcome.

Selection bias (also allocation bias): A systematic bias in selecting participants for study groups, so that the groups have differences in prognosis and/or therapeutic sensitivities at baseline. Randomisation (with concealed allocation) of patients protects against this bias.

Sensitivity analysis: A means of representing uncertainty in the results of economic evaluations. Uncertainty may arise from missing data, imprecise estimates or methodological controversy. Sensitivity analysis also allows for exploring the generalisability of results to other settings. The analysis is repeated using different assumptions to examine the effect on the results. See also: One-way simple sensitivity analysis; Multi-way simple sensitivity analysis; Threshold sensitivity analysis; Probabilistic sensitivity analysis.

Sensitivity (of a search): The proportion of relevant studies identified by a search strategy expressed as a percentage of all relevant studies on a given topic. It describes the comprehensiveness of a search method (that is, its ability to identify all relevant studies on a given topic). Highly sensitive strategies tend to have low levels of specificity and vice versa.

Specificity (of a test): The proportion of individuals classified as negative by the gold (or reference) standard, who are correctly identified by the study test.

Sensitivity (of a test): The proportion of individuals classified as positive by the gold (or reference) standard, who are correctly identified by the study test.

Stakeholder: Those with an interest in the use of a technology under appraisal or a guideline under development. Stakeholders include manufacturers, sponsors, healthcare professionals, and patient and carer groups.

Statistical power: The ability to demonstrate an association when one exists. Power is related to sample size; the larger the sample size, the greater the power and the lower the risk that a possible association could be missed.

Synthesis of evidence: A generic term to describe methods used for summarising (comparing and contrasting) evidence into a clinically meaningful conclusion in order to answer a defined clinical question. This can include systematic review (with or without meta-analysis), qualitative and narrative summaries.

Systematic review: Research that summarises the evidence on a clearly formulated question according to a predefined protocol using systematic and explicit methods to identify, select and appraise relevant studies, and to extract, collate and report their findings. It may or may not use statistical meta-analysis.

Threshold sensitivity analysis: the critical value of parameters above or below which the conclusions of the study will change are identified.

Time horizon: The time span used in the NICE appraisal which reflects the period over which the main differences between interventions in health effects and use of healthcare resources are expected to be experienced, and taking into account the limitations of supportive evidence.

Treatment allocation: Assigning a participant to a particular arm of the trial.

Treatment options: The choices of intervention available.

User: Any one using the guideline.

Utility: A measure of the strength of an individual's preference for a specific health state in relation to alternative health states. The utility scale assigns numerical values on a scale from 0 (death) to 1 (optimal or 'perfect' health). Health states can be considered worse than death and thus have a negative value.

Glossary specific to the guideline

Active warming: a process that transfers heat to the patient.

Circulating water mattress: An active patient warming device which conducts heat to the front and/or back of the body.

Electric warming mattress: An active patient warming device placed underneath the patient delivering warming at a low voltage (24V). A control unit is used to maintain the mattresses at the user-selected temperature. Surfaces are anti-static, latex-free polyurethane with fully welded seams.

Fluid warming: An active fluid warming device which allows for the infusion of warm fluids set to a specified temperature.

Forced air warming: a temperature management unit where heated air is used to warm patients through convection. The warming unit draws ambient air through a filter and warms the air to a specified temperature. The warmed air is delivered through a hose to a blanket or gown.

Heated-Humidfiers: warming devices designed to deliver gases to a patient's airway at close to physiologically normal levels of temperature and humidity.

Hyperthermia: An acute condition which occurs when the body produces or absorbs more heat than it can dissipate.

Hypothermia: For the purpose of this guideline, hypothermia is defined as a core temperature less than 36.0°C (96.8°F). Severity of hypothermia was defined as follows: mild hypothermia: core temperature 35.0°C to 35.9°C; moderate: 34.0°C to 34.9°C severe: ≤ 33.9°C.

Intraoperative phase: Defined as the period from time of anaesthetic intervention to entry into the operating room

Normothermia: For the purpose of this guideline, normothermia is defined as a core temperature range of 36.5°C to 37.5°C.

Postoperative phase: 24 hours postoperatively, commencing from transfer to the recover room and including the clinical area (e.g. ward, ICU)

Preoperative phase: Defined as the period from the time of preparation for surgery/administration of premedication to the time of first anaesthetic intervention

Thermal insulation: An intervention that prevents heat loss by reducing conduction, convection or radiation.

Warmed cotton blankets: For the purpose of this guideline, cotton blankets warmed in a thermostatically controlled incubator are defined as an active patient warming mechanism.

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1 EXECUTIVE SUMMARY

Inadvertent perioperative hypothermia (IPH) is a preventable complication of perioperative procedures. The guideline definition of hypothermia is a patient temperature less than 36°C. IPH is a common occurrence, with adult surgical patients at risk of developing hypothermia at any stage of the perioperative pathway. In preventing this adverse event, the guideline defines the preoperative period as 1 hour prior to induction of anaesthesia (when the patient is prepared for surgery on the ward/in the emergency department), the intraoperative period as total anaesthetic time, and the postoperative period as the 24 hours after entry into the theatre recovery area (which will include transfer to and time spent on the ward).

The phrase 'comfortably warm' is used in recommendations relating to both the preoperative and postoperative phases, and refers to the expected normal temperature range of adult patients (between 36.5°C and 37.5°C).

During the first 30 to 40 minutes of anaesthesia, a patient's core temperature can drop to less than 35°C. Reasons for this include the loss, under general or regional anaesthesia, of the behavioural response to cold and the impairment of thermoregulatory heat-preserving mechanisms, anaesthetic-induced peripheral vasodilation (with associated heat loss) and patients getting cold while waiting for surgery on the ward or in the emergency department.

Why is it important to prevent IPH? Evidence synthesis demonstrates that it is both clinically and cost effective to warm patients who have a high risk of IPH (ASA grade greater than I and with increased risk of a morbid cardiac event [for example age over 50 years]) for all procedures, and to warm all other patients who have a duration of anaesthesia longer than 30 minutes. Key priorities for implementation provide strong direction for healthcare professionals in optimising the adult surgical patient's perioperative journey.

Key Priorities for Implementation

These were produced through a GDG nominal group technique, determining the top eight recommendations that can maximise the impact of the guideline through focused implementation activity.

These are presented to reflect the different phases of the perioperative pathway, and are seen below:

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Preoperative phase

Each patient prior to transfer to the theatre suite should be assessed for their risk of inadvertent perioperative hypothermia and potential adverse consequences. Patients with any two of the following should be managed as higher risk (see section 4.1.2.5):

- ASA grade greater than I (the higher the grade, the greater the risk);
- preoperative core temperature below 36.0°C;
- undergoing combined general and regional anaesthesia;
- undergoing major or intermediate surgery;
- at risk of cardiovascular complications (for example, age over 50 years). **4.1.1.1**

Patients and their carers should be informed that:

- staying warm before surgery will lower the risk of postoperative complications;
- the hospital environment may be colder than their own home;
- they should bring additional clothing, such as a dressing gown, a vest, warm clothing and slippers, to help them keep comfortably warm;
- staff should be told if the patient feels cold at any time during their hospital stay. **4.1.1.2**

If the patient's temperature is below 36.0°C:

- forced air warming should be applied (unless there is a need to expedite surgery due to clinical urgency, for example bleeding or critical limb ischaemia);
- forced air warming should be maintained throughout the intraoperative period. **4.1.1.6**

Intraoperative phase

Healthcare professionals:

- should measure and document the patient's temperature prior to induction of anaesthesia and every 30 minutes until the end of surgery;
- should not commence induction of anaesthesia unless the patient's temperature is above 36.0°C. **4.1.2.2**

Healthcare professionals should ensure that intravenous fluids (500ml or more) and blood products are warmed to 37°C using a fluid warming device. **4.1.2.3**

Patients having anaesthesia for less than 30 minutes and who are at higher risk of inadvertent perioperative hypothermia (see section 4.1.1.1) should be warmed intraoperatively using a forced air warming device (minimum setting 38°C) from induction of anaesthesia. **4.1.2.5**

All patients having anaesthesia for longer than 30 minutes should be warmed intraoperatively using a forced air warming device (minimum setting 38°C) from induction of anaesthesia. **4.1.2.6**

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Postoperative phase

The patient's temperature should be measured and documented on admission to the recovery room and then at 15-minute intervals.

- Ward transfer can be arranged once the patient's temperature is above 36.0°C.
- If their temperature is below 36.0°C, the patient should be actively warmed to near 36.5°C using forced air warming. **4.1.3.1**

These recommendations represent the heart of the guideline and focus the reader's attention onto key parts of the perioperative pathway.

In order to maximise visual impact, recommendations are summarised in a patient algorithm which is seen below.

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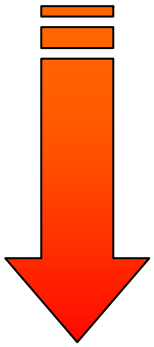
The Inadvertent Perioperative Hypothermia Patient Pathway (October 07)

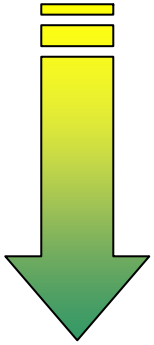
Ask patient to bring additional clothing, including dressing gown, vest, warm clothes and slippers
Assess preoperative risk of IPH and adverse consequences

- **Keep the patient comfortably warm (36.5°C to 37.5°C) on ward or in emergency department**
- **Patients should be provided with at least one sheet and two blankets or alternatively a duvet**
- **Record patient temperature in the hour prior to transfer to the theatre suite (should be above 36°C)**
- **Encourage the patient to walk to theatre, wearing their dressing gown and slippers.**



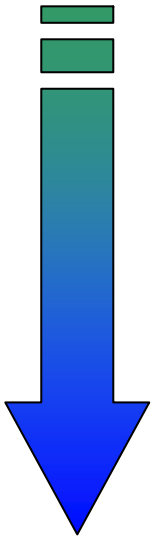
AT INDUCTION OF ANAESTHESIA

- **Theatre suite temperature should be maintained at a minimum of 21°C**
- **Measure and record patient temperature at induction and every 30 minutes until end of surgery**
- **Induce anaesthesia only if patient core temperature is above 36.0°C except for clinical urgency**
- **Apply forced air warming (minimum 38°C) for patients with high risk of IPH**
- **Apply forced air warming (minimum 38°C) for patients with procedures longer than 30 minutes**
- **Warm intravenous fluids (500ml or more) and blood to 37°C using a fluid warming device**



INTRAOPERATIVE PATIENT TEMPERATURE MAINTAINANCE

- **Continue forced air & intravenous fluid warming (adjust settings to maintain normothermia)**
- **Cover patients adequately and only expose patients for surgical preparation**
- **Theatre temperature should be a minimum of 21° C * (Consider cooling the scrubbed surgical team)**
- **Warm fluids used for intracavity washout and irrigation to 40°C**
- **Record patient temperature every 30 minutes intraoperatively**



ON ARRIVAL INTO THE RECOVERY AREA AND FOR 24 HOURS POSTOPERATIVELY

- **Measure and record patient temperature every 15 minutes in recovery**
- **The patient can be discharged to ward once patient temperature is above 36.0°C**
- **If patient temperature falls below 36.0°C apply forced air warming to as near 36.5°C.**
- **Record patient temperature on ward and repeat in routine 4 hourly observations; if rewarming record patient temperature every 30 minutes**
- **Keep patients comfortably warm with at least one sheet and two blankets or alternatively a duvet**

In

2 PRINCIPLES OF PRACTICE

The principles outlined below describe the ideal context in which to implement the recommendations contained in this guideline.

These have been adapted from the NICE clinical practice guideline: *Assessment and prevention of falls in older people* (2004).

2.1 Person-centred care

- People who are at risk of developing Inadvertent Perioperative Hypothermia (IPH) should be made aware of the guideline and its recommendations, and should be referred to the *Understanding NICE Guidance* version of the guideline.
- All adult surgical patients should be involved in shared decision–making about individualised care in preventing perioperative hypothermia.
- Healthcare professionals are advised to respect and incorporate the knowledge and experience of people in shared decision making.
- All adult surgical patients should be informed about the potential risks and/or associated complications of IPH.

2.2 Collaborative interdisciplinary approach to care

- All members of the interdisciplinary team should be aware of the guidelines and all care should be documented in the patient's health care records.
- A collaborative, multi-disciplinary approach should be provided by appropriately trained professionals.
- The roles of parents/carers and health professionals in implementing the guideline recommendations should be sensitively negotiated.

2.3 Organisational issues

- There should be an integrated approach to the prevention and management of IPH across the three phases of the perioperative patient experience, these being the preoperative, intraoperative and postoperative phases.
- Care should be delivered in a context of continuous quality improvement, where improvements to care following guideline implementation are the subject of regular feedback and audit.
- The health care team should have received appropriate training and have demonstrated their competence in the prevention and management of IPH.
- Commitment to and availability of education and training are required to ensure that all staff, regardless of their profession, are given the opportunity to update their knowledge, and are able to implement the guideline recommendations.

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- Adult surgical patients should be cared for by personnel who have undergone appropriate training and who know how to initiate and maintain appropriate prevention and management of IPH. Staffing levels and skill mix should reflect the needs of patients.

2.4 Background to the current guideline

In January 2006, The National Collaborating Centre for Nursing and Supportive Care (NCC-NSC) was commissioned by NICE to develop a clinical guideline on the 'Management of perioperative hypothermia (IPH)' for use in Primary Care in England and Wales.

2.5 Clinical need for the guideline

Inadvertent perioperative hypothermia (IPH) is a preventable complication of perioperative procedures. The main aim of this guideline is to indicate the optimal clinical and cost-effective management of adult surgical patients in both preventing and managing IPH.

For the purpose of this guideline, the definition of hypothermia is a core temperature of less than 36°C. This definition applies regardless of the patient's initial temperature. Inadvertent perioperative hypothermia is distinguished from therapeutic hypothermia, which is the deliberate induction of hypothermia. Inadvertent perioperative hypothermia is a recognised and common occurrence during surgery, with the adult surgical patient at risk of developing hypothermia at any stage of the perioperative pathway. In addressing this potential adverse event, the guideline considers the period from 1 hour prior to induction of anaesthesia (when the patient is prepared for surgery on the ward or in the emergency department, including possible use of premedication), the intraoperative time (measured as total anaesthetic time) and the postoperative period (24 hours after entry into the recovery room).

It is not unusual for a patient's core temperature to drop to less than 35°C within the first 30 to 40 minutes of anaesthesia. If the perioperative team do not manage this risk throughout the perioperative patient pathway, as many as 70% of patients undergoing routine surgery may be hypothermic on admission to the recovery room. The reasons for hypothermia include the loss, under general or regional anaesthesia, of the behavioural response to cold and the impairment of thermoregulatory heat-preserving mechanisms, anaesthetic-induced peripheral vasodilation (with associated heat loss), patients getting cold while waiting for surgery (exposure of the body during surgery and environmental factors), fluid deprivation before anaesthesia (which varies from 2 to more than 12 hours) resulting in patients being dry and poorly perfused, impairing heat distribution and the use of unwarmed intravenous or irrigation solutions.

The degree of heat loss is also influenced by ambient temperature, airflow in the theatre and factors associated with skin preparation. Patients at high risk of perioperative hypothermia include are generally those who are assessed by the perioperative team as having an ASA grade of greater than 2, and those patients who are at increased risk of a morbid cardiac

event, typically these patients are around 50 years of age, with an ischaemic heart disease profile. Duration of anaesthesia has been identified as an IPH risk, and whether the patient is having medium to major surgery, which usually correlates to duration of anaesthesia, i.e. the larger the surgical procedure the longer duration of anaesthetic time. The guideline includes a risk of developing IPH systematic review, and findings have informed both the economic modelling and recommendations.

Why prevent? Typically this question is answered by looking at the impact on both the patient and resources if an adverse outcome does present; in this guideline it is if the patient becomes hypothermic. Expressed as a consequence, if hypothermia does develop then patients can experience increased perioperative blood loss, longer post-anaesthetic recovery, postoperative shivering and thermal discomfort, morbid cardiac events including arrhythmia, altered drug metabolism, increased risk of wound infection, reduced patient satisfaction with the surgical experience and possibly a longer stay in hospital. This has been difficult to determine from the literature, mainly because of how contemporary surgical procedures not requiring the patient to have an overnight stay in hospital.

2.6 Management Issues

The aetiology of IPH is explained within the guideline. The focus of the GDG's work has been to identify key information for patients and healthcare professionals that relate to each part of the perioperative pathway. This is summarised on the IPH algorithm, and identified as:

- Maintaining patient thermal comfort preoperatively through encouraging the patient to wear their own warm clothing
- Assessment of IPH risk by a member of the perioperative team
- Maintaining ambient temperature in ward, emergency departments and theatre suite
- Recording patient core temperature at regular intervals; these are immediately prior to leaving the ward or emergency department, very 30 minutes intraoperatively and every 15 minutes in the recovery area until a core temperature of 36.0˚C is recorded, and then at hourly intervals until the patient reaches normothermia (36.5˚C).
- Only commencing induction of anaesthesia if the patient's core temperature is above 36.0˚C
- Active warming of the patient using a combination of warmed fluids and warming devices.

3 AIMS OF THE GUIDELINE

The aims of the guideline are:

- To evaluate and summarise the clinical and cost evidence relating to all aspects of the prevention and treatment of Inadvertent Perioperative Hypothermia (IPH)
- To highlight gaps in the research evidence
- To formulate evidence-based cost effective clinical practice recommendations relating to the prevention and treatment of IPH
- To formulate consensus recommendations shaped around available evidence and expert GDG opinion in those areas of prevention and treatment of IPH where there is no clear clinical and cost effective evidence base.

3.1 Who the guideline is for

The guideline is of relevance to all adults undergoing surgery, carers for those people who are undergoing surgery and all healthcare professionals/hospital workers who care for patients who are undergoing surgery at any point of the preoperative pathway.

3.2 Groups covered by the guideline

Adults (over 18 years of age) undergoing elective and emergency surgery (including surgery for trauma), under general and regional (central neuraxial block) anaesthesia.

Subgroups will be considered, based on patient demographics, concurrent medication, duration of anaesthesia and surgery, and/or grade of surgery (see 'Preoperative tests: the use of routine preoperative tests for elective surgery' [*NICE clinical guideline* no. 3]).

3.3 Groups not covered

- Pregnant women
- Patients who have been treated with therapeutic hypothermia
- Patients undergoing operative procedures under local anaesthesia
- Patients with severe head injuries resulting in impaired temperature control.

3.4 Healthcare setting

It is recognised that the NHS is rapidly developing patterns of service delivery, with primary and secondary care borders blurring. The guideline is relevant to secondary and tertiary care provision. Current variation to service delivery and in particular rates of day surgery is noted. The focus of the guideline is, however, applicable to all healthcare service delivery in relation to the management of patients undergoing surgery.

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3.5 IPH management and interventions covered

The following areas of practice will be covered. They have been sequenced throughout guideline documents to reflect the logical progression of patients through their perioperative journey. This is separated into three main phases: the Preoperative phase (1 hour pre-induction of anaesthesia in ward environment or emergency department); the Intraoperative phase (from induction of anaesthesia to end of surgery), and; the Postoperative phase (24 hours following admission to recovery, incorporating transfer back to the ward and immediate management on the ward). This sequencing has shaped the patient algorithm, mapping out the patient journey.

3.5.1 Preoperative phase - assessment of risk

Assessing potential risk factors that contribute to the development of IPH is an important area of contemporary practice. This should be performed by members of the perioperative team, which should include allied healthcare professionals, nurses, ward based doctors, anaesthetists and surgeons. What are the mechanisms of heat loss and distribution, pre-, intra- and postoperatively?

3.5.2 Preoperative phase – patient information

This section of the guideline reviews the importance of clear information to both patients and their carers and healthcare professionals. It emphasises the importance of simple interventions, such as wearing warm clothing and being asked to walk to theatre. It also highlights the importance of increasing patient and healthcare professional awareness in relation to the risks contributing to IPH.

3.5.3 Preoperative phase – preparing the patient for surgery

This section of the guideline reviews the practical aspects of preparing the patient for surgery, and through consensus recommendations gives direction relating to maintaining patient warmth and comfort. Variations to ambient temperature in ward and/or emergency departments are acknowledged, but a recommendation is made on minimum temperature consistent with NHS estates policy.

3.5.4 Intraoperative phase – induction of anaesthesia

This section provides clinical/cost effectiveness and consensus based recommendations on patient warming and temperature management. It includes ambient temperature management, active warming, fluid management and temperature monitoring and recording.

3.5.5 Intraoperative phase – during surgery

This section provides clinical/cost effectiveness and consensus based recommendations on patient warming and temperature management. It includes ambient temperature management, active warming, fluid management and temperature monitoring and recording.

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3.5.6 Postoperative phase – from PACU (recovery) to the ward environment

This section provides clinical/cost effectiveness and consensus based recommendations on patient temperature management, and targets management interventions on maintaining patient core temperature at 36.0˚C or greater. It emphasises the importance of simple interventions (such as wearing warm clothing) emphasising the importance of patient warmth and comfort.

3.6 Interventions not covered

Pre-operative care before arrival in the ward/accident and emergency department, and postoperative care beyond the initial 24-hour period following surgery are not covered by the guideline.

3.7 Guideline Development Group

The guideline recommendations were developed by a multidisciplinary and lay Guideline Development Group (GDG) convened by the NICE-funded National Collaborating Centre for Nursing and Supportive Care (NCC-NSC) with membership approved by NICE. Members included representatives from patient groups, nursing, anaesthesia, surgery, research and the technical team from the NCC-NSC.

The GDG met 13 times between July 2006 and September 2007. All members of the GDG were required to make formal declarations of interest at the outset. GDG members were also asked to declare interests at the beginning of each GDG meeting. This information is recorded in the meeting minutes and kept on file at the NCC-NSC.

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4 RECOMMENDATIONS AND EVIDENCE TO RECOMMENDATIONS

4.1 GUIDELINE RECOMMENDATIONS

The phrase 'comfortably warm' is used in recommendations relating to both the preoperative and postoperative phases, and refers to the expected normal temperature range of adult patients, which is between 36.5°C and 37.5°C.

The numbering of the recommendations is as per the numbering in the NICE version of the guideline.

4.1.1 Preoperative phase

The preoperative phase is defined as the 1 hour prior to induction of anaesthesia when the patient is prepared for surgery on the ward or in the emergency department, including possible use of premedication.

4.1.1.1 Each patient prior to transfer to the theatre suite should be assessed for their risk of inadvertent perioperative hypothermia and potential adverse consequences. Patients with any two of the following should be managed as higher risk (see section 4.1.2.5):

- ASA grade greater than I (the higher the grade, the greater the risk)
- preoperative core temperature below 36.0°C
- undergoing combined general and regional anaesthesia
- undergoing major or intermediate surgery
- at risk of cardiovascular complications (for example, age over 50 years).

4.1.1.2 Patients and their carers should be informed that::

- staying warm before surgery will lower the risk of postoperative complications
- the hospital environment may be colder than their own home
- they should bring additional clothing, such as a dressing gown, a vest, warm clothing and slippers, to help them keep comfortably warm
- staff should be told if the patient feels cold at any time during their hospital stay.

4.1.1.3 Healthcare professionals should ensure that patients are kept comfortably warm while waiting for surgery by providing all patients with at least one cotton sheet plus two blankets, or alternatively a duvet.

4.1.1.4 Healthcare professionals should take special care to keep patients comfortably warm when they are given premedication (for example, benzodiazepines such as midazolam and opioids).

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4.1.1.5 The patient's preoperative temperature should be measured and documented in the hour prior to them leaving the ward or emergency department.

4.1.1.6 If the patient's temperature is below 36.0°C:

- forced air warming should be applied (unless there is a need to expedite surgery due to clinical urgency, for example bleeding or critical limb ischaemia)
- forced air warming should be maintained throughout the intraoperative period.

4.1.1.7 The patient's temperature should be above 36.0°C prior to transfer from the ward or emergency department.

4.1.1.8 On transfer to the theatre suite:

- the patient should be kept comfortably warm
- the patient should be encouraged to walk where appropriate.

4.1.2 Intraoperative phase

The intraoperative phase is defined as total anaesthetic time, from the first anaesthetic intervention to patient transfer to the recovery area of the theatre suite.

4.1.2.1 The theatre suite temperature should be at least 21°C. In order to maintain comfortable working conditions for the scrubbed surgical team, consideration should be given to using equipment to cool the team, rather than reducing the operating theatre temperature.

4.1.2.2 Healthcare professionals:

- should measure and document the patient's temperature prior to induction of anaesthesia and every 30 minutes until the end of surgery
- should not commence induction of anaesthesia unless the patient's temperature is above 36.0°C.

4.1.2.3 Healthcare professionals should ensure that intravenous fluids (500 ml or more) and blood products are warmed to 37°C using a fluid warming device.

4.1.2.4 In order to conserve heat, patients should be adequately covered throughout the intraoperative phase, being exposed only during surgical preparation.

4.1.2.5 Patients who are having anaesthesia for less than 30 minutes and who are at higher risk of inadvertent perioperative hypothermia (see section 4.1.1.1) should be warmed intraoperatively using a forced air warming device (minimum setting 38°C) from induction of anaesthesia.

4.1.2.6 All patients having anaesthesia for longer than 30 minutes should be warmed intraoperatively using a forced air warming device (minimum setting 38°C) from induction of anaesthesia.

4.1.2.7 The temperature setting on forced air warming devices should be set at maximum and then adjusted with the aim of maintaining a patient core temperature of at least 36.5°C.

4.1.2.8 All irrigation fluids used intraoperatively should be warmed in a thermostatically controlled cabinet (38– 40°C).

4.1.2.9 When using forced air warming and fluid warming devices:

- they should be used and maintained in accordance with manufacturers' and suppliers' instructions
- local infection control policies should be complied with.

4.1.3 Postoperative phase

The postoperative phase is defined as the 24 hours after the patient has entered the recovery area in the theatre suite.

4.1.3.1 The patient's temperature should be measured and documented on admission to the recovery room and then at 15-minute intervals.

- Ward transfer can be arranged once the patient's temperature is above 36.0°C.
- If their temperature is below 36.0°C, the patient should be actively warmed to near 36.5°C using forced air warming.

4.1.3.2 Patients should be kept comfortably warm when back on the ward:

- their temperature should be measured and documented on arrival at the ward
- temperature should be re-measured as part of routine 4-hourly observations
- they should be provided with at least one cotton sheet plus two blankets or alternatively a duvet (see section 4.1.1.3).

4.1.3.3 If the patient's temperature falls below 36.0°C:

- they should be warmed using forced air warming until they are comfortably warm
- their temperature should be monitored at least every 30 minutes during warming.

4.2 Evidence to recommendations

4.2.1 Introduction

For the purpose of this guideline, it is necessary to bring together all of the evidence in order to make recommendations that are relevant for the whole patient journey. This is in contrast to the often-used approach of looking at single interventions as prevention or management

approaches. The focus of the systematic review work is to enable the GDG to interpret the evidence, which, at times, is not of sufficient strength to give full confidence without clinical application and interpretation. Studying single interventions in relative isolation across the perioperative patient pathway would have been a more exact methodological approach, but the reality is to assess the combination of interventions across the three different phases of the pathway (preoperative, intraoperative and postoperative) is the only pragmatic way to provide recommendations for perioperative practice. The interdependence of the evidence across these three phases provides the context for this clinical guideline, which has a primary outcome (hypothermia) as its driving force, rather than a discrete clinical condition or disease. Given this approach, the technical team with the GDG's support, have chosen to combine all the evidence to recommendations sections, supported by consensus recommendations into this single chapter, facilitating understanding of how efficacy data has informed economic modelling and recommendations made.

4.2.2 Prevention of IPH

The GDG considered several aspects of prevention of hypothermia, notably 'why we should attempt to prevent hypothermia (the consequences of IPH)?', 'who was most likely to be at risk of IPH and its consequences?' and 'how to prevent it effectively?'

4.2.3 Consequences of hypothermia and patient information

The evidence from the consequences review (section 8) demonstrated that IPH increases the patient's risk of medical complications: these include morbid cardiac events (depending on age and cardiac health), surgical wound infections, pressure ulcers, increased requirement for blood transfusion and mechanical ventilation. IPH also increases the length of stay in hospital and the recovery time in PACU, the latter having an impact on the throughput of patients in the theatre suite with a potential negative effect on surgical list management. The GDG recognised the importance of all health care professionals understanding the serious consequences of IPH and recommended that these provide the basis for economic modelling when determining effective management of patients through the perioperative pathway.

The GDG also recognised the importance of patients being fully informed of the need to stay warm to prevent postoperative complications. They wished to counter the perception that hospitals are always warm and to encourage patients to bring additional clothing such as a dressing gown, a vest, warm clothes and slippers. Patients should be advised to inform staff if they felt cold at any time in hospital.

In addition, the GDG emphasised that it was important for health care professionals to be aware of their responsibility to keep patients 'comfortably warm' on the wards or in the emergency department, and on transfer between the wards and the theatre suite. The provision of sufficient bedding was an important aspect of this, with a minimum of one sheet

and two blankets or a duvet being recommended. The term 'comfortably warm' refers to the expected normal temperature range of adults, this range is supported by the physiology review and is between 36.5 and 37.5°C.

4.2.4 Risk factors for hypothermia

The GDG considered it important to know who was at higher risk of hypothermia and its consequences. This was contextualised by determining who would benefit most from preventative measures (informed by the cost effectiveness analyses).

The risk factors review highlighted that the following factors increased the risk of hypothermia:

- ASA grade higher than I
- Lower patient preoperative temperature
- Combined regional and general anaesthesia
- Major or intermediate surgery
- Unwarmed intravenous fluids, irrigation fluids and blood
- Lower theatre temperature.

Unwarmed IV fluids, irrigation fluids and blood were not used for case finding of those at higher risk because the GDG had recommended that all fluids and blood should be warmed.

Lower theatre temperature, was also not used for case finding because the GDG had recommended that the theatre temperature should be at least 21°C.

Lower patient preoperative temperature, has been used to inform other recommendations, these are:

- That patients should be kept warm preoperatively and on transfer to the theatre suite
- That induction should not be commenced if the patient temperature is below 36.0°C.

The GDG included this risk factor for case finding in order to include patients undergoing urgent surgery, whose temperatures may be below 36.0°C. The GDG determined the temperature threshold by consensus.

The GDG recognised that it is essential to consider which patients are more likely to experience the adverse consequences associated with IPH. Health economic modelling showed that it was particularly important to highlight patients who were at an increased risk of cardiac complications as these have the greatest potential to result in long-term morbidity. Age is an important indicator of an increased risk of cardiac complications, but is not an independent risk factor for IPH. The observational study used for inputs in the health economic modelling identified preoperative ischaemic heart disease as an independent predictor of major cardiac complications (Lee 1999). There is evidence from a large data set

(British Heart Foundation Statistics) indicating that the incidence of ischeamic heart disease increases with age. The GDG noted that routine NHS practice was to carry out ECGs at age 65 and above because it is accepted that cardiac abnormalities can manifest themselves in this patient population that often are asymptomatic of cardiac disease.

The GDG decided that patients at increased risk of IPH or of cardiac complications should be identified as 'higher risk' and the threshold for intervention should be lower in these patients. Consequently, the GDG identified the following risk factors for case finding: ASA grade higher than I, a preoperative temperature below 36.0°C, intermediate or major surgery, combined general and regional anaesthesia and increased risk of cardiac complications. After considering the variation in cost-effectiveness across different risk groups, the GDG were able to interpret that two factors should define higher risk patients.

Pharmacological agents that increase IPH risk, including midazolam (and, by extension, other benzodiazepines and CNS depressant drugs) when given in the preoperative phase, and the analgesics tramadol and nefopam given in different operative phases. Many patient risk factors and pharmacological agents did not affect the incidence of IPH. The GDG decided not to make a recommendation on tramadol and nefopam because they are not widely used in the UK. The GDG noted that the benzodiazepines tend to induce a poikilothermic state in the patient, where core temperature approaches that of the surroundings because of the peripheral vasodilatation that these drugs produce. In such clinical circumstances, it is important for healthcare professionals to keep the patient warm.

Environmental preventative measures

Evidence from the risk factors review was used to inform discussions on environmental preventative measures. The review showed that a lower theatre suite temperature was a risk factor for IPH, and there was weak evidence to suggest that an appropriate cut-off temperature was 21°C. Looking at patient end outcomes, higher temperatures were likely to be advantageous. The GDG recognised the difficulty of making recommendations in this area, and focused their recommendations on the theatre suite temperature, balancing these with the need for comfortable working conditions for the scrubbed perioperative team. To this end, they concurred that consideration should be given to using equipment to cool the perioperative team, rather than reducing theatre suite temperatures. Weak evidence suggested the promotion of ambient temperature being between 21°C and 24°C. The GDG interpreted this and recommended that a minimum theatre temperature of 21°C should be experienced. The GDG noted from the risk factors review that theatre humidity is not an important factor.

The GDG recognised that it was implausible to make recommendations on ward or emergency department temperatures, choosing to focus their consensus recommendations on preventative measures for the patient.

4.2.5 Warming devices and pharmacological interventions to prevent IPH – Clinical effectiveness evidence summary

The clinical effectiveness evidence for warming mechanisms is generally not good: there are many small studies, data extraction from graphs was often necessary – and sometimes these graphs lacked information or there were inaccuracies or inconsistencies with the text. In addition, several studies had baseline differences in core temperature that have potential to confound the results. Furthermore, the interventions vary and may be used with or without other warming mechanisms, for example, forced air warming versus usual care with warmed fluids in both arms of the trial.

An agreed GDG approach was only to consider acceptable or good evidence, as being sufficiently reliable to inform recommendations. Most of the comparisons meeting these criteria were used for the economic modelling, but, for the comparisons with usual care, only those showing a significant effect were selected. GDG members were surprised by the poor quality and paucity of evidence, but recognised the importance of having sufficient certainty in the evidence before making recommendations. The evidence base considered as acceptable for the purposes of informing recommendations is summarised below

A. Acceptable or good evidence for warming mechanisms and pharmacological agents

Intraoperative

1. Forced air warming versus usual care for general anaesthesia had significantly higher core temperatures at 30, 60 and 120 minutes intraoperatively and at the end of surgery and in ICU.
2. Water mattress versus usual care for general anaesthesia had significantly higher core temperatures at 120 minutes intraoperatively but there was no statistically significant difference at 60 minutes.
3. Forced air warming versus reflective blanket for regional anaesthesia had significantly higher core temperatures at 60 and 120 minutes intraoperatively but there was no statistically significant difference at 30 minutes.
4. Forced air warming versus warmed cotton blankets for general anaesthesia had a significantly lower incidence of IPH in PACU and significantly higher core temperatures at 120 minutes intraoperatively.
5. Forced air warming versus electric heating pad for general anaesthesia had significantly higher core temperatures at 120 minutes intraoperatively but there was no statistically significant difference at 30 or 60 minutes intraoperatively.
6. Warmed IV fluids (1.3 to 1.8 litres) versus usual care for general anaesthesia had significantly higher core temperatures at 15, 30 and 60 minutes intraoperatively.
7. Forced air warming plus warmed fluids (2.97 litres) versus Forced air warming plus unwarmed fluids (1.77 litres) for general anaesthesia had significantly higher core temperatures at 30 and 120 minutes intraoperatively but there was no statistically

significant difference at 60 minutes and we note that the amount of fluids was significantly different between the two groups.

8. Forced air warming aggressive versus forced air warming conventional for regional anaesethesia had significantly higher average core temperatures and at the end of surgery.
9. Urapidil versus placebo, given at the end of surgery, GA – no significant difference at 15 and 60 minutes post extubation.

Pre and intraoperative

10. Reflective blanket versus usual care for general anaesthesia had significantly higher core temperatures at 30 and 45 minutes but the difference was small 0.21°C at 45 minutes.
11. Forced air warming plus warmed fluids (1.1 litre) versus usual care for general anaesthesia had significantly higher core temperatures at the end of surgery (56 min) and the lowest core temperatures (at 25 and 35 minutes) were significantly higher. Forced air warming also significantly decreased the incidence of IPH at the end of surgery (RR 0.32)
    - We note that, of the patients receiving usual care, 29% of patients assigned to the routine care arm received forced air warming and 9% received warmed fluids at the discretion of the anaesthetist. This is likely to underestimate the size of the effect.
12. Infusion of amino acids versus placebo for general anaesthesia had significantly higher patient core temperatures for amino acids at 120 minutes intraoperatively but there was no statistically significant difference at 60 minutes.

Preoperative

13. Forced air warming versus warmed cotton blankets for general anaesthesia had a significantly lower incidence of IPH in PACU and a higher core temperature in PACU.

Evidence with methodological limitations

There were some studies that the GDG decided had methodological limitations and so could not be used reliably to make recommendations. These included:

Sheng (2003) (2): this study randomised 52 patients to reflective hats and jackets or usual care preoperatively and then re-randomised them to a reflective blanket or usual care intraoperatively. Data extraction was from a graph that did not state if the error bars were confidence intervals, standard errors or standard deviations – the latter were deduced from the p values given. The GDG noted that there was a large significant effect of preoperative hats and jackets (mean difference in core temperature of 0.98°C for a control group temperature of 35.5°C at 30 minutes), and wished to investigate this further in a research recommendation.

The Sheng (2003) study also recorded the comparison of reflective blankets versus usual care and the GDG considered this to be similarly unreliable, both on its own and in meta-analysis with the small Ouellette (1993) study.

The studies comparing electric blankets with usual care were either too small (less than 20 patients) or were fairly small (22 patients). In addition, the GDG noted that electric blankets are not in use in the UK.

Use of clinicial effectiveness data in cost-effectiveness modelling

From the clinical effectiveness evidence, the GDG decided that the following interventions should be modelled (indicating where there is no significant difference in core temperature).

Intraoperative phase

- Forced air warming (versus usual care)
- Forced air warming plus warmed IV fluids (from head-to-head with forced air warming plus unwarmed IV fluids)
- Warmed fluids
    - Insufficient evidence at 120 minutes
- Electric heating pad (from head to head with FAW)
    - No significant difference at 30 and 60 min
- Circulating water mattress
    - 120 minutes only
- Reflective blanket for regional anaesthesia (from head to head with FAW)
    - 120 minutes only
- Warmed cotton blanket (from head to head with FAW)
    - 120 minutes only

Pre and intraoperative phase

- Reflective blanket
    - No data at 60 or 120 minutes
- Forced air warming plus warmed IV fluids
    - No data at 120 minutes
    - Effect underestimated because some of the control group were warmed
- Amino acids
    - No data at 30 minutes.

Preoperative phase

- Forced air warming (from comparison with warmed cotton blankets)
    - At 120 minutes.

Time points chosen by the GDG were: 30, 60 and 120 minutes. These times typically represent short, medium and longer duration operations. It is recognised that this is an

approximation, particularly for the 30 minutes results, because this time point in a longer operation will be under different anaesthetic conditions to those of a 30 minute total anaesthesia time.

We note that, for some of these interventions, the efficacy was not available at all time points.

4.2.6 Warming devices and pharmacological interventions to prevent IPH – interpreting the clinical and cost-effectiveness evidence

For the cost effectiveness analyses, the net benefit per hypothermic case prevented depended on the risk of each consequence of hypothermia, and of particular importance was the risk of morbid cardiac events, which, in turn, depended on age. The net benefit also depended on the risk of hypothermia, the relative risk for prevention of IPH and the cost of the intervention. The cost effectiveness model has been run for different scenarios represented by various combinations of each of the risk factors for IPH and age as a risk factor for morbid cardiac events.

Whilst the economic model provides evidence on the cost-effectiveness of various interventions and combinations of interventions across different risk groups, the GDG recognised the need to make clinically workable recommendations that could be applied across the population covered by the guideline without the need for complicated algorithms. During the interpretation of the cost and clinical effectiveness evidence, the GDG were mindful of the importance of clear recommendations that ensure that the guideline can be implemented.

Fluid warming

The GDG noted that, for all scenarios modelled, fluid warming was cost effective compared with usual care (unwarmed fluids). This was applicable for the volumes of fluids used in the trials. The GDG noted that the clinical effectiveness review showed that when warmed fluids were given, there was a significant difference in core temperature at 15 minutes, at which time it was estimated that a minimum of 200 ml of warmed fluid had been delivered to the intervention group and at least 200 ml room temperature fluid to the control group. The GDG also considered it clinically negligent not to warm intravenous fluids, other than those for the delivery of drugs. Taking all these things into consideration, they recommended that when IV fluids of 500 ml or more are given, they should be warmed using a fluid warming device and not taken from a warming cabinet.

Forced air warming

The GDG decided to make separate recommendations for shorter and longer durations of anaesthesia. These were divided at 30 minutes duration:

Duration of anaesthesia of at least 30 minutes

For the interventions that were modelled, the GDG took into consideration the cost effectiveness results and concluded that, for patients at higher risk of IPH and its consequences, the most effective preventative method at 60 and 120 minutes of anaesthesia was forced air warming with warmed fluids given in the intraoperative phase. For the lower risk groups at these times, the most cost effective measure was warmed fluids alone, but for all groups, forced air warming was more cost effective than usual care, particularly because it prevented the consequences of hypothermia.

The GDG's view was that the effectiveness of warmed fluids was likely to depend on the volume of fluids given and this depended on other perioperative factors, including clinician preference. The GDG considered that the approach of using warmed fluids as the sole means of heat transfer could be unreliable, because the patient who did not require much fluid might not be adequately warmed, and there was no independent control over the warming mechanism. If the volume of fluids given was lower than represented in the trials – as might be the case in minor surgery – then the forced air warming plus warmed fluids option would become more likely to be the most cost effective strategy. The GDG also took into consideration the fact that forced air warming was cost effective compared with usual care and that the consequences of not warming patients were serious.

The GDG considered that the adverse effects of forced air warming did not pose a significant risk in comparison to the potential benefits - provided manufacturers' instructions for use and maintenance were followed.

Although the time points considered in the modelling were 60 and 120 minutes, the GDG considered it reasonable to extrapolate these results to all durations above 30 minutes. Therefore, they recommended that the combination of forced air warming and warmed fluids should be given to all patients having anaesthesia durations of 30 minutes and over.

Anaesthesia duration of less than 30 minutes

At 30 minutes anaesthesia duration, the health economic modelling showed that the strategies forced air warming plus warmed fluids and warmed fluids alone had similar likelihoods of being optimal in patients at higher risk of IPH and its consequences. In patients at lower risk the optimum strategy was warmed fluids alone.

The GDG also considered what would be the best option for those patients who do not receive fluids, or who only receive small volumes perioperatively. For these patients, the problem reduced to whether or not forced air warming alone was cost effective compared with usual care. The GDG noted that, for all patients, forced air warming is more cost effective than usual care under the basecase assumptions for anaesthesia durations of 30 minutes.

The GDG then considered whether these 30-minutes results applied to durations shorter than 30 minutes. They were concerned that the efficacy values for short operations were largely based on measurements taken at 30 minutes during longer operations, which could lead to uncertainty in the reliability of these efficacy values. Secondly, they believed that forced air warming took time to work and might not be effective at short times, but they noted that the clinical effectiveness review showed that when warmed fluids were given, there was a significant difference in core temperature at 15 minutes into a longer operation. Finally, the GDG believed that the risks of hypothermia and infection, at shorter times, for this population, would be lower than in the basecase. They noted the sensitivity analysis which showed that when the risk of hypothermia was lower than assumed in the basecase (50% reduction), forced air warming was still cost-effective compared to usual care for most of the scenarios considered, but the cost per QALY ratio was in the £20,000 to £30,000 range for the lowest risk group.

The GDG also considered the balance of benefits and harms, taking into account the risk of adverse effects from forced air warming, even though this risk is low.

In view of their reservations about the applicability of the evidence to short operations, the uncertain effectiveness of forced air warming at short times, and taking into account the sensitivity analyses, the GDG decided to adopt a more conservative approach for the shorter operations, and recommended that only patients at higher risk of IPH and its consequences should receive forced air warming for anaesthesia durations less than 30 minutes. The GDG was also interested to know if preoperative warming mechanisms could be useful in preventing hypothermia for short operations and therefore proposed a research recommendation.

The risk factors were:

- ASA grade greater than I
- Preoperative temperature less than 36.0°C
- Undergoing combined general and regional anaesthesia
- Intermediate or major surgery
- Risk of cardiovascular complications.

The GDG noted that age is particularly important in determining the risk of cardiovascular complications and took into account the age of 50 years given normal epidemiological trends in increasing cardiovascular risk and the age of 65 years used routinely in practice. They also noted that patients over 65 years would routinely have an electrocardiogram to establish if they have any cardiac rhythm disturbance indicative of increased cardiac morbidity, as often rhythm disturbance may be asymptomatic. The GDG decided it that was most helpful to

qualify their recommendation's 'risk of cardiovascular complications' from the epidemiological data and gave age over 50 years as an example.

The GDG concluded that all patients at higher risk of IPH for anaesthesia durations less than 30 minutes and all patients receiving anaesthesia lasting more than 30 minutes should be given warmed fluids and forced air warming. Patients at lower risk of IPH should receive warmed fluids only.

Circulating water mattress

The Matsusaki (2003) and Hynson (1992) studies both reported change scores from baseline for forced air warming versus circulating water mattress. The GDG noted that the weighted mean difference in core temperature at 60 minutes was significantly higher for forced air warming. The GDG noted that the comparison of circulating water mattress versus usual care was not significant at 30 or 60 minutes, but there was weak evidence to show a small effect at 120 minutes. This was much lower than for the comparison of forced air warming versus usual care (0.39 versus 0.91°C). Although these are indirect comparisons, the GDG took them into consideration, together with the head-to-head comparison, and decided that forced air warming was more clinically effective and likely to be more cost effective than a circulating water mattress.

Electric heated mattress

There were two studies that compared the Inditherm mattress with forced air warming, one of which was described on the Inditherm website. The latter did not give standard deviations, and although attempts were made to obtain further data from the authors, none were forthcoming. There was weak evidence to suggest that there was no significant difference in core temperature for the two warming mechanisms in a direct comparison, but the study was small. The GDG also recognised that the Inditherm mattress did not require any disposables and therefore had the potential to be more cost-effective than FAW if it were shown to be equally effective. The GDG concluded that further investigation was needed to determine how effective the Inditherm mattress might be, and included the comparison in a research recommendation.

Irrigation fluids

There was weak evidence from two studies that were inconsistent – one, using active warming of fluids (at least 5 litres) showed a significant difference in core temperature, but the other, using passive warming of fluids (8.4 litres) showed no significant difference. It was unclear if the difference between studies was concerned with the type of warming or the amount or any other factor. The GDG considered that warming irrigation fluids is unlikely to increase costs significantly, as it is already standard practice in many hospitals and the warming cabinets are likely to be available currently in most theatre suites. They also noted the considerable cost

savings and health benefits that can be achieved by preventing the adverse consequences associated with IPH, as demonstrated by the economic modelling, and believed that using unwarmed irrigation fluids would put the patient at significant increased risk of developing IPH, and that it would be clinically negligent not to warm irrigation fluids. Therefore they recommended that irrigation fluids should be warmed before use, in warming cabinets.

Actively warmed versus passively warmed fluids

There was weak evidence to show no significant difference between different methods of warming IV fluids, but there was insufficient information on the volume of fluids and the method of significance testing. This evidence was used to inform GDG discussions, but the GDG decided to err on the side of caution and recommend the use of active fluid warming.

Pre-warming

There was weak evidence from indirect comparisons to suggest that pre-warming did not have a large additional effect on core temperatures intraoperatively. The GDG also noted that applying forced air warmers on the ward would require training in their use and there might be infection control issues in transferring the forced air warming device into the theatre area.

Forced air warming (aggressive) versus forced air warming conventional

The Winkler (2000) study gave acceptable evidence to show a significant difference in core temperature for patients warmed using aggressive forced air warming, this study promoted maintenance of normothermia (a temperature of at least 36.5°C), by adjusting the temperature setting on the warming device, and this intervention was compared with warming to 36.0°C. This study was not modelled because the costs would be very similar for each group, apart from some minor differences in electricity usage. This study is discussed further in the section on treatment of hypothermic patients.

Phenylephrine

The pharmacological agent, phenylephrine, a vasoconstrictor, showed some potential for increasing core temperatures in comparison with placebo and reported a large increase at 60 minutes, but the study was too small (18 patients) to make a recommendation. The GDG was interested to determine if phenylephrine was effective in a larger study, and noted that the use of drugs would have to be in addition to forced air warming and warmed fluids, rather than as an alternative. The GDG therefore proposed a research recommendation for phenylephrine and other alpha adrenergic antagonists.

Thermogenesis solutions

The nutritional solutions of amino acids and fructose showed some potential for prevention of IPH. The economic modelling showed that amino acids given pre and intraoperatively were not cost-effective, in indirect comparison with warming mechanisms, but the GDG wished to

know the adjunctive effect of these solutions for patients who were already receiving FAW and warmed IV fluids. The small study investigating fructose solutions had wide confidence intervals, although the effect was significant. The GDG also took into consideration other potential benefits of nutritional agents, such as healing from protein synthesis and general nourishment and well being in fasted patients. The GDG therefore proposed a research recommendation.

Forced air warming – device settings

Finally, the GDG considered the settings of the forced air warming device. The majority of studies in the reviews used a setting of 'high'. The GDG considered the adverse effects review evidence and noted that there might be an increased risk of burns if the setting was too high. Their view was that regular monitoring would allow the perioperative team to adjust settings to maintain a core temperature of at least 36.50°C.

The GDG also took into consideration the adverse effects review and noted that adverse effects could be minimised if forced air warmers were used in accordance with manufacturer's instructions and if adequate infection control measures were put in place (e.g. decontaminating the end of the hose).

Optimising usual care to prevent IPH

The GDG recognised variability in the ways health care professionals manage patient temperature on the ward, and made consensus recommendations focussed on some simple measures to optimise 'usual care'.

Healthcare professionals should encourage patients to bring warm clothes, such as a dressing gown and slippers to the hospital. Healthcare professionals should ensure that the patient has at least one sheet with two blankets or a duvet.

The GDG also discussed the merits of patients walking to theatre (where possible). The reasons for this arose from the physiology review, which demonstrated the relationship between physical activity (in this case walking) and heat conservation. The GDG agreed that there may be benefits to the patient by promoting this simple intervention. When walking to theatre, the patient should wear their dressing gown and slippers. For less mobile patients, the GDG recommended that they were kept warm on transfer to the theatre suite.

In the theatre, the GDG recommended that patients remained covered, only being exposed for surgical preparation.

4.3 Treatment of inadvertent perioperative hypothermia

The GDG considered two main aspects of the treatment of IPH: temperature monitoring and the detection of IPH and then focussed on how best to treat hypothermia once detected.

Temperature monitoring and detection of IPH

The GDG was concerned that temperature should be monitored effectively, so that any trend towards hypothermia could be dealt with as quickly as possible. They noted that temperature measurement equipment is likely to be available already in all wards and theatre suites. The GDG also noted the considerable cost savings and health benefits that can be achieved by preventing the adverse consequences associated with IPH, as demonstrated by the economic modelling, and recognised that temperature monitoring is necessary in order to determine which patients are at risk of these complications and to treat where appropriate. They therefore considered the frequency of temperature monitoring, based on the significant clinical experience within the group. GDG consensus indicated that the frequency of measurement should vary according to the perioperative phase. This reflects best practice and acknowledges the likely ease of implementation of the recommendations. Consensus was:

- Preoperatively, a baseline temperature should be measured and documented prior to the patient leaving the ward. The preoperative period is defined as I hour before induction of anaesthesia and the recommendation reflects this.
- Intraoperatively, the temperature should be recorded prior to induction and then every 30 minutes until the end of surgery.
- In PACU, temperatures should be recorded every 15 minutes.
- In the postoperative ward, the temperature should be measured and documented as part of routine four hourly observations. However, if warming were necessary, temperatures should be monitored every 30 minutes to avoid overheating.

Recognising normal physiology, the GDG agreed that the temperature should be raised above 36.0°C and ideally to as near to 36.5°C as possible, returning patients to normothermia, which is between 36.5°C and 37.5°C for most patients. The GDG considered it preferable to have a temperature excess of 0.5°C above the hypothermia threshold so that any further loss of heat would not immediately make the patient hypothermic. In effect this would act as a buffer that protected against hypothermia development. This approach, whilst preferable, is unable to be supported by available evidence for the following reasons:

- The economic modelling is based on a threshold of 36.0°C, which was determined by the GDG's definition of hypothermia to be core temperatures below 36.0°C.
- There is a paucity of clinical effectiveness evidence to support warming to 36.5°C, with no indication that a 0.5°C buffer is cost effective for the patient. There was weak evidence from a small number of patients to show it took about 60 minutes to increase the temperature from 36.0 to 36.5°C when the patients were given forced air warming.

- There is physiological evidence that temperature has an upwards gradient following the end of anaesthesia, not a downwards gradient. Intuitively, this means that the patient is likely to get warmer and not cooler.

The GDG also took into consideration observational data collected by one of its members. This was a large data set comprising more than 20,000 patients, some of whom were warmed. The data were recognised to be characteristically representative of a typical NHS Trust, and were used as indirect evidence in concluding decisions relating to endpoint patient temperature. This indirect evidence demonstrated that a high percentage (more than 60%) of patients never reached 36.5°C before discharge from recovery. A higher temperature end point (36.5°C) would create significant challenges to throughput of patients in recovery following surgery. After robust discussion, the GDG were confident that 'above 36.0°C' was the right temperature endpoint to recommend for patient discharge from recovery to the ward environment. This was based on the consideration that if a patient's temperature remained above 36.0°C throughout their stay in recovery, transfer could be arranged as they are unlikely to drop their temperature when sufficiently awake for ward transfer. The GDG recognised that patients whose temperatures were below 36.0°C should be actively warmed to near 36.5°C to prevent a second period of IPH developing.

The GDG was also concerned that healthcare staff should be trained in how to use the temperature monitoring equipment in their local area.

Summary of clinical evidence for the treatment of IPH

The GDG then considered the evidence regarding methods of treating hypothermia, should it occur. Again, the approach taken was to consider the different perioperative phases separately.

The evidence is summarised by quality and significance of the effect. The GDG decided to omit the evidence from indirect populations (e.g. those who had undergone therapeutic hypothermia, but then experienced an afterdrop following re-warming). This section also presents evidence, in the preoperative phase, for the effectiveness of warming patients who are not hypothermic, to give an indication of the relative merits of different warming mechanisms. Again the GDG considered that only acceptable or good evidence should be used for informing recommendations and this is summarised below.

Acceptable or good evidence relating to warming mechanisms used to treat IPH

Preoperative phase – patients not hypothermic

1. Forced air warming versus usual care for general anaesthesia had significantly higher core temperatures at the end of prewarming for patients who were not hypothermic.
2. Forced-air warming versus warmed cotton blanket for general anaesthesia had

significantly higher core temperatures in at the end of prewarming for patients who were not hypothermic.

3. Thermal insulation (reflective hat, reflective hat and jacket, reflective blanket) versus usual care for general anaesthesia had no significant difference in the core temperature in the holding area for patients who were not hypothermic (acceptable: meta-analysis of 3 studies; duration not stated).

Postoperative phase – hypothermic patients

1. Reflective blankets and reflective head covering versus warmed blankets had no significant difference in the time taken to reach 36.0°C from an initial mean temperature of 34.8 or 35.0°C.

Treatment of hypothermia – interpreting the clinical and cost-effectiveness evidence

The majority of the evidence is for treatment in the postoperative phase and the quality of that evidence was generally weak. Therefore, economic modelling was not carried out specifically for the treatment of hypothermia, and general guidance was taken from the modelling for prevention. In particular, the GDG noted that since it is cost-effective to warm patients to prevent IPH, when not all patients will develop IPH under usual care, it must be cost-effective to treat people who are hypothermic preoperatively as they are already at higher risk of developing the adverse consequences associated with IPH. Secondly, the GDG noted that warming mechanisms that can be used to cover both prevention and treatment will be more cost-effective than switching from one mechanism to another, because of the investment in disposables. This dual approach includes (i) warming hypothermic patients in the preoperative phase and continuing that warming into the intraoperative phase, and (ii) warming patients intraoperatively to prevent IPH, and then continuing the same method if treatment is needed postoperatively. In these situations, the additional cost of postoperative treatment will be small because disposables associated with warming devices can be kept in place. Using the same warming mechanism for prevention and treatment will also reduce the need to invest in equipment and staff training for several different warming mechanisms.

<u>Duration of warming</u>

It was noted that, under usual care in ICU or PACU, it took about two hours to raise the temperature from about 35°C to 36.0°C and about three hours to reach 36.5°C. Preoperatively, there was weak evidence from one small study to show that forced air warming increased the temperature of hypothermic patients from about 35°C to above 36.0°C in about 75 minutes.

In the intraoperative phase, there were two small studies that randomised hypothermic patients to forced air warming or usual care, when they became hypothermic. In one study this was at induction of anaesthesia and in the other it was two hours after induction. Each study

reported significantly higher temperatures for the forced air warming group compared with usual care. In the latter study, the usual care group had a mean core temperature of 34.8°C four hours after becoming hypothermic, but even with forced air warming, the patients in the intervention group required four hours of warming to reach temperatures above 36.0°C. The GDG considered this evidence and noted that, although these are small studies, there is some evidence that it is difficult to raise the temperature of a patient once they have become hypothermic, and that 'prevention is better than cure'.

When treatment should commence

The GDG considered when and where treatment should commence, and concluded that this should be whenever the temperature dropped below 36.0°C, unless there was a need for urgent surgery. Preoperatively, treatment should be initiated on the ward or in the emergency department, and this warming should be maintained throughout the intraoperative period. The GDG also noted, from the risk factors review, that a lower preoperative patient temperature was a risk factor for IPH, and further recommended that if a patient had a temperature below 36.0°C on arrival in the theatre suite, anaesthesia should not be induced unless there was a need for urgent surgery.

Which warming mechanisms?

The GDG then considered which warming mechanisms should be used in different phases to treat hypothermia. The GDG was keen to emphasise that treatment was only in response to hypothermia, and the objective was to prevent IPH from occurring at the outset.

Preoperative phase

The GDG took into consideration additional evidence from the preoperative review.

There was good or acceptable evidence in patients who are not hypothermic to show that forced air warming increased the temperature significantly more than usual care or warmed blankets. For this patient group, there was good evidence to show no significant difference in treatment effect between thermal insulation of any type compared with usual care. The weak evidence from one small preoperative study in hypothermic patients suggested that forced air warming was significantly more effective than usual care.

The GDG was concerned that all possible simple methods should be carried out to ensure patients were kept warm (see prevention above), but if these measures failed (possibly because the patient was at higher risk of IPH) and the patient's temperature fell below 36.0°C, the GDG recommended that patients should be warmed using forced air warming devices. These should be continued into the intraoperative phase.

Intraoperatively

The evidence for treatment in the intraoperative phase is that forced air warming is significantly more effective than usual care in treating patients who have become hypothermic intraoperatively. The GDG also took into consideration the Winkler study in which patients receiving aggressive forced air warming reached significantly higher core temperatures than those receiving conventional warming. Taking these factors into account, the GDG recommended that forced air warming should be applied intraoperatively, together with adjustment of settings and monitoring of the core temperature.

Postoperatively

The GDG took into consideration the weak evidence from the postoperative treatment review. They noted that forced air warming and radiant heat appeared to be the best choices for the treatment of hypothermia, and that electric blankets, reflective blankets and warmed cotton blankets were comparatively less effective. The GDG commented that radiant heaters were not widely used in the UK, and noted that many patients would already have forced air warmers on arrival in PACU. The GDG observed that it would be more cost-effective to continue any intraoperative warming mechanism already in use than to switch mechanisms. The GDG therefore recommended that forced air warming should be continued until the patient's core was 36.5°C, but that transfer to the ward could be arranged once the temperature reached 36.0°C provided other discharge criteria were met.

The GDG was concerned that all possible simple methods should be carried out on the ward to ensure patients were kept warm (see prevention above). However, if the patient's temperature dropped below 36.0°C, the GDG recommended that forced air warming should be used to raise the patient's temperature.

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5 METHODS USED TO DEVELOP THE GUIDELINE

5.1 Summary of development process

The methods used to develop this guideline are based on those outlined by Eccles and Mason (2001). The structure of the recommendations section (i.e. recommendations, evidence statements, evidence narrative and guideline development group commentary) came from McIntosh et al. (2001).

The stages used in the development of this guideline were as follows:

- Guideline scope development following referral from the Department of Health
- NICE stakeholder review and feedback
- Multidisciplinary guideline development group convened with formal appointment of the clinical lead and chair of the group by competitive interview
- Establish key clinical questions
- Identify sources of evidence
- Retrieve potential evidence
- Evaluate potential evidence relating to clinical and cost effectiveness, quality of life, for eligibility, quality and relevance
- Extract relevant data from studies meeting methodological and clinical criteria
- Interpret each paper, taking into account the results (including, where reported, beneficial and adverse effects of the interventions, cost, comfort and acceptability to patients), the level of evidence, the quality of the studies, the size and precision of the effect, and the relevance and generalisability of the included studies to the scope of the guideline
- Analyse, where appropriate using statistical synthesis, the results reported in the studies
- Prepare evidence reviews and tables which summarize and grade the body of evidence
- Formulate conclusions about the body of available evidence based on the evidence reviews by taking into account the above factors
- Agree final recommendations
- Submit drafts (short version and full version) of guideline for feedback from NICE registered stakeholders
- Consider stakeholders comments (GDG)
- Submit final version of the guideline to NICE.

NCC-NSC technical team members searched bibliographic databases for evidence, examined and quality assessed the evidence. The technical team compose successive drafts of the recommendations and guideline documents (including the full version of guideline; the NICE version and the quick reference guide), based on the evidence reviews and GDG input and deliberations. The GDG having interpreted the evidence formulated the recommendations.

The NICE patient and public involvement programme produced the *Understanding NICE guidance* version, using the NICE version of the guideline, in collaboration with the NCC-NSC. The general methods for the evidence reviews are reported in sections 5.2 and 5.3. This linear relationship, demonstrating the relationship between the clinical and cost effectiveness results, evidence statements and resulting recommendations, is reported in chapter 4.

For the purpose of this guideline, it is necessary to consider the evidence within the context of the whole patient journey. This is in contrast to often looking at single interventions as prevention or management approaches. The focus for systematic review work for this guideline is to enable the GDG to interpret the evidence, which, at times is not of sufficient strength to have full confidence without clinical application and interpretation. Single interventions in relative isolation across the perioperative patient pathway would have been a preferred methodological approach. The reality is that assessing the combination of interventions across the three different phases of the pathway (preoperative, intraoperative and postoperative) is the only pragmatic way to provide recommendations for practice. The interdependence of the evidence across these three phases provides the context for this clinical guideline which has a primary outcome (hypothermia) as its main focus, rather than a discrete clinical topic/disease. Given this context, all clinical and cost effectiveness evidence informing recommendations, with consensus recommendations, is included as a single chapter, rather than incorporated into individual reviews.

The search strategies for the reviews are presented in Appendix B. The included studies for each review are reported in Appendix C. The methodological assessments of the included studies are in Appendix D and the studies excluded from each review are listed in Appendix E.

5.2 Clinical effectiveness review methods

This section describes the methods of reviewing that are common to all reviews of intervention studies and the methods used for the risk factors review. Further specific details are given in the individual reviews.

SELECTION CRITERIA

The following selection criteria were to be applied to studies to determine their suitability for inclusion in the reviews:

Types of studies

For intervention studies, the randomised trial (RCT) was to be the primary trial design. Quasi randomised studies could also be included (e.g. allocation by alternation, date of birth, etc). Where there was insufficient evidence from RCTs or quasi RCTs, cohort studies could be considered.

For the risk factor reviews, randomised trials (RCTs) comparing groups with different risks (e.g. types of surgery) and cohort studies (prospective and retrospective) investigating the incidence of perioperative hypothermia were to be the main study designs. We note that, for some risk factors (e.g. age), the randomised trial cannot be used as the study design. If there are no cohort studies available, case-control studies and cross-sectional surveys could be considered, with allowance made for the fact that they have increased potential for bias.

Studies were to be limited to the English language, with the exception of studies translated for Cochrane reviews or as directed by the GDG, but the date was not to be restricted.

Types of participants

Participants were to be adults (18 years and older). However, studies could be included if they had some participants slightly below 18 years, provided that the mean age indicated the majority were adults.

For all studies, participants were to be undergoing surgery or other procedures under general or regional or combined general/regional anaesthesia. Studies reporting patients receiving local anaesthesia or sedation were not to be included, nor were studies in which the patients received therapeutic hypothermia (but see also indirect evidence, below). Studies in patients with head injuries resulting in impaired temperature control or those in volunteers not receiving anaesthesia were to be excluded (but see also below for indirect evidence in the latter).

For studies reporting the *treatment* of inadvertent perioperative hypothermia, the patients were to be hypothermic, defined as a temperature below 36.0°C, and categorised as: mild (35.0 to 35.9°C), moderate (34.0 to 34.9°C) and severe (less than or equal to 33.9°C). Studies were to be included if the mean patient core temperature was less than 36.0°C, regardless of where it was measured. Preferably, though, temperatures should have been measured at one of the following sites: tympanic membrane, bladder, pulmonary artery, nasopharynx and oesophagus. Measurements at the temporal artery, rectum and mouth were to be regarded as more indirect; and studies recording only the skin or axilla temperatures were to be excluded, since these sites are peripheral.

Indirect evidence was considered for some reviews, where direct evidence was not available, or insufficient. In all cases, indirect evidence was used to provide additional information, and its quality was downgraded accordingly. Indirect evidence was not combined in a meta-analysis with direct evidence.

Specifically, the following patient groups were considered as providing indirect evidence:

- Volunteers receiving anaesthesia only without surgery
- Pregnant women

- Patients undergoing therapeutic hypothermia in the post-bypass phase after re-warming ("after drop").

Types of intervention

The interventions to be considered varied across reviews and are detailed at the beginning of the individual reviews.

For prevention of perioperative hypothermia, some interventions could be given over a variable time period and some could be given at a particular time relative to the first anaesthetic intervention or to the start of surgery; this interval could also be varied.

Interventions could be given during one or more of the three phases of the perioperative pathway. The following definitions are used for the three phases:

Preoperative phase: from the time of preparation for surgery/administration of premedication to the time of first anaesthetic intervention.

Intraoperative phase: from the time of first anaesthetic intervention to entry into the recovery room.

Postoperative phase: covering the period 24 hours postoperatively (24 hours refers to the time of delivery of interventions, rather than the time outcomes are recorded), commencing from transfer to the recovery room, and including the clinical area (e.g. Ward, ICU).

Interventions could also be applied across more than one phase (e.g. both pre and intraoperatively).

Types of outcome measures

Inadvertent perioperative hypothermia principally occurs when the patient is under anaesthesia, but consequences of IPH are found in the postoperative phase too.

1. Interventions for the prevention of IPH

For studies of interventions for the prevention of IPH, the following primary outcomes were to be considered:

- Incidence of hypothermia
  - Mild (core temperature 35.0°C to 35.9°C)
  - Moderate (34.0°C to 34.9°C)
  - Severe (≤33.9°C)
- Shivering
- Patient centred outcomes

- Harms/adverse effects associated with the intervention (e.g. burns).

The incidence of hypothermia outcome may have been measured in a dichotomous way, i.e. the number of patients with hypothermia, or in a continuous way, by recording the final value of the core temperature (after intervention). It is noted that the change in temperature compared to baseline is a surrogate outcome.

Temperatures should have been measured at one of the following sites: direct tympanic membrane, bladder, pulmonary artery, nasopharynx and oesophagus. Measurements at the temporal artery, rectum and mouth were to be regarded as indirect outcomes. Skin or axilla temperature measurements were to be excluded, since these sites are peripheral.

Secondary outcomes which should be considered are:

Intraoperative

- Blood loss
- Blood transfusion
- Haematology complications (e.g. Disseminated Intravascular Coagulation)
- Cardiac complications
- Death
- Time to extubation.

Postoperative

- Length of stay in post anaesthesia care unit (PACU)
- Unplanned transfer to ICU/HDU
- Length of hospital stay
- Cardiac event/ Arrhythmia - myocardial infarction complications
- Wound infection
- Pressure ulcer development
- Pain
- Blood loss
- Blood transfusion
- Death
- Postoperative nausea and vomiting (for pharmacological interventions).

Postoperative complications - general

Postoperative complications were to be grouped into two main areas:

- Therapeutic/medical outcomes (e.g. morbid events)
- Humanistic (e.g. shivering, discomfort, pain).

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We note that, sometimes, 'discomfort' is more correctly classified as an adverse effect of the treatment (e.g. overheating).

Categorical outcomes were to be dichotomised, e.g. grouping together 'severe shivering' and 'mild shivering'.

2. Intervention studies for the treatment of IPH

For intervention studies for the treatment of IPH, the same outcomes were to be considered as for prevention. The time to reach a particular temperature (especially 36.0°C) and the rate of warming (temperature change divided by time) were also to be recorded as primary outcomes.

3. Risk factor studies

For risk factor studies the following outcomes were to be considered:

- Incidence of hypothermia
- Core temperature
- Rate of rewarming.

Ideally, the incidence of hypothermia should have been determined for patients who were not warmed, but studies in which some or all of the patients were warmed could also be included. The GDG considered that the risk associated with particular factors may be different in warmed patients. Preferably patient warming would have been included as a variable in multivariate analyses.

SEARCH STRATEGY

The search strategies and the databases searched are presented in detail in Appendix B. All searches were carried out on the following core databases: Medline, Embase, Cinahl (all using the OVID interface) and The Cochrane Library.

For this guideline, a general set of terms was produced relating to inadvertent perioperative hypothermia to produce an IPH search filter. The relevance of terms connected with anaesthesia, surgery and postoperative complications was explored. It was decided that combining these terms with the IPH filter was too restrictive. Initially it was decided to search for all interventions at once and not to use additional terms related to the interventions. This broad search was supplemented where necessary with more specific searches. Where appropriate, study design filters (RCT and systematic review) were applied. Results were limited to papers published in English where possible. All searches were updated to August 2007.

Hand-searching was not undertaken following NICE advice that exhaustive searching on every guideline review topic is not practical or efficient (Mason 2002). Reference lists of articles were checked for studies of potential relevance.

Sifting process

Once the search had been completed, the following sifting process took place:

- 1st sift: One reviewer sifted the title/abstract for articles that potentially met the eligibility criteria.
- 2nd sift: Full papers were ordered that appeared relevant and eligible or where relevance/eligibility was not clear from the abstract.
- 3rd sift: Full papers were appraised that meet eligibility criteria. Generally, one reviewer appraised the papers using an inclusion criteria form, and this was checked where necessary by a second reviewer.

Once individual papers were retrieved, the articles were checked for methodological rigour (see below), applicability to the UK and clinical significance. Assessment of study quality concentrated on dimensions of internal validity and external validity. At this stage, some studies were excluded if the interventions were not licensed for use in the UK or they were not regularly used in the UK. Studies in which the interventions were obsolete were also excluded.

DATA EXTRACTION

Data from included studies were extracted by one reviewer for each review, and randomly checked by a second reviewer, and entered into a Microsoft Access relational database that had been especially designed for the guideline. The use of the database provided a more structured extraction, for example, only certain choices could be made for some items, although free text fields were also completed. The main advantage of using a database for this purpose is that a large measure of detail can be input, and then an overview obtained using database sorting procedures.

Intervention studies

For intervention studies, the following data were extracted:

- Review being addressed
- Study details: study design (RCT, quasi-randomised, cohort study, etc); country where trial conducted; study size; perioperative phase; funding
- Participants
    - Patient characteristics: age (mean and range), gender (ratio male:female), comorbidities, inclusion/exclusion criteria, ASA grade. For treatment of IPH, mean temperature of patients and method of its measurement
    - Anaesthesia: premedication, type of anaesthesia (general/regional/combined), duration of anaesthesia, anaesthesia drugs used, height of regional block

  - Surgery: type of surgery (elective/emergency), surgical speciality, surgery grade (classified as in the NICE preoperative tests guideline), duration of surgery
  - Conditions in other perioperative phases: warming intraoperatively and postoperatively (both arms of trial) – i.e. concurrent treatments that are the same in each arm.
  - Other: ward or operating room temperature, irrigation fluid/IV fluid (warmed/not; active/passive); spontaneously breathing/ventilated (for postoperative measurements)
- Interventions: class (e.g. active warming); sub-class (e.g. forced air warming); intervention details, duration of intervention/time given; dose/temperature setting/power where appropriate; part of body exposed to the intervention; percentage of body area covered by the intervention; perioperative phase(s) in which the intervention was given
- Comparator: usual care; placebo (details of what it is); other intervention
- Outcome: including time measured; site of temperature measurement; scales used (validity); definition of success (if using 'improved', 'complete response', etc).

For the prevention of IPH, the GDG indicated that where possible, core temperature measurements should be extracted at various stages in the perioperative pathway: during or at the end of the preoperative period; during the intraoperative period (at 15, 30, 60 minutes and at 2 and 3 hours from induction of anaesthesia); at the end of surgery and on arrival in PACU.

In addition, the lowest intraoperative temperatures reached by the intervention and control groups should be compared (regardless of the time in which this lowest point occurs), and the times of lowest temperature should also be recorded.

For the treatment of IPH, measurements should be extracted for the post treatment period at 15, 30, 45, 60 minutes and at 2 and 3 hours from the start of treatment.

Other data extracted were:

- Study quality (see below)
- Results for each outcome.

Risk factor reviews

For the risk factor reviews, data were extracted on the following for each study:

- Study details: study design (cohort study/RCT etc); study size; country of the study (relevance to UK populations), perioperative phase.
- Patient characteristics: definition of hypothermia (less than 36.0°C; less than 35.5°C; less than 35.0°C); method of temperature measurement; ASA grade; warming mechanisms used; number of patients with hypothermia.
- Anaesthesia/surgery details: operating room temperature; type of surgery; type of

anaesthesia; duration of anaesthesia/surgery.

- Risk factor details: including distribution of risk factors; multivariate analysis details; comparators.
- Study quality (see below)
- Results for each outcome.

If studies were published more than once, data were extracted from the most recent report where there were differences, otherwise all papers were used for data extraction.

Masked assessment, whereby data extractors are blind to the details of journal, authors etc, was not undertaken.

APPRAISAL OF METHODOLOGICAL QUALITY

The methodological quality of each trial was assessed by one reviewer and randomly checked by a second. Quality items were assessed by type of study.

An important quality criterion for non-randomised studies is how account is taken of confounding by factors other than those under investigation. In the randomised trial, confounders are nullified by the randomisation process: if the studies are sufficiently large, randomisation will ensure an equal distribution of confounders, known and unknown, across groups. However, account can also be taken of confounders in RCTs using analysis of covariance (ANCOVA) methods.

For randomised trials, the following factors were considered in assessing the potential for bias:

- *A priori* sample size calculation:
  - whether or not this was carried out;
- Method of generation of the randomisation sequence:
  - the means by which interventions are distributed amongst the participants
  - whether the method was reported or unclear (i.e. no details given)
  - whether the reported method was adequate, inadequate or partial (Table 1);
- Allocation concealment at randomisation:
  - the means of preventing the treatment assignment being known *before* the time of allocation
  - whether the method was reported or unclear (no details)
  - whether the reported method was adequate, inadequate or partial (Table 1);
- Baseline comparability of treatment groups:
  - for relevant risk factors;
- Patients stated to be blinded, especially for comparisons with placebo:
  - blinding involves hiding the nature of the intervention from participants, clinicians and treatment evaluators *after* allocation has taken place

- blinding may be not be possible depending on the nature of the interventions
- blinding may be more important for some outcomes than others:

- Outcome assessor stated to be blinded
- No loss to follow up for each outcome:
  - studies with at least 20% of data missing from any group were considered to be potentially biased
  - those with moderate loss to follow up (20 to 50%) were considered in sensitivity analyses
  - those with 50% or more patients missing from any one group were regarded as flawed and not analysed further;
- Intention to treat analysis:
  - Trial participants should be analysed in the groups to which they were randomised regardless of which (or how much) treatment they actually received, and regardless of other protocol irregularities and all participants should be included regardless of whether their outcomes were actually collected.

Table 1:

Adequate sequence generation
• Coin toss, throwing a dice, shuffling, drawing lots (from a container). **Partial** drawing a card from a pack.
• Computer or calculator generated sequence (including minimisation and biased-coin/urn design). **Partial**: "random permuted blocks".
• Random number table or statistical tables. **Partial**: random numbers, randomisation table.
• Randomised Latin square design.
Inadequate sequence generation
• For example, allocation by alteration, birthdate, day of week.
Adequate allocation concealment
• Central randomisation: with contacting details and/or statement that central office retained schedule; must apply to all patients. **Partial**: vague statement of central randomisation.
• Independent third party: allocates interventions *and* retains schedule, or statement that *allocator* has no knowledge of patients. **Partial**: third party, but unclear treatment allocation.
• Third party cluster randomisation: third party has no knowledge of clusters. **Partial**: unclear what third party knew.
• Different parties (including one of the authors): should have no knowledge of the patients *and* retain schedule.
• Secure computer assisted method, e.g. locked file. **Partial**: as adequate, but unclear access.
• Sequentially numbered, opaque, sealed envelopes – all required, else **partial**.

• Serially numbered, identical containers, allocated sequentially – all required, else **partial**.
Inadequate allocation concealment
• For example, schedule known in advance, birthdate, case record number.

Cohort studies were assessed using criteria based on the Newcastle-Ottawa checklist and the NICE Guidelines Manual. The following criteria were considered:

1) Representativeness of the exposed cohort:
   a) Truly representative of the community e.g. random sample from general population*****
   b) Somewhat representative of the community e.g. men; all non cardiac operations*
   c) Selected group e.g. cardiac operations under normothermia
   d) No description of the derivation of the cohort or unclear.

2) Selection of the non exposed cohort:
   a) Drawn from the same community as the exposed cohort*
   b) Drawn from a different source – e.g. compared with general population levels in epidemiological studies
   c) No description of the derivation of the non exposed cohort or unclear.

3) Ascertainment of exposure:
   a) Temperature recording at an adequate site (e.g. tympanic membrane, pulmonary artery)*
   b) Temperature recording at a partially adequate site (e.g. adequately positioned sublingual)*
   c) Temperature recording with an inadequate method (e.g. oral temperature without details)
   d) No description.

4) Demonstration that outcome of interest was not present at start of study:
   a) Yes*
   b) No.

5) Prospectiveness:
   a) Prospective study*
   b) Retrospective study
   c) Unclear.

6) Comparability of cohorts on the basis of the design or analysis:
   a) Cohorts balanced at baseline for important factors (see below)*

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b) Adjusted for confounding factors in analysis and does not have too many factors in the analysis for the number of events or patients*
c) Study has 8 to 10 events per factor and adjusted for 3 of 4 relevant factors in the analysis*
d) Study adjusts for some confounders (or keeps them constant): 2 of 4 included
e) Study has less than 8 to10 events per factor in the analysis
f) Study does not adjust for confounders.

In cohort studies, the best way to adjust for confounders is to use regression methods to adjust for all the factors at once in a multivariate analysis. For validity, there should be at least ten patients for each factor in the regression equation for continuous outcomes, and at least ten patients having the event (e.g. IPH) per factor for dichotomous outcomes. However, if there are insufficient relevant factors taken into account, the quality of the study should be downgraded. The relevant factors that had to be included in the analysis were decided *a-priori* by the GDG using consensus methods. They were: age; ASA grade; type of anaesthesia; and duration of anaesthesia/surgery or magnitude of surgery. To qualify as a well adjusted study, the analysis should include at least 3 out of 4 of these factors (or they should be kept constant).

6) Ascertainment of outcome:
   a) Temperature recording at an adequate site (e.g. tympanic membrane, pulmonary artery)*
   b) Temperature recording at a partially adequate site (e.g. adequately positioned sublingual)*
   c) Temperature recording with an inadequate method (e.g. oral without details)
   d) No description.

7) Adequacy of follow up of cohorts:
   a) Complete follow-up: all subjects accounted for*
   b) Subjects lost to follow-up unlikely to introduce bias: more than 80% follow up*
   c) Follow-up rate less than 80% and no description of those lost
   d) No statement.

Studies were considered to be of acceptable quality if the asterisked statements were met, otherwise their quality rating was downgraded.

DATA SYNTHESIS

I. For intervention studies

Meta-analysis of similar trials, where appropriate, was carried out using *The Cochrane Collaboration's* analysis software, Review Manager (Version 4.2). Trials were pooled using a

fixed effects model and plotted on forest plots. Where there was significant heterogeneity, a random effects model was used as a sensitivity analysis.

For dichotomous studies, we used intention to treat analyses (including all participants according to their assigned groups) where reported by the study authors, and failing that, available case analyses (all those reporting an outcome) as reported by the authors were used. Where there were incomplete data reported (more than 20% missing in any one group), we carried out sensitivity analyses, excluding these studies.

Where it was possible to combine studies, outcomes were summarised for dichotomous data using odds ratios (as default), relative risks (where the event rate was greater than 20%), or Peto odds ratios (where there were studies with no events in one arm). Numbers needed to treat, with their 95% confidence intervals and the control group rate (range of rates) to which they apply, were calculated from the risk difference where appropriate. The number needed to treat (NNT) is the number of patients who would have to be treated for one to have an improved outcome.

For continuous data, weighted mean differences were used and where the studies had different scales, standardised mean differences were used. Studies reporting final values or change scores were combined if the scales used were the same, otherwise they were reported separately. If both final values and change scores were reported, the former were used. Summary statistics and their 95% confidence intervals (95% CI) were reported where sufficient detail allowed their calculation, together with the control group range.

We assessed heterogeneity between trials by visual inspection of forest plots, noting where there was poor overlap of horizontal lines, and by using statistical measures: the X^2 test for heterogeneity and the level of inconsistency, I^2 ($I^2 = [(\chi^2 - df)/ \chi^2] \times 100\%$, where df is the degrees of freedom). We considered that there was heterogeneity if the heterogeneity p-value was less than 0.1 and/or I^2 was greater than 50%. Any heterogeneity was explored further and unexplained heterogeneous results were not used as the basis for recommendations.

Stratifications

We planned to consider separately the following groups:

- Trauma patients – elective and emergency surgery to be considered together initially
- Patients with comorbidities that affect metabolism, such as hypothyroidism
- Patients with hyperthermia.

Other stratifications were planned depending on the review.

Subgroup analyses

Randomised trials generally report four different types of subgroup analyses:

- Between-trial, in which the *studies* are separated according to the particular variable considered (e.g. dose).
- Within-trial subgroup analyses, with stratification of the *participants* by the particular characteristic (e.g. type of surgery) followed by randomisation.
- *A-priori* defined within-trial subgroup analyses, in which the *participants* were not stratified, but later separated according to prespecified characteristics. These analyses were included cautiously, because the interventions were not randomised to the subgroups.
- Post-hoc within-trial subgroup analyses, in which the *participants* were separated afterwards without prespecification.

All subgroup analyses are non-randomised comparisons between the different subgroups, however, types 1 and 2 are more reliable. Type 3 analyses were included in meta-analyses with caution, and post-hoc within-trial subgroup analyses were considered to be data-driven and were included only under exceptional circumstances.

Most commonly in the guideline, the term 'subgroup analysis' refers to between-study comparisons.

Subgroup analyses were carried out in order to investigate heterogeneity or to investigate prespecified features.

The following general pre-specified factors were proposed for subgroup analyses:

- Age (below 60, 60 to 80, over 80 years)
- BMI (below 18, 18 to 25, 25 to 35, over 35 kg/m^2)
- Type of surgery (elective/emergency)
- Spontaneous breathing/ventilated patients
- ASA grade (I to II and III and over)
- Grade of surgery (see NICE preoperative tests guideline)
- Duration of anaesthesia (less than 30 minutes; 30 to 60 minutes; over 1hour)

Subgroup analyses specific to each review were also carried out.

Sensitivity analyses

Sensitivity analyses were carried out to investigate assumptions within the analyses. These included the following:

- Methodological quality
- Fixed effects model
- Other features specific to each review.

In terms of methodological quality, we paid particular attention to allocation concealment, loss to follow-up and baseline comparability. We did not include studies with more than 50% loss to follow-up in the analyses. Otherwise we carried out sensitivity analyses on studies that had between 20 and 50% withdrawals or protocol deviations in any group (that were eliminated from the study's analyses). Where quasi-randomised studies (e.g. sequence generation by alternate allocation or date of birth) represented the only evidence, they were downgraded accordingly.

The other methodological factor considered was the comparability of the core temperature at baseline across groups. If there was a significant temperature difference at baseline, we considered how similar it was to the effect size. Where the difference in baseline was 20% or more of the mean difference between interventions at a particular perioperative time, we excluded the outcome for that study. Other significant baseline differences (e.g. duration of surgery) were considered for importance by the GDG.

Significance: sometimes the effect was statistically significant, but small in size. Therefore, the GDG decided what was a clinically important difference for a particular outcome. For the primary outcome of core temperature, the GDG decided on two ranges of clinical importance: below 36.0°C, a difference between intervention and control of 0.2°C or more was considered important; above 36.0°C, a difference of 0.5°C was clinically significant.

Some meta-analyses gave pooled summary statistics close to the null value. Where the confidence interval was narrow, we considered this to be 'evidence for little difference' between interventions and the approach became similar to that of an equivalence trial (Alderson 2004). Where the confidence interval was wide, there was considered to be insufficient information to determine if there was a difference between interventions. For most outcomes, the GDG judged what constituted a wide confidence interval; if there was any doubt, they decided there was uncertainty. For core temperature, a confidence interval of between 0.5 and 1.0°C was defined as 'fairly wide' and one more than 1.0°C as 'wide'.

II. For cohort studies (risk factor reviews)

Cohort studies in the risk factor reviews were included, either if they kept known confounders constant and investigated another factor, or if they carried out multivariate regression analysis. Studies that only carried out univariate analyses were not considered further.

The principle of regression analysis is to assume that the outcome being measured depends on contributions from a number of risk factors. For example, for a continuous outcome, an example of a regression equation is:

$$y = a + b_1x_1 + b_2x_2 + b_3x_3 + \ldots$$

where b_1, b_2, b_3, etc are the partial regression coefficients; b_1 represents the amount y increases on average if we increase x_1 by 1 unit and keep all the other x's the same. Often these coefficients are reported as standardised coefficients, designated ß, which means the b coefficients are standardised so that they have variances of 1 (this is done by subtracting the mean (a) and dividing each b by the standard deviation of its x). $ß_1$ represents the change in y (in standard deviation units) that results from a change of one standard deviation in x_1 if all the other x's are kept constant.

For dichotomous outcomes, logistic regression is used, in which the probability of an event occurring is considered. This is defined by:

$$\text{Prob(event)} = \frac{1}{1+e^{-z}}$$

where z is $b_0 + b_1x_1 + b_2x_2 + ...$

The logistic regression equation is more usually rearranged into a linear form by converting the probability into a log odds or logit.

$$\log [\text{Prob(event)}/\text{Prob(no event)}] = b_0 + b_1x_1 + b_2x_2 + \ldots b_Px_P$$

This produces a relationship similar to that for multiple regression, except that now each one-unit change in a predictor is associated with a change in log odds rather than the response directly. This is more difficult to interpret and is best explained by an example:

Consider an equation, log [p(IPH)/p(no IPH)] = -4.353 + 0.038 age

If b is the logistic regression coefficient for *age*, then exp(b) is the odds ratio corresponding to a one unit change in age. For example for age=a,

$$\text{odds(IPH|age=a)} = \exp(-4.353 + 0.038\ a)$$

while for age=a+1

$$\text{odds(IPH|age=a+1)} = \exp(-4.353 + 0.038\ (a+1))$$

Dividing one equation by the other gives:

$$\frac{\text{odds(IPH|age=a+1)}}{\text{odds(IPH|age=a)}} = \exp(0.038)$$

which equals 1.0387. Thus, the odds that an older individual has IPH increases 3.87% over that of a younger individual with each year of age. For a 10 year age difference, say, the increase is $\exp(b)^{10}$ [$= 1.0387^{10}$] = 1.46, or a 46% increase.

In multiple regression, these covariates (x's) are assumed to be independent, but we are aware that some risk factors for this review are not. For example, the use of warming devices: these may be given to those patients perceived to be at highest risk in a preventative way.

Some studies suggest there may be an interaction between two or more factors, e.g. the operating room temperature and type of anaesthesia. There are also some parameters that may have a threshold effect, for example, a value above which a further increase makes no additional difference to the outcome. Possible parameters of this type include operating room temperature, duration of anaesthesia/surgery and age.

Continuous variables such as age are dealt with in one of three ways: as a continuous variable, as a dichotomous variable (above or below a particular threshold) and as a categorical variable (e.g. age less than 40; 40 to 64 years; 65 years and over). For categorical variables, the usual approach in regression analyses is to compare the upper sets of values with the lowest category.

Another feature to take into consideration for continuous variables is their range. For example, a narrow range of operation times may mean that the analysis concludes, possibly erroneously, that the duration of surgery is not an important risk factor for IPH.

Where possible, the odds ratios relating to each factor were extracted for dichotomous outcomes (and the standardised regression coefficients for continuous outcomes), with their 95% confidence intervals, in order to determine the contribution from each risk factor to the overall odds ratio (or mean) for the comparison of those with hypothermia versus those without.

Meta-analysis, where appropriate, was carried out on results from two or more studies. Combination of studies in a meta-analysis was based on the following principles:

i) Studies should not be separated by definition of hypothermia (less than 36.0°C; less than 35.5°C; less than 35.0°C).
ii) Results from cohort studies should not be combined with those from case control studies, but cohort studies and RCTs may be combined (but as subgroups in the analysis).
iii) Cohort studies should be confined to those in which there is a multivariate analysis or

comparability at baseline.

If there was heterogeneity, subgroup analyses were to be based on the following:

- Different definitions of hypothermia (<36.0, <35.5, <35.0°C)
- Type of study design (RCT, cohort)
- Theatre temperature (22°C and above, below 22°C)
- Duration of anaesthesia (shorter than 1 hour, 1 hour and above)
- Type of anaesthesia (general, regional, combined)
- Magnitude of surgery (major, intermediate, minor).

Sensitivity analyses were to be carried out to examine the assumption of a fixed effects model.

GENERAL APPROACH TO REVIEWING

The clinical effectiveness reviews seek to determine answers to the following questions, which were investigated using the bulleted comparisons:

- Does the intervention work? (and is it harmful):
  - Direct comparisons of intervention with usual care/placebo;
- Is there a dose/setting effect?
  - Direct dose/setting comparisons
  - Subgroup analyses (across trials) of intervention versus usual care/placebo by dose/setting;
- Is the duration of treatment important?
  - Direct duration comparisons
  - Subgroup analyses of intervention versus usual care/placebo by duration;
- Is the intervention better than another treatment?
  - Direct comparisons
  - Subgroup analyses of intervention versus usual care/placebo by type of intervention;
- Is the intervention useful as an adjunct to another treatment?
  - Direct comparisons (A + B versus B alone);
- Does an intervention given in one phase work as an adjunct to the intervention in another phase?
  - Direct comparisons
  - Subgroup analyses of intervention versus usual care/placebo by phase;
- Are there (pre-specified) subgroups of patients for whom the intervention is more effective?
  - E.g. older patients
  - Subgroup analyses: preferably within trials (stratification then randomisation for each subgroup) or across trials; less acceptably, within trials.

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We note that the best type of information is from direct comparisons in which two values of the variable considered (e.g. dose 1 and dose 2) are randomised to different groups of patients. However, some useful information can be obtained from between-study subgroup analyses.

GRADING EVIDENCE

We used the GRADE* scheme (Atkins 2004) informally as a guide to assess the quality of the evidence for each outcome using the approach described below, and evidence statements based on these were produced for each review.

The procedure adopted when using GRADE is:

1. A quality rating is assigned, based on the study design: for example, RCTs start as high and observational studies as low.
2. This rating is up or downgraded according to specified criteria: study quality, consistency, directness, preciseness and reporting bias. These criteria are detailed below. Criteria are given a downgrade mark of -1 or -2 depending on the severity of the limitations.
3. The downgrade/upgrade marks are then summed and the quality rating revised. For example, a decrease of -2 points for an RCT would result in a rating of 'low'.
4. Wherever possible, reasoning was explained for the downgrade marks.

Study quality

Study quality was assessed against standard criteria, depending on the study design. For randomised trials, we took into account the adequacy of allocation concealment, loss to follow-up and comparability at baseline, particularly of the core temperature. If the evidence was a meta-analysis of several studies, we took into consideration the proportion and weighting of poor quality studies, and in some instances carried out sensitivity analyses disregarding these studies and giving a separate rating for the new meta-analysis.

Consistency

When several RCTs have widely differing estimates of treatment effect (heterogeneity or variability in results) the results are regarded as inconsistent. We defined this by a p-value for heterogeneity less than 0.1 or an I^2 value more than 50%. Where this was the case, we gave a downgrade mark of -1. Where possible, we carried out predefined subgroup analyses to investigate heterogeneity and reported these results separately.

Directness

Directness refers to the extent to which the population, interventions, comparisons and outcome measures are similar to those defined in the inclusion criteria for the reviews. Indirectness is only relevant if there is a compelling reason to expect important differences in the size of the effect. For example, many interventions have more or less the same relative

* GRADE – Grading of Recommendations Assessment, Development and Evaluation

effects across patient groups, so extrapolation is possible and reasonable. There were two main types of indirectness found in the studies:

- Indirect populations, such as pregnant women, post-bypass patients and those receiving anaesthesia but not surgery were regarded as indirect populations and their evidence quality downgraded accordingly.
- Studies using surrogate outcomes generally provide less direct evidence than those using outcomes that are important to people. In this category were bacterial colony counts instead of rates of infection in the adverse effects review and change from baseline temperatures.

Preciseness

This is a rather subjective, but nevertheless important category. Evidence is considered to be imprecise if:

- The sample size is small. This is a subjective measure and is more important in a single study. We decided not to use the results from power calculations to determine if a study was 'small', mainly because some studies suggested very small sample sizes would power the study. This would be inconsistent with the principles of true randomisation. Instead we used the rule of thumb that if the study had less than 20 patients, this was too small and if less than 50 patients the evidence was weak. The rationale for this was that below 25 patients per arm, assumptions about normal distributions become much less valid.
- There are sparse data (only a few events and they are uninformative).
- The confidence intervals are sufficiently wide that the effect estimate is consistent with both important harms and important benefits, and would lead to conflicting recommendations. This category requires the GDG to decide what are important harms and benefits for that outcome measure. For core temperature, we defined a confidence interval of between 0.5 and 1.0°C as 'fairly wide' and one more than 1.0°C as 'wide'. Where the confidence intervals were wide, we gave a downgrade mark of -2.

Reporting bias

Reporting bias occurs in two main ways:

- Publication bias, in which papers are more likely to be published if their results are statistically significant. The existence of publication bias in the studies in a meta-analysis can be investigated in a limited way using funnel plots, in which the standard error is plotted against the log odds ratio, the log relative risk or the mean difference. Asymmetry about the summary statistic effect for the meta-analysis is indicative of reporting bias. This method is usually only useful when there are at least 5 studies. Industry sponsored studies are also regarded as potentially biased.

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- Outcome bias, in which authors do not report some outcomes (probably because they have non-significant results), even though they say in the methods section that they have measured them.

Evidence Statements

The GRADE approach was used to help devise evidence statements, which were based on the scheme in Table 2.

Table 2: Evidence statements

Description	Quality		Quantity
Good evidence	Good quality	AND	Large amount of data/meta-analysis
Moderate evidence	OK quality	AND	Reasonable amount
Weak evidence	Poor quality	OR	Not much evidence; trial size less than 50 patients
Insufficient evidence	Biased/flawed	OR	Not enough evidence to judge: trial size less than 20 patients or wide confidence interval

5.3 Cost effectiveness methods

Health economic evidence is useful in guideline development as it assesses the costs and benefits of alternative courses of action which could be recommended within the guideline. Cost-effectiveness evidence can be used to determine whether a particular recommendation would result in the efficient use of NHS resources by considering whether it achieves additional health gain at an acceptable level of cost. Whilst cost-effectiveness was an important consideration for all recommendations made within the guideline, one area was identified as being a priority area for which cost-effectiveness evidence would have particular importance for informing recommendations. This was identified by the health economist in conjunction with the GDG after consideration of the importance of each clinical question in terms of the number of patients likely to be affected and the impact on costs and health outcomes for those patients.

The use of warming mechanisms and pharmacological interventions to prevent IPH was considered to be a high priority area for economic evaluation for the following reasons. Firstly, the use of these interventions in a large number of surgical patients would have significant implications for the use of NHS resources, so it was necessary to determine which patients are at sufficient risk of IPH to make preventative methods worthwhile. Secondly, preventing the adverse consequences of hypothermia would have significant benefits for patients and

would also reduce the amount of NHS resources used in treating hypothermia and managing the adverse consequences of hypothermia.

5.3.1 Economic literature review

The aim of the economic literature review was to identify published economic analyses which could be used to inform recommendations in any of the areas covered by the guideline.

Types of studies

The types of studies included in the review were trial or model based economic evaluations including cost-effectiveness analyses, cost-utility analyses and cost-benefit analyses. Cost-minimisation studies were excluded except where therapeutic equivalence had been demonstrated. Partial economic evaluations in which only a few of the relevant costs and benefits had been assessed were excluded as they were not deemed to be too limited to be used to inform recommendations.

Outcomes

The outcomes assessed by the review were: cost per QALY; cost per LY; cost per correct diagnosis; cost per unit of clinical effect; cost-benefit ratio; net benefit.

Search strategy for identification of studies

An economic filter was applied to the broad search used to identify efficacy evidence. This identified 1095 titles which were sifted by a health economist. No relevant economic evaluations which could be used to inform recommendations were identified from this search.

5.3.2 Cost-effectiveness modelling

As no published economic evidence had been identified by the literature review, it was necessary to carry out a new economic analysis to inform recommendations. The health economist decided, in conjunction with the GDG, that any new economic analysis should focus on the cost-effectiveness of strategies to prevent hypothermia, as this was an area for which cost-effectiveness evidence would have particular importance for informing recommendations.

For those clinical questions not prioritised for economic analysis, the GDG considered the likely cost-effectiveness of associated recommendations by making a qualitative judgement on the likely balance of costs, health benefits and any potential harms.

Whilst a large number of warming mechanisms and pharmacological interventions have been included in the clinical effectiveness reviews, it was decided that only those interventions with acceptable evidence of clinical effectiveness should be evaluated for cost-effectiveness. An economic model was developed to estimate the incremental cost and benefit of several

strategies to prevent IPH compared to usual care. In the economic model benefits were measured in terms of the quality-adjusted life-years (QALYs) gained and cost were assessed from an NHS and personal social services perspective. The net present value of future costs and benefits were discounted at 3.5% (NICE 2004).

The GDG considered the incremental cost per QALY for each strategy compared to usual care. The incremental QALY is the balance of the QALY gain achieved from preventing IPH and its adverse consequences and any QALY loss due to adverse effects of the intervention. The incremental cost is the balance of cost savings from preventing IPH and its adverse consequences and the cost of providing the intervention. Where the strategy was more effective and less costly than usual care it was said to "dominate" usual care and was considered to be a cost-effective strategy. Where one strategy was more effective but also more costly than usual care, the incremental cost per QALY was estimated and this was compared to a cost-effectiveness threshold of £20,000 to £30,000 per QALY in line with the principles laid out in the NICE Guidelines Manual (NICE 2007). Where several strategies were found to be cost-effective compared to usual care it was necessary to determine which would result in the most cost-effective use of NHS resources. For this the GDG estimated the incremental net benefit (INB) of each strategy compared to usual care. The INB is the monetary value of a strategy compared to an alternative for a specific cost-effectiveness threshold and is calculated as follows when using a threshold of £20,000:

INB = (incremental QALY gain compared to usual care)*£20,000
- (incremental cost compared to usual care)

Strategies with a positive INB are cost-effective compared to the alternative and the strategy with the highest INB is the optimal strategy. The cost-effectiveness model was used to estimate the optimal strategy for various patient scenarios and this was used by the GDG to inform recommendations.

Further details on the economic model are given in Chapter 13 but the following general principles were followed:

- Modelling was carried out using the best available evidence and according to the NICE reference case for economic evaluations (NICE 2004).
- Assumptions made in the model have been described explicitly. The validity of these assumptions was discussed with the GDG during the development of the model and the interpretation of the cost-effectiveness results.
- The importance of model assumptions was examined through univariate sensitivity analysis.
- Parameter uncertainty was explored by carrying out a probabilistic sensitivity analysis (PSA).

- The variation in cost-effectiveness across the population covered by the guideline was explored by estimating the cost-effectiveness for various clinical scenarios which capture the variation in three factors: risk of IPH, risk of the adverse consequences of IPH and cost and QALY impact of adverse consequences.
- Limitations of the analysis are explicitly discussed alongside the cost-effectiveness results.

Identifying evidence on the consequences of IPH

In order to estimate the cost-effectiveness of interventions to prevent IPH, it was necessary to quantify the adverse impact of IPH on resource use and health related quality of life (HRQoL). Several adverse consequences of IPH, such as increased blood loss, morbid cardiac events and surgical wound infection, had been identified during scoping and these were expected to have an important impact on costs and HRQoL. It was necessary to quantify the relationship between IPH and these consequences in order to estimate the number of adverse consequences that can be prevented by interventions to prevent IPH. A rapid literature review was carried out to identify data which could be used to inform the health economic modelling. The aim of this review was to determine the rate of adverse health outcomes in patients who are hypothermic compared to patients who are normothermic. The methods and results of this review are given in section 8 along with a description of how the data was used to inform the economic modelling.

5.4 Submission of evidence

No formal request was made for submission of clinical effectiveness evidence. In order to secure data that enabled economic modelling of the equipment used to maintain patient core temperature throughout the perioperative pathway, companies marketing warming devices identified from the clinical effectiveness literature were asked to submit the costs for these devices. This information enabled health economic modelling to underpin recommendations made by the GDG.

5.5 Formulating recommendations and determining key recommendations

EVIDENCE TO RECOMMENDATIONS

The GDG considered the combined evidence from each of the reviews in drafting the recommendations. This included consideration of all the clinical and cost effectiveness evidence; an indication of the factors the GDG took into account, including the balance between benefits and harms; the GDG's reasoning and conclusions, and, where relevant, the level of agreement amongst the group.

An evidence to recommendations chapter has been produced, summarising the evidence, describing GDG consensus discussions and detailing how the GDG interpreted the evidence,

and how this led to the recommendations. The evidence to recommendations chapter illustrates the linear relationship between published clinical and cost effective evidence and recommendation for clinical practice.

KEY RECOMMENDATIONS

Methodology

There are generally three main methods reported for developing consensus. These are Delphi, consensus development panels and nominal group processes (Bowling 2002). The nominal group technique (NGT) was originally developed by Delbecq et al (1971) as an organisational planning tool. The methodology allows individuals to work in the presence of others, but verbal interaction is prevented, enabling consensus to be developed without the social pressures normally exerted through open dialogue (Zastrow and Navarre 1977). Individual ideas are shared within the group, with facilitated discussion enabling the group to see how individuals are expressing their ideas. Normal practice is for the facilitator to then ask the group to prioritise, with aggregated rankings recorded. This methodology works extremely well towards the end of guideline development, particularly in relation to developing consensus agreement.

The GDG worked together effectively throughout the 14 month development period and had become a mature working group. Individuals within the group were able to express their views relating to key recommendations within a social setting (GDG meetings). This was important for the group, who were able to use this experience and the content of discussion to then go into a round of voting to move agreed recommendations into a potential top 10 list, which reflected the key priorities for the guideline. Iteration is usual within consensus methodology, and a second round of voting is sometimes necessary in order to gain full consensus within the group.

Process

The GDG was asked to vote on key recommendations by secret email ballot using an Excel spreadsheet. This incorporated the full list of recommendations, and votes were allocated to the group in order to try to determine the key priorities for the guideline. Developing consensus through validated instruments is important in ensuring that the final list of up to ten key recommendations fully reflects the group as a whole. This enables all constituent members of the group to have equal weighting of opinion with the process moving individual opinion to a consensus group position. Typically, NGT works well for small groups, with 12 to 15 people widely acknowledged in the literature as the maximum number of people involved in this process.

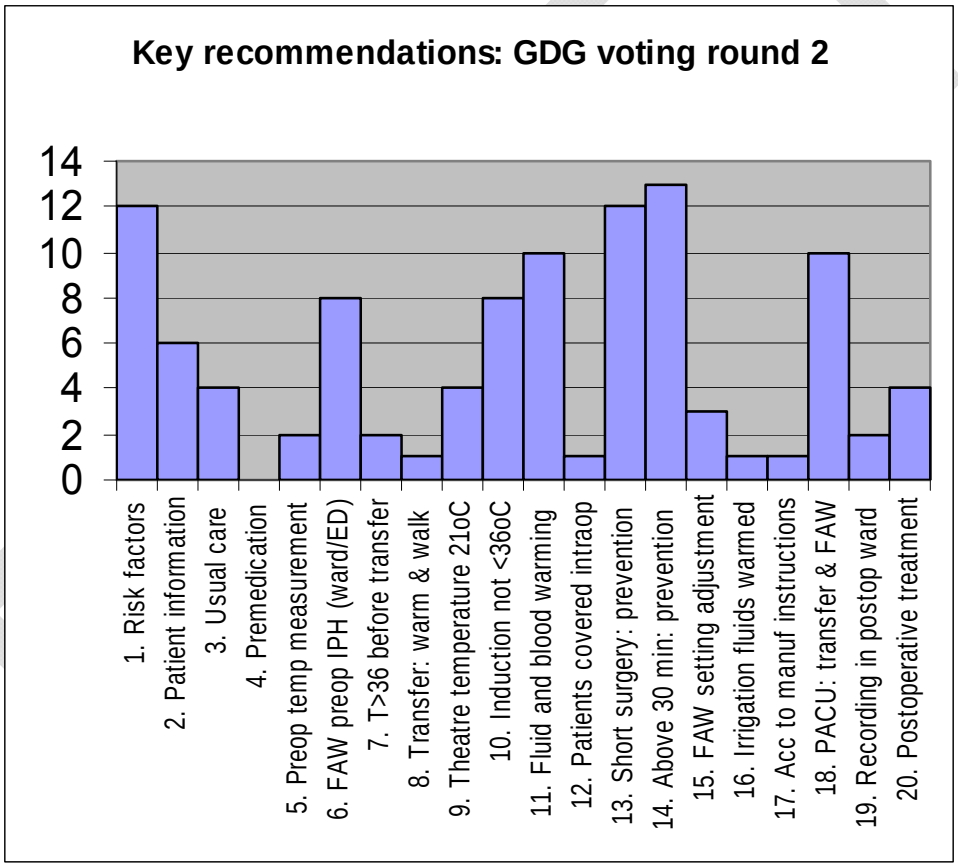
Results in round 1: 12 GDG members voted (92%), providing their 8 key recommendations as priorities for implementation. What quickly emerged as the group were voting was a lack of

'buy in' to the final wording of recommendations. We received feedback on the possibility of changing wording, removing ambiguity and developing greater consistency across the recommendations. Whilst it would have been possible to present a graphical representation of the 22 recommendations and how priority votes were allocated, the technical team felt that this round had to be voided. The importance of GDG members feeling that they owned the recommendations, were happy with final wording, style and content determined the need to amend recommendations as presented in Round 1. This iterative process reduced the number of recommendations to 20, enabling the technical team to fully integrate feedback provided by the GDG and from an expert medical editor. This produced in effect a second round of voting.

Results in Round 2:

13 GDG members voted (100%). Results are seen below in table 1.

Table 1.



All recommendations with more than 50% of the vote (n=7) were selected automatically as key recommendations and therefore priorities for implementation. An eighth recommendation with 46% of the GDG vote (n=6) had clear water between itself and other recommendations that had received GDG votes, with 4 votes being the next most popular. A further iteration and refinement to the final list of key recommendations meant that the technical team requested voting members' opinion on whether this should be added to the other seven key

recommendations. Feedback was received from 10 voting members of the group (77%) which strongly supported it's inclusion in the final list of key recommendations.

Summary

The NGT works well in developing consensus opinion, with iteration and feedback enabling the group to determine the 8 key recommendations for effective implementation of this guideline. The selected recommendations represent the heart of the guideline and focus the reader's attention onto key parts of the perioperative pathway. Having circulated the final list of recommendations, a sense of integrity to the process and GDG satisfaction quickly emerged in feedback provided.

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6 PHYSIOLOGY OF IPH

Clinical question:
What are the mechanisms and underlying physiology that cause inadvertent perioperative hypothermia

Introduction and context

Inadvertent perioperative hypothermia (IPH) is a recognised and common side effect occurring during surgery. IPH is a recognised side-effect of general and regional anaesthesia when normal thermoregulation is inhibited. Hypothermia is defined as a core temperature less than 36°C (96.8°F). It is not unusual for patient core temperatures to drop to less than 35°C within the first 30 to 40 minutes of surgery and if not managed intra-operatively, many of these are likely to be hypothermic on admission to the recovery ward. Approximately 6 million patients undergo surgery in England each year, so the burden of related complications is likely to be significant.

Hypothermia may be found at any stage of the perioperative pathway, from pre-induction through to the postoperative recovery. Reasons for hypothermia include the loss, under anaesthesia, of the behavioural response to cold and the impairment of thermoregulatory heat preserving mechanisms. Further to this are:

- Anaesthetic-induced peripheral vasodilation (with associated heat loss) means that patients can often get cold while waiting for surgery
- Exposure of the body during preparation for surgery
- Fluid deprivation as part of the fasting regime before induction of general anaesthesia (large variations in current practice from 2 hours to more than 12 hours), often resulting in patients being dry and poorly perfused
- Impaired heat distribution which can be further complicated by the lack of warming of intravenous solutions.

Definition of perioperative hypothermia

For the purpose of this guideline, the definition of hypothermia is a core temperature less than 36.0°C.

Selection criteria

The selection criteria for this narrative review focussed on analysing relevant literature related to thermoregulation and heat balance (the aetiology of inadvertent hypothermia). The purpose of the review is to provide context for the GDG relating to the causes and impact of hypothermia. It contextualises hypothermia within the perioperative patient journey/ experience, and recognises IPH as an adverse event.

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Types of studies

Published literature on related physiology and thermoregulation was included. This resulted in an explosion search strategy, and during sifting it was clear that once a relatively small number (10 to 15) of seminal papers had been identified, that saturation of data was achieved. For this purpose, a pragmatic cut-off was established, once seminal work had been cross-checked and assurances reached within the GDG that relevant work was included.

Search strategy for identification of the literature

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additional databases were not searched for this review.

Methodology for this review

Applying the quality assurance principles advocated by Oxman et al (1994), a valid review article can provide the best possible source of information that can lay a foundation for clinical decisions to be made. There is an argument that focused narrative reviews for individual outcomes, in this case the development of inadvertent hypothermia, are more likely to provide valid results that are useful for clinicians.

Physiological concepts in temperature control

Thermoregulation

The human body has been described as having two main areas that relate to temperature control; a core thermal compartment and a peripheral compartment. Within the thermal compartment, tissues are usually well perfused and temperature is typically constant, maintained by neuro-thermoregulatory mechanisms. The peripheral compartment comprises arms and legs, and typically peripheral temperature can be 2 to 4˚C lower than core thermal temperature.

Temperature is regulated by central structures, receiving information from the skin surface, neuroaxis and deep tissues. Control is maintained through reference temperatures for each regulatory response. Homeothermy is defined by the Thermal Physiology Commission Sciences as ‘a pattern of temperature regulation in which the cyclic variation in core temperature, either nychthermally or seasonal, is maintained within arbitrary limits despite much larger variations in ambient temperature’. The concept of homeothermy, is dependent on the body sensing body temperature and appropriately driving the mechanisms controlling heat loss and gain in order to maintain normal temperature. This has been described as a closed-loop system. The physiological principle is about balancing heat gains with heat losses, operating always within a normal ambient range, ideally without metabolic expenditure through peripheral vaso-dilation/constriction.

Heat gains

These are gains that occur independently of central thermoregulation processes, with muscular exercise being the most common source of metabolic heat. Light walking increases metabolic rate above basal and severe exercise can produce as much as a twenty fold increase, known as obligatory heat gains. Facultive heat gains are produced to restore thermal imbalance, and can be classified as shivering and non-shivering. Shivering can produce a four to six fold increase in heat production, with 80% of heat produced in this way retained by the body as compared with 50% for voluntary exercise. Non-shivering is evident in other physiological responses. A good example of this is the conversion of brown adipose tissue in neonates. This can produce a two to three fold increase in metabolic rate.

Heat losses

Heat is lost from the body only at points of contact with the environment, this being skin and the respiratory tract. At rest, 75% is lost through convection, conduction and radiation. Of these convection is the main cause of heat loss. The remaining 25% is lost through sweating and through the respiratory tract. Sweating is the major cause of heat loss under thermoregulatory control.

Normothermia

Body temperature is usually maintained somewhere within the range of 36.0˚C and 37.5˚C (Guyton 1996). Circadian influences within this range typically see the body's highest core temperature in late afternoon (5 to 6pm) and at its lowest core temperature early in the morning (2am).

Preoperative core temperature target range

For the purpose of this guideline, it is important to establish what normal temperature range is. This in effect becomes a target range for any active warming of patients undergoing anaesthesia and operative procedures. Mitchell and Kennedy (2001) in a prospective study obtained sublingual temperatures from adults having elective surgery (n=446). Preoperative core temperatures ranged from 35.7˚C to 37.8˚C; mean temperature was reported as 36.5˚C (SD 0.4). This is consistent with the baseline temperature recorded in the trial evidence used throughout the IPH guideline, reporting mean temperature in the control arm of trials as 36.5˚C. Recognising the standard error reported in devices used to record patient temperature, supported by this evidence, for the purpose of this guideline, normothermia is defined as 36.5˚C to 37.5˚C

IPH Clinical Guideline normothermia range

36.5˚C to 37.5˚C

The effect of general anaesthesia

A high proportion of adult patients receiving general anaesthesia prior to surgery will experience significant heat loss, developing a clinical hypothermia, defined in this clinical guideline as patient core temperature that is lower than 36.0˚C. Patients undergoing surgery will have a typical core temperature heat loss of between 1 to 3˚C (Sessler and colleagues). This heat loss is dependent on a number of variables, of which length (dose) of anaesthesia and amount of body exposure during surgery are central factors. Sessler (2000) over many years of research and clinical experience was able to demonstrate a pattern which is characteristic of normal physiological responses in the surgical patient.

Mechanism of heat loss

General anaesthesia promotes vasodilation by reducing the vasoconstriction threshold to well below core temperature, inhibiting central nervous system mediation (neuro-thermoregulation responses). This induces peripheral vasodilation. The effect of this is to allow fairly rapid heat loss from the peripheries because it is no longer controlled by the protected thermal compartment of the body. The net effect is that an artificially high peripheral temperature may be recorded, which does not usually correlate to patient core temperature, and is not dependent on ambient environmental temperature. That said, if patients are exposed to cooler air temperatures (because of body exposure due to surgical procedures), hypothermia will inevitably worsen.

Pattern of heat loss

During the first hour of any surgical procedure (including induction of anaesthesia), core temperature will fall by 1 to 1.5˚C. This steep fall in core temperature in the first hour is followed by a slower, linear decrease in core temperature during the next 2 to 3 hours. Core temperature then plateaus (see Figure 1). The aetiology of this is not fully understood, but it appears to be a combination of pharmokinetic actions produced by anaesthetic and sedative drugs, reduced metabolism and changes to the body's normal control (autonomic) of both vasodilation and vasoconstriction in normal cardiac functioning.

Figure 1. Typical pattern of hypothermia during general anaesthetic (characterised by three phases as seen in the diagram below).

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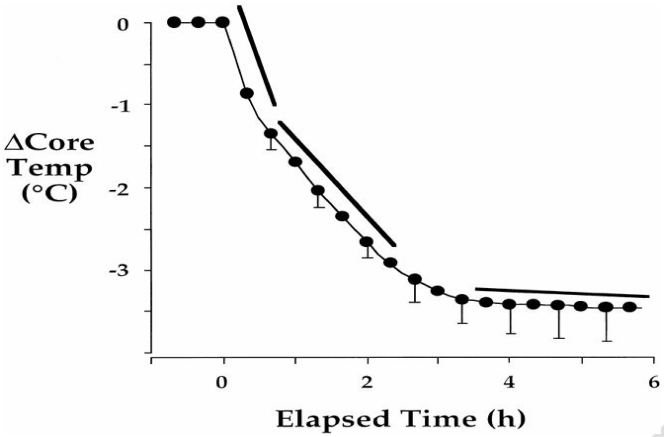


Kurz A, Sessler DI, Christenson R, Dechart M (1995). Heat blance and distribution during the core temperature plateau in anaesthetised humans. Anesthesiology 83: 491-9

Anaesthesia inhibits vasoconstriction and shivering far more than it inhibits sweating. The central effects on thermoregulation are that vasoconstriction thresholds fall, with the shivering response inhibited, occurring in both general and regional anaesthesia. In considering both heat loss and heat production, and if we conceptualise this as a continuum, the physiological processes of radiation, convection (air currents in relation to this are particularly important), conduction (from a warmed or cool bed, from warmed or unwarmed intravenous/irrigation fluids) and evaporation all play a role. Given this, the perioperative team need to minimize where possible heat losses identified through radiation, convection, conduction and evaporation.

Understanding normal patterns of heat losses and gains in non-anaesthetised humans is essential if hypothermia is to be avoided as a consequence of anaesthetic and surgical procedures (see Figures 2 and 3).

Figure 2. Patterns of heat losses and gains in non anaesthetised humans

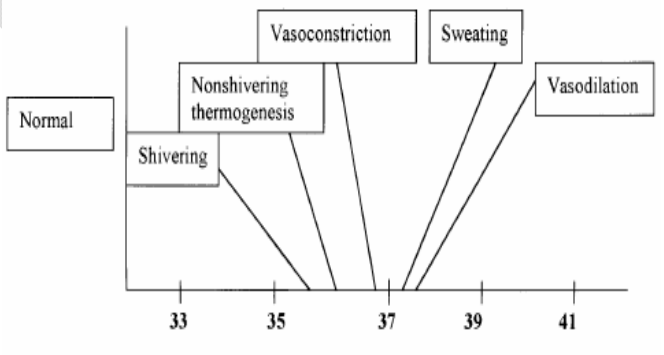
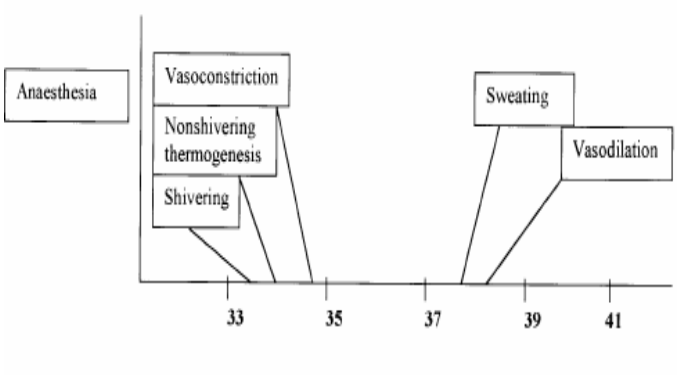


Figure 3. Patterns of heat losses and gains in anaesthetised humans

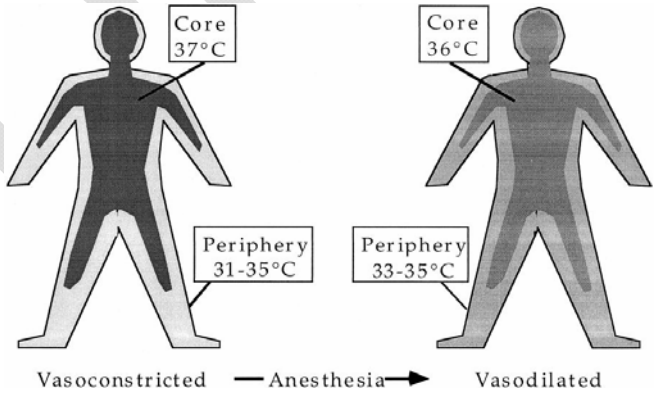


For patients undergoing anaesthesia as part of a surgical procedure, the effect of anaesthesia as seen in Figures 2 and 3 is a disproportionate shift to the left of the temperature scale, with core temperature being much lower when normal body controls, such as vasoconstriction and shivering, commence in order for heat to be gained. This in effect means that patients do not display either physical or physiological signs of heat generation until their core temperature is significantly lower when compared to normal physiology.

Physiological principles of redistribution of heat in anaesthetised patients

Body heat content is not normally distributed evenly. Instead, thermoregulatory vasoconstriction maintains a core-to-peripheral temperature gradient as seen in Figure 4. Induction of general anaesthesia inhibits vasoconstriction, and this allows a core-to-peripheral redistribution of body heat. If periopertaive hypothermia is to be prevented, understanding of this core to peripheral temperature gradient is essential.

Figure 4. Cartoon showing redistribution hypothermia after induction of general anaesthesia



Sessler DI (2000): Temperature monitoring, Anesthesia, 4th edition. Edited by Miller RD. New York, Churchill Livingstone.

The patient response to induction of general and regional anaesthesia

Hypothermia during general anaesthesia develops with a characteristic three-phase pattern (see Figure 1). The initial rapid fall in core temperature after induction of anaesthesia results from an internal redistribution of body heat. Redistribution results because anaesthetic drugs inhibit the tonic vasoconstriction that normally maintains a large core-to-peripheral temperature gradient. As a result, patient core temperature decreases at a rate determined by the difference between heat losses and gains.

When surgical patients become hypothermic (<36.0˚C), physiological triggers initiate thermoregulatory vasoconstriction, which restricts core-to-peripheral flow of heat. Constraint of metabolic heat, in turn, maintains a core temperature plateau (despite continued systemic heat loss), with the normal core-to-peripheral temperature gradient re-established. These mechanisms indicate that alterations in the distribution of body heat contribute more to changes in core temperature than to systemic heat imbalance in most patients. Just as with general anaesthesia, redistribution of body heat is the major initial cause of hypothermia in patients administered spinal or epidural anaesthesia.

The patient response to neuraxial anaesthesia

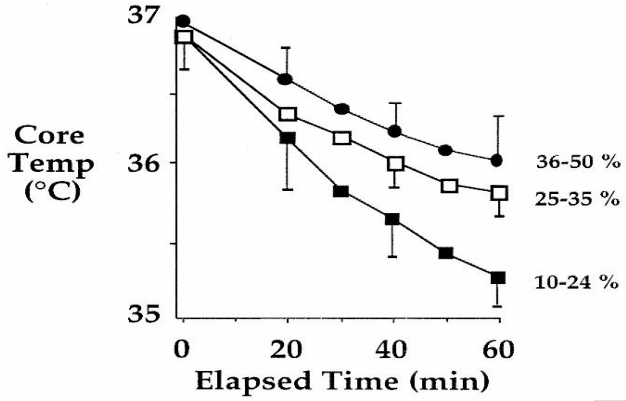
This process of heat redistribution during neuraxial anaesthesia is different, in that it is generally restricted to the lower body (legs). Consequently, redistribution decreases core temperature about half as much when compared with other anaesthesia. As during general anaesthesia, patient core temperature decreases at a rate determined by the difference between heat losses and gains.

The major difference is that this decrease is not discontinued by the physiologically driven response of thermoregulatory vasoconstriction. This is because constriction in the legs is blocked peripherally. This means that for patients with long neuraxial anaesthetic times (major surgery), there is the potential of serious hypothermia.

Slowing of the reduction in patient core temperature to plateau phase

Patient core temperature decreases at a rate determined by the difference between heat losses and gains. When patients reach a point on this gradient, and thermoregulatory vasoconstriction has been triggered, core-to-peripheral flow of heat continues. Metabolic heat production maintains a core temperature plateau (despite continued systemic heat loss), eventually re-establishing the normal core-to-peripheral temperature gradient. This physiologically driven process indicates that alterations in the distribution of body heat contribute more to changes in patient core temperature than to systemic heat imbalance. The perioperative team should note that residual anaesthesia and opioids given for treatment of postoperative pain are likely decrease the effectiveness of these responses. Return to normothermia (defined in this guideline as 36.5˚C to 37.5˚C) often needs considerable postoperative time (reported as between two and five hours), depending on the degree of hypothermia and the comorbidity profile of the patient.

Figure 5. Patient core temperature plateau during anaesthesia



Kurz A, Sessler DI, Christenson R, Dechart M (1995). Heat balance and distribution during the core temperature plateau in anaesthetised humans. Anaesthesiology 83: 491-9

Other reported effects of lowered core temperature in anaesthetised patients

- Platelet *function* is impaired (local phenomenon) with ↓ release of thromboxane A2
- Fibrinolytic activity is unaffected (clot formation affected rather than ↑ lysis)
- Standard coagulation tests remain unchanged at 37°C, but are prolonged when performed at a reduced patient temperature

Summary

The control of normal body temperature is a well established, and changes to body temperature have been discussed in this narrative review. Whilst a normal range exists for body temperature, adult patients being prepared for surgery can experience largely downward trends within this normal range, which is then compounded by induction of anaesthesia. Typical patterns following induction of anaesthesia see a dramatic fall to core temperature in the first hour of anaesthesia, with as much as 1.5°C lost to core temperature, and the body's normal thermoregulatory response to initiating heat gain impaired due to anaesthesia. Physiological principles discussed in this review are well established and supported by trials in anaesthetised and non-anaesthetised humans. This review and its findings provide an essential foundation for the IPH clinical guideline. Normal body temperature range for the purpose of this guideline is 36.5°C to 37.5°C, enabling all preventive measures (active warming) to aim to restore patient core temperature to at least 36.5°C.

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7 RISK FACTORS FOR INADVERTENT PERIOPERATIVE HYPOTHERMIA

Clinical question

What risk factors contribute to perioperative hypothermia?

Background

Perioperative hypothermia develops in three characteristic phases: a rapid decrease in core temperature in the first hour due to core to peripheral redistribution of body heat – which is mediated by the use of volatile anaesthetic agents; a slow linear decrease in core temperature due to heat loss exceeding metabolic heat gain; a plateau in temperature in which vasoconstriction decreases heat loss from the skin. The pattern of development of these phases will be influenced by risk factors.

Numerous factors contribute to the risk of inadvertent perioperative hypothermia. Risk is perceived to depend on patient characteristics (such as age or BMI); surgery factors (such as magnitude of the procedure or whether body cavities are open); anaesthesia factors (such as type or duration of anaesthesia); perioperative pharmacological agents (such as premedication); environmental factors (e.g. theatre temperature) and any preventative measures (such as the use of forced air warming devices). Risk factors are not necessarily independent and combinations of risk factors may be important, for example, patient age may be a relevant factor only for long surgical procedures. Furthermore, for continuous variables, such as age, there may be thresholds above which inadvertent perioperative hypothermia (IPH) is more likely to occur.

It may also be important to distinguish between factors that make the patient more likely to become hypothermic, and those that put the patient at greater risk of prolonged hypothermia and/or at greater risk of complications from hypothermia because of their inability to recover quickly from the hypothermic state. Where possible we will examine the incidence of hypothermia and the rate of recovery.

The purpose of this review is to examine systematically the evidence base to elucidate the variety of factors that contribute to an individual's risk of inadvertent perioperative hypothermia. This will provide a framework for targeting limited resources, if necessary, to those individuals at highest risk.

The risk factors review is split into two: one concerned with hypothermia risks associated with pharmacological agents used perioperatively for any purpose (Section 7.1), and the other

covering all other risk factors (Section 7.2).

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7.1 RISK FACTORS FOR IPH: PHARMACOLOGICAL AGENTS

SELECTION CRITERIA

Types of study design

Pharmacological agents as risk factors should be examined primarily in randomised trials because they are interventions.

Types of intervention

Any pharmacological agent used perioperatively. This includes, but is not restricted to, the following drug classes:

Premedications:

- Alpha$_2$-adrenergic antagonist (e.g. clonidine);
- Benzodiazepines (e.g. midazolam).

Reversal of benzodiazepines:

- Benzodiazepine antagonists (e.g. flumenazil; used to reverse the effects of benzodiazepines and counter the unwanted effects of anaesthetics, in order to speed recovery of motor and cognitive function).

Muscle relaxants:

- Anti-muscarinic drugs (e.g. atropine).

Reversal of muscle relaxants:

- Cholinesterase inhibitor (e.g. physostigmine).

Induction of anaesthesia:

- Barbiturate (e.g. thiopentone);
- N-methyl-D-aspartate (NMDA) receptor antagonist (e.g. ketamine; used for induction of anaesthesia and analgesia).

General anaesthesia drugs:

- General anaesthesia drugs (e.g. halothane, isoflurane, propofol).

Analgesia (for pain control):

- Opioid (e.g. pethidine);
- Other centrally-acting analgesics (e.g. tramadol, nefopam).

Control of nausea:

- Serotonin-receptor antagonist (e.g. dolasetron, ondansetron).

Types of comparison

The following comparisons were to be included:

- Intervention versus placebo / no intervention;
- Intervention 1 + intervention 2 versus intervention 2 alone;
- Drug A versus drug B (both drugs in same class);
- Duration 1 versus duration 2;

- Dose 1 versus dose 2.

It was decided to combine the two types of comparison: (i) intervention versus placebo / no intervention and (ii) intervention 1 + intervention 2 versus intervention 2 alone, and examine this assumption using sensitivity analyses.

Outcomes

Studies were to be included if they reported either core temperature intra- or post-operatively, or the incidence of inadvertent perioperative hypothermia. Studies reporting only the incidence of shivering were excluded.

Stratification and subgroup analyses

We planned to stratify the studies by the following:

- Classes of drugs;
- Perioperative phase of intervention;
- Trauma patients – elective and emergency surgery considered together initially.

The following subgroups were to be considered:

- Type of pharmacological agent;
- Dose;
- Duration intervention given preoperatively.

METHODS OF THE REVIEW

Search strategy for identification of studies

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additional databases were not searched for this review. The search strategies are given in Appendix B.

The titles and abstracts from the search strategy were assessed. Thirty studies met the inclusion criteria for the review. The reference lists of the retrieved studies were inspected for further potential papers, but none were identified. The excluded studies are listed in Appendix E, along with reasons for exclusion.

DESCRIPTION OF STUDIES INCLUDED IN THE REVIEW

30 studies met the inclusion criteria for the review (Alfonsi 1998; Bilotta 2002; Buggy, abstract; Cheong 1998; Crozier 2004; Delauney 1991; De Witte 1995; De Witte 1998; Goto 1999; Grover 2002; Holdcroft 1978; Hong 2005; Horn 1997; Horn 1998; Ikeda 2001; Kelsaka 2006; Kimberger 2007; Kinoshita 2004; Mao 1998; Mathews 2002; Matsukawa 2001; Mizobe 2005; Piper 2002; Piper 2004; Powell 2000; Röhm 2005; Sagir 2007; Stapelfeldt 2005; Toyota 2004; Weinbroum 2001).

Two studies were conducted in the UK (Holdcroft 1978; Powell 2000); 15 were in the rest of Europe; six in Japan; one in Israel; one in Kuwait; one in India; one in Singapore; one in South Korea; one in Taiwan and one in the USA.

Seventeen studies had 50 patients or fewer in each comparison (Alfonsi 1998; Buggy, abstract; Delauney 1991; De Witte 1995; De Witte 1998; Goto 1999; Grover 2002; Holdcroft 1978; Horn 1997; Horn 1998; Ikeda 2001; Kimberger 2007; Kinoshita 2004; Matsukawa 2001; Mizobe 2005; Stapelfeldt 2005; Toyota 2004), one of which had fewer than 20 patients (Mizobe 2005). Six studies had more than 100 patients in total (Cheong 1998: 80 in each arm; Hong 2005: 30, 30 and 29 in the three arms; Mathews 2002: 50 in each of three arms; Piper 2004: 73 to 76 in each of the five arms; Sagir 2007: 40 in each of three arms; Weinbroum 2001: 34 to 50 in each of six arms. Eighteen studies had more than 2 arms, giving a total of 66 comparisons.

Population and details of surgery and anaesthesia

The mean age (where given) ranged across the studies from 28 to 73 years. Toyota (2004) included participants from the age of 13 to 52 years (median around 26 years). From the mean and standard deviation (mean 33 years; SD 13 years for ketamine group; mean 37 years, SD 16 for propofol group), one other RCT may have included some children (Ikeda 2001).

Surgery was carried out under general anaesthesia in 19 studies (Alfonsi 1998; Buggy, abstract; Cheong 1998; Crozier 2004; Delauney 1991; De Witte 1995; De Witte 1998; Goto 1999; Grover 2002; Holdcroft 1978; Horn 1997; Horn 1998; Ikeda 2001; Mathews 2002; Piper 2002; Piper 2004; Powell 2000; Röhm 2005; Stapelfeldt 2005; Toyota 2004; Weinbroum 2001); regional anaesthesia in five studies (Bilotta 2002; Hong 2005; Kelsaka 2006; Kinoshita 2004; Mao 1998; Sagir 2007); mixed general and epidural anaesthesia in one study (Mizobe 2005) and in two studies the anaesthesia type was unclear (Kimberger 2007; Matsukawa 2001).

Anaesthesia duration was more than 1 hour in 12 studies (Cheong 1998; Crozier 2004; De Witte 1998; Ikeda 2001; Kelsaka 2006; Mathews 2002; Piper 2002; Piper 2004; Röhm 2005; Stapelfeldt 2005; Toyota 2004; Weinbroum 2001); less than 1 hour in one study (De Witte 1995), and not stated in 17 studies (Alfonsi 1998; Bilotta 2002; Buggy; Delauney 1991; Goto 1999; Grover 2002; Holdcroft 1978; Hong 2005; Horn 1997; Horn 1998; Kimberger 2007; Kinoshita 2004; Mao 1998; Matsukawa 2001; Mizobe 2005; Powell 2000; Sagir 2007).

The types of surgery in the studies were orthopaedic (Alfonsi 1998; Bilotta 2002; Buggy, abstract; Kelsaka 2006; Toyota 2004); gynaecological (De Witte 1995; Grover 2002; Holdcroft

1978); ENT (Crozier 2004; Horn 1997; Horn 1998); neurosurgical (Kimberger 2007; Stapelfeldt 2005); urological (Mao 1998; Sagir 2007); abdominal (De Witte 1998; Goto 1999; Mizobe 2005); mixed (Cheong 1998; Ikeda 2001; Kinoshita 2004; Mathews 2002; Piper 2002; Piper 2004; Powell 2000; Röhm 2005; Weinbroum 2001) or unclear (Delauney 1991; Matsukawa 2001). There was one indirect study (Hong 2005) in which the patients were undergoing Caesarean section; the study was only considered if there were insufficient data for direct populations.

Surgery lasted less than 30 minutes in one study (Grover 2002); 30 to 60 minutes in 3 studies (De Witte 1998; Hong 2005; Horn 1997); 1 to 3 hours in 11 studies (Alfonsi 1998; Bilotta 2002; Buggy 1997, abstract; Delauney 1991; Horn 1998; Ikeda 2001; Kelsaka 2006; Piper 2002; Piper 2004; Röhm 2005; Weinbroum 2001); over 3 hours in one study (Stapelfeldt 2005) and was not stated in 14 studies (Cheong 1998; Crozier 2004; De Witte 1995; Goto 1999; Holdcroft 1978; Kimberger 2007; Kinoshita 2004; Mao 1998; Mathews 2002; Matsukawa 2001; Mizobe 2005; Powell 2000; Sagir 2007; Toyota 2004).

Ten studies recorded tympanic temperatures, six rectal, six oesophageal, two bladder, three aural canal and two nasopharyngeal.

Risk factors

The following pharmacological agents were examined; where applicable, we have indicated if the anaesthesia is not general, but have analysed the studies together regardless of type of anaesthesia.

A. Premedication:

- Alpha$_2$-adrenergic antagonists:
  - Clonidine: eleven studies (Buggy 1997; Delauney 1991; Horn 1997; Horn 1998; Mizobe 2005; Piper 2000; Piper 2001; Piper 2002; Piper 2004; Stapelfeldt 2005; Mao 1998, regional).
- Benzodiazepines, midazolam:
  - Four studies: (Grover 2002; Toyota 2004); unclear anaesthesia (Kimberger 2007; Matsukawa 2001).

B. Reversal of benzodiazepines:

- Benzodiazepine antagonists:
  - Flumenazil: one study (Weinbroum 2001).

C. Muscle relaxants:

- Anti-muscarinic agents:
  - Atropine: one study (Matsukawa 2001, unclear);

- Glycopyrronium: one study (De Witte 1995).

D. Reversal of muscle relaxants:

- Cholinesterase inhibitor:
  - Physostigmine: two studies (Horn 1998; Röhm 2005).

E. Induction of anaesthesia:

- N-methyl-D-aspartate (NMDA) receptor antagonist:
  - Ketamine: three studies (Ikeda 2001, general; Kinoshita 2004, regional; Sagir 2007, regional).

F. General anaesthesia drugs:

- General anaesthesia drugs:
  - Halothane: one study (Holdcroft 1978);
  - Isoflurane: one study (Sahin 2002);
  - Propofol: one study (Sahin 2002);
  - Xenon: one study (Goto 1999);
  - Nitrous oxide: one study (Goto 1999).

G. Analgesia:

- Opioid:
  - Pethidine: four studies (Horn 1998; Piper 2000, regional; Hong 2005, indirect; Kelsaka 2006);
  - Morphine: one study (Hong 2005, regional, indirect);
  - Remifentanil: one study (Crozier 2004);
  - Alfentanil: one study (Crozier 2004).
- Other centrally-acting analgesics:
  - Tramadol: four studies (Bilotta 2002, regional; De Witte 1998; De Witte 1995; Mathews 2002)
  - Nefopam: three studies (Bilotta 2002, regional; Piper 2004; Röhm 2005).

H. Control of nausea:

- Serotonin-receptor antagonist:
  - Dolasetron: one study (Piper 2002);
  - Ondansetron: two studies (Kelsaka 2006, regional; Powell 2000);
  - Granisetron: one study (Sagir 2007, regional).

Other warming during the studies

Some studies used other methods to warm all the patients:

- Warmed IV fluids (Ikeda 2001; Kelsaka 2006);

- Forced air warming (Crozier 2004).

Two studies gave the patients warmed sheets (Horn 1997; Horn 1998), which is likely to have a negligible warming affect. In the other studies, patients received no active warming (Alfonsi 1998; Bilotta 2002; Buggy 1997; Cheong 1998; Delauney 1991; Goto 1999; Holdcroft 1978; Hong 2005; Kimberger 2007; Kinoshita 2004; Mao 1998; Matsukawa 2001; Mizobe 2005; Piper 2004; Powell 2000; Röhm 2005; Toyota 2004).

Interventions

The comparisons were also separated by the perioperative phase in which the pharmacological agent was given.

A. Premedication

1. Alpha$_2$-adrenergic antagonist (e.g. clonidine; used as a premedication)

Intervention versus placebo / no intervention

Preoperative phase:

- Clonidine versus placebo (Mao 1998, regional; Mizobe 2005, combined general and epidural)

Intraoperative phase:

- Clonidine versus placebo (Buggy 1997; Delauney 1991; Horn 1997; Horn 1998; Piper 2000; Piper 2001; Piper 2002; Piper 2004; Stapelfeldt 2005).

2. Benzodiazepines (e.g. midazolam; used as a premedication)

Intervention versus placebo / no intervention

Preoperative phase:

- Midazolam versus no premedication (Toyota 2004);
- Midazolam versus usual care (Kimberger 2007, unclear);
- Midazolam versus placebo (Matsukawa 2001, unclear).

Intervention 1 + intervention 2 versus intervention 2 alone

Preoperative phase:

- Midazolam plus active warming versus active warming alone (Kimberger 2007, unclear)
- Midazolam plus atropine versus atropine alone (Matsukawa 2001, unclear).

Intraoperative phase:

- Midazolam versus placebo (Grover 2002).

B. Reversal of benzodiazepines

1. Benzodiazepine antagonists

Intervention versus placebo / no intervention

Intraoperative phase:

- Flumenazil versus placebo (Weinbroum 2001).

C. Muscle relaxants

1. Anti-muscarinic agents

Intervention versus placebo / no intervention and

Preoperative phase:

- Atropine versus placebo (Matsukawa 2001, unclear anaesthesia type).

Intervention 1 + intervention 2 versus intervention 2 alone

Preoperative phase:

- Atropine plus midazolam versus midazolam alone (Matsukawa 2001, unclear);
- Glycopyrronium versus placebo (De Witte 1995).

D. Reversal of muscle relaxants

1. Cholinesterase inhibitor

Intervention versus placebo / no intervention

Intraoperative phase:

- Physostigmine versus placebo (Horn 1998; Röhm 2005).

E. Drugs for induction of anaesthesia:

1. N-methyl-D-aspartate (NMDA) receptor antagonist

Intervention versus placebo / no intervention

Intraoperative phase:

- Ketamine versus placebo (Sagir 2007, regional).

Intervention 1 + intervention 2 versus intervention 2 alone

Intraoperative phase

- Ketamine plus granisetron versus granisetron alone (Sagir 2007, regional);
- Ketamine plus propofol versus propofol alone (Kinoshita 2004, regional).

Comparison of two drugs in different classes

Intraoperative phase:

- Ketamine versus propofol (Ikeda 2001).

F. General anaesthesia drugs

Comparison of two drugs in the same class

Intraoperative phase:

- Isoflurane versus propofol (Sahin 2002);
- Xenon versus isoflurane (Goto 1999);
- Nitrous oxide versus isoflurane (Goto 1999).

Different doses of same drug

All phases:

- Halothane 0.5% versus halothane 1% (Holdcroft 1978).

G. Analgesia:

1. Opioid (e.g. pethidine; used for pain control)

Intervention versus placebo / no intervention

Intraoperative phase:

- Pethidine versus placebo (Horn 1998; Piper 2000; Kelsaka 2006, regional).

Intervention 1 + intervention 2 versus intervention 2 alone

Intraoperative phase:

- Morphine plus bupivacaine versus bupivacaine alone (Hong 2005, regional, indirect);
- Pethidine (pethidine) plus bupivacaine versus bupivacaine alone (Hong 2005, regional, indirect).

Comparison of two drugs in the same class (opioids)

Intraoperative phase:

- Pethidine versus morphine (Hong 2005, regional, indirect);
- Remifentanil versus alfentanil (Crozier 2004).

Different doses of same drug

All phases:

- Morphine 0.1mg versus morphine 0.2mg (Hong 2005, regional, indirect).

2. Other centrally-acting analgesics (e.g. tramadol, nefopam; used for pain control)

Intervention versus placebo / no intervention

Preoperative phase

- Tramadol versus placebo (De Witte 1998).

Intraoperative phase

- Nefopam versus placebo (Bilotta 2002, regional; Piper 2004; Röhm 2005)
- Tramadol versus placebo (Bilotta 2002, regional; Mathews 2002).

Intervention 1 + intervention 2 versus intervention 2 alone

Preoperative phase

- Tramadol plus glycopyrronium versus glycopyrronium only (De Witte 1995).

Comparison of two drugs in the same class

Intraoperative phase:

- Nefopam versus tramadol (Bilotta 2002, regional).

Different doses of same drug

Intraoperative phase:

- Nefopam 0.2mg/kg versus nefopam 0.1mg/kg (Piper 2004);
- Nefopam 0.2mg/kg versus nefopam 0.05mg/kg (Piper 2004);
- Nefopam 0.1mg/kg versus nefopam 0.05mg/kg (Piper 2004).

H. Control of nausea:

1. Serotonin-receptor antagonist (e.g. dolasetron, ondansetron)

Intervention versus placebo / no intervention

Intraoperative phase:

- Ondansetron 4mg or 8 mg versus saline control (Powell 2000)
- Dolasetron versus placebo (Piper 2002)
- Granisetron versus placebo (Sagir 2007, regional)
- Ondansetron versus placebo (Kelsaka 2006, regional)

Intervention 1 + intervention 2 versus intervention 2 alone

Intraoperative phase:

- Granisetron plus ketamine versus ketamine alone (Sagir 2007, regional).

METHODOLOGICAL QUALITY

The quality assessment for the included trials is shown in Appendix D. An adequate method of randomisation was reported in six studies (computer generated: Bilotta 2002; De Witte 1998; Kimberger 2007; Matsukawa 2001; Mizobe 2005, table of random numbers; Cheong 1998). The other studies did not state the method of randomisation.

Allocation concealment (variants on the sealed envelopes method) was reported in nine studies (Crozier 2004 (partial); Hong 2005 (partial); Kimberger 2007 (adequate); Mathews 2002 (partial); Mizobe 2005 (partial); Piper 2004 (partial); Powell 2000 (partial); Sagir 2007 (partial); Stapelfeldt 2005 (partial)). Allocation concealment was not reported or unclear in the other studies.

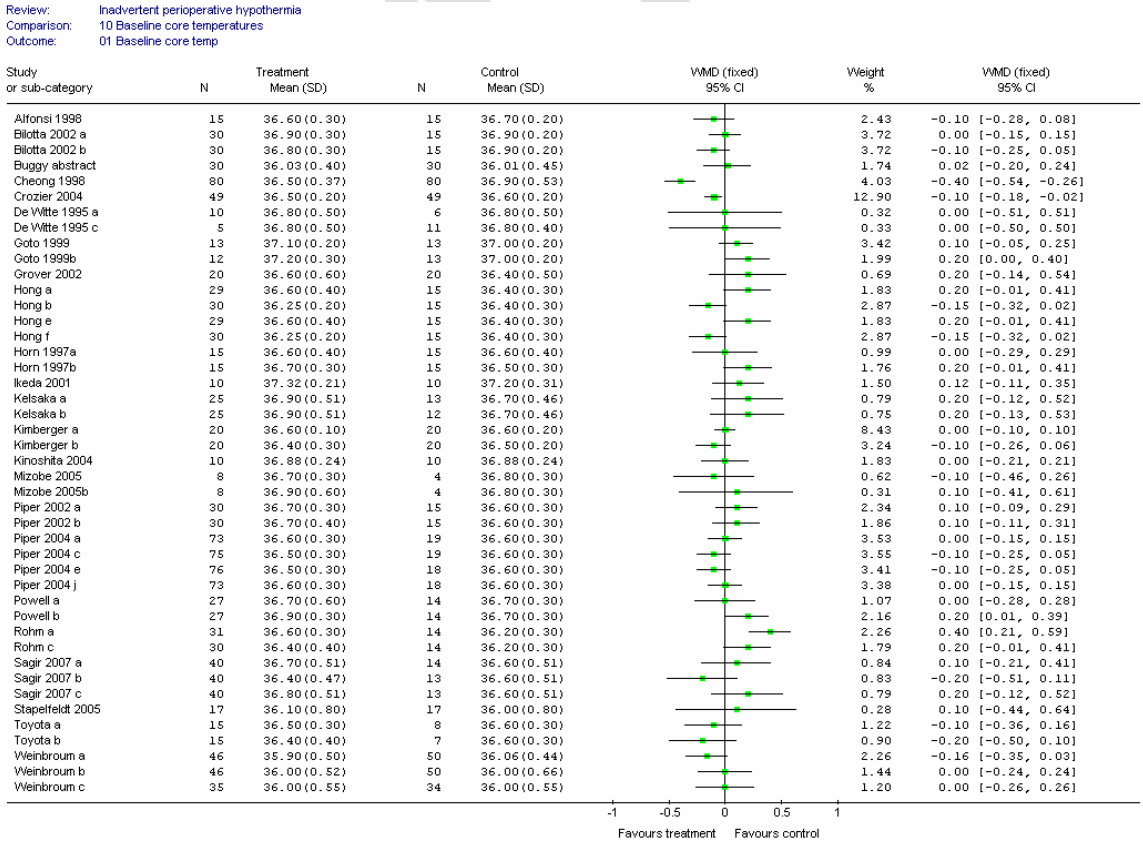
All studies but four reported that the outcome assessors and the patients were blinded to the interventions; blinding was not stated in Goto 1999; Holdcroft 1978; Ikeda 2001; Kinoshita 2004.

Ten studies (Bilotta 2002; Hong 2005; Kelsaka 2006; Kimberger 2007; Piper 2004; Röhm 2005; Sagir 2007; Stapelfeldt 2005; Toyota 2004) described an *a-priori* power calculation. These calculations suggested that the sample size should be 30 patients per group (Bilotta

2002); 27 (Hong 2005); 24 (Kelsaka 2006); 16 (Kimberger 2007); 27 (Piper 2002); 73 (Piper 2004); 27 (Röhm 2005); 40 (Sagir 2007); 17 (Stapelfeldt 2005) and 15 (Toyota 2004). All studies used an intention to treat analysis.

All studies included in the review demonstrated baseline comparability of the groups on characteristics such as age, gender, duration of surgery, and ambient air temperature. The comparability of baseline core temperatures is shown Figure 1. Delauney 1991, De Witte 1998, Holdcroft 1978, Horn 1998, Mao 1998, Mathews 2002 and Matsukawa 2001 did not report baseline core temperatures in the groups before the intervention. Figure 1 suggests that in four studies, baseline temperatures were significantly different between groups (Cheong 1998; Hong 2005; Powell 2000; Röhm 2005). However, core temperatures were described as 'similar between the groups' in Hong (2005) and Röhm (2005). The sizes of the differences in temperatures were 0.4ºC in Cheong (1998) and Röhm (2005); 0.2ºC in Hong (2005) and Powell (2000b), and 0.1°C in Crozier (2004). These differences in baseline were compared with the effect size, and only outcomes in which the baseline difference was less than 20% of the effect size were included in the analysis.

Figure 1: Baseline core temperatures



The risk of bias was assessed for each included study. Cheong (1998), Crozier (2004), Powell (2000b) and Röhm (2005) were treated with caution because of significant differences in baseline.

RESULTS

A. Premedication

1. Alpha$_2$-adrenergic antagonist versus placebo

1.1 Intervention given in the preoperative phase

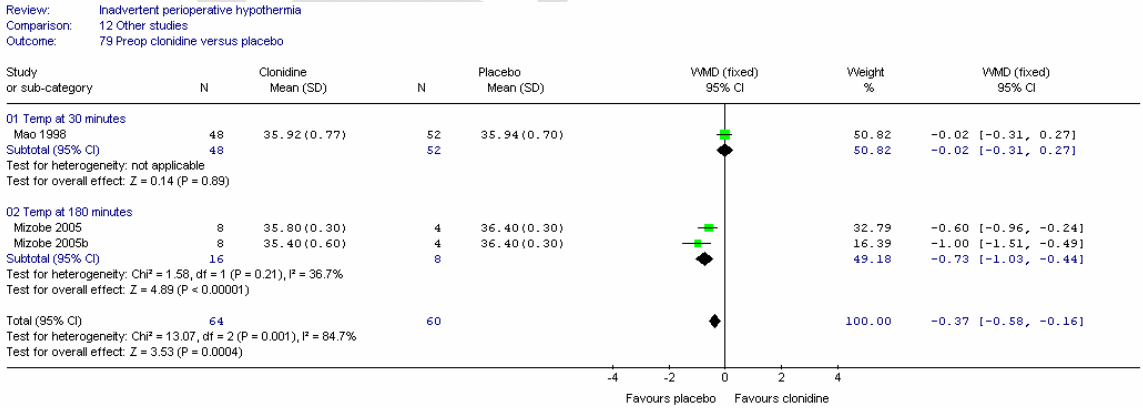
Mao (1998) compared clonidine 150µg, given orally 90 minutes before induction of spinal anaesthesia, with placebo (two starch tablets) in 100 patients. The ambient temperature was 22 to 23ºC. Mizobe (2005) compared clonidine versus placebo, given orally 30 minutes before entering the operating room, in patients having combined general plus epidural anaesthesia. Eight patients received 150µg clonidine, eight received 300µg clonidine, and eight received placebo. The ambient temperature was 24ºC.

a) Core temperature intraoperatively

The Mao (1998) study in 100 patients showed no significant difference in core temperature at 30 minutes after spinal anaesthesia. The confidence interval is fairly wide.

At 180 minutes, meta-analysis of the two Mizobe (2005) comparisons in 24 patients showed a significantly higher mean core temperature for the placebo group, with a fairly wide confidence interval: WMD -0.73°C (95%CI -1.03, -0.44).

Figure 2: Core temperature



1.2 Intervention given in the intraoperative phase at induction

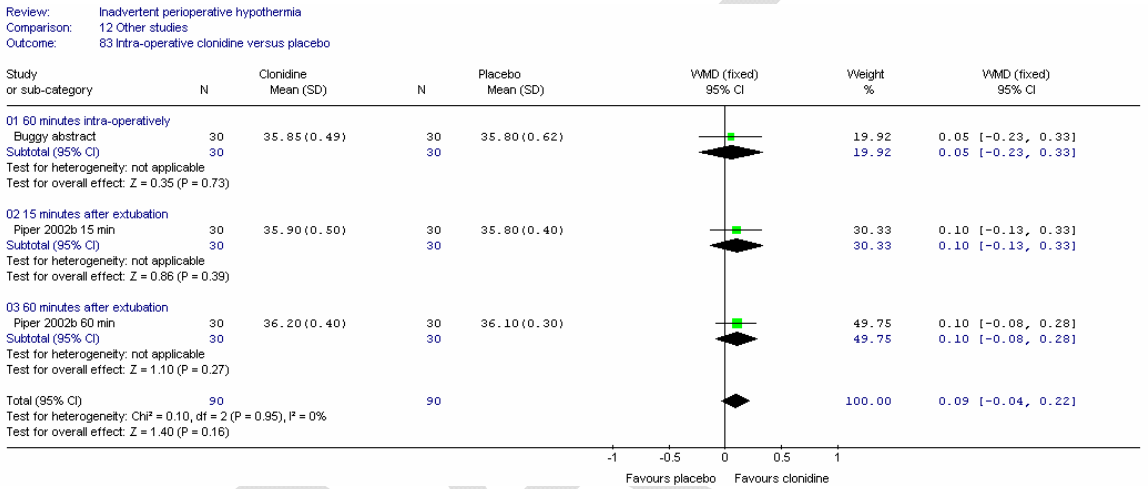
Two studies gave clonidine or placebo at induction of anaesthesia (Buggy abstract: 150µg IV; Piper 2002: 3µg/kg IV).

The Buggy (1997) study gave few details. In the Piper (2002) study, the mean duration of surgery was 74.1 (SD 42.3) minutes in the clonidine group and 74.3 (SD 34.4) for the placebo group.

a) Core temperatures intraoperatively

The Buggy (1997) study recorded the temperature at 60 minutes intraoperatively in 60 patients. There was no significant difference between interventions; the confidence interval is fairly wide (Figure 3).

Figure 3: Intraoperative clonidine measured intra and postoperatively



b) Core temperatures postoperatively

The Piper (2002b) study in 60 patients recorded the temperature at 15 and 60 minutes after extubation (Figure 3). There was no significant difference between interventions (Figure 3).

1.3 Intervention given in the intraoperative phase at the end of surgery

Six studies evaluated the effect of clonidine given at the end of surgery (for the prevention of shivering):

Delauney (1991) compared clonidine versus control (isotonic saline) given at the end of surgery as an infusion over 20 minutes, before transfer to the recovery room. Rectal temperatures were measured in the recovery room (at some point during the first hour in recovery; exact time of measurement not stated).

Horn (1998) compared clonidine versus control (saline), given at the end of surgery; patients were extubated 5 minutes later. Patients were covered with warmed sheets during anaesthesia; ambient temperature was 23ºC.

Piper (2000) compared clonidine 3µg/kg with placebo, given at the end of surgery. The mean duration of surgery was 93.1 (SD 48.2) minutes in the clonidine group and 86.6 (SD 26.9) in the placebo group.

Piper (2001) compared clonidine 3µg/kg with placebo, given at the end of surgery. The mean duration of surgery was 91.0 (SD 52.1) minutes in the clonidine group and 77.9 (SD 34.9) in the placebo group.

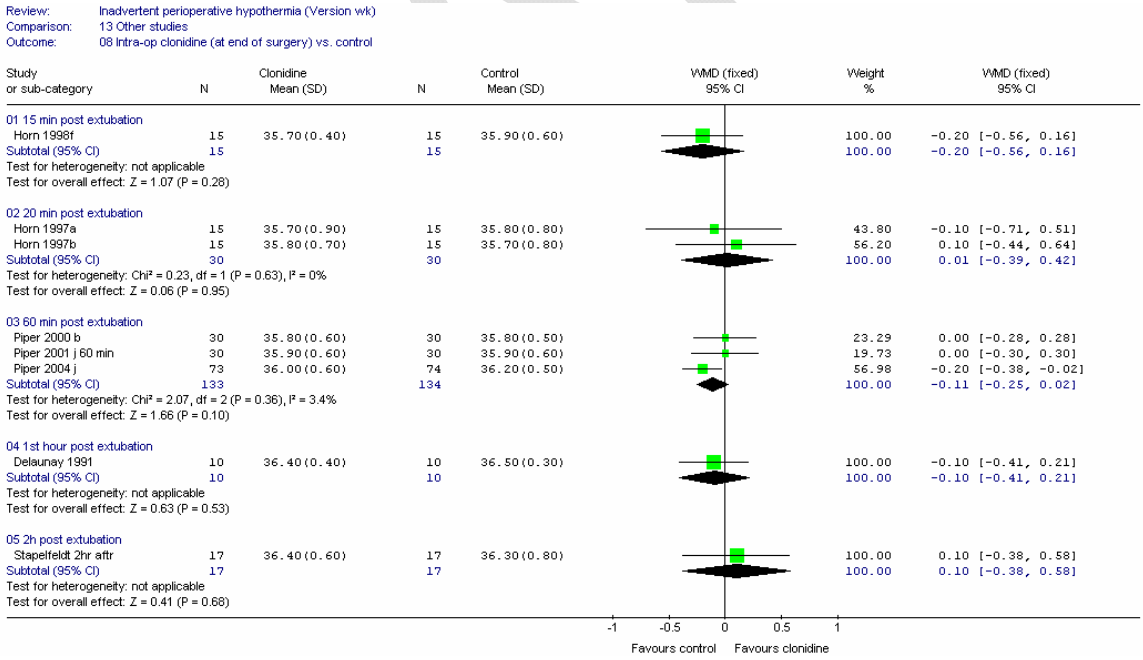
Piper (2004) compared clonidine 1.5 µg/kg IV with placebo, given at the end of surgery.

Horn (1997) compared clonidine 3µg/kg with saline placebo 5 minutes before extubation. In two groups, these interventions were in addition to isoflurane anaesthesia, and in two further groups, clonidine or saline were combined with propofol anaesthesia. The temperature was measured 20 minutes after extubation.

a) Core temperatures postoperatively

Meta-analysis across these studies was carried out for temperatures measured 20 and 60 minutes post-extubation, in 60 and 267 patients respectively. Other results are given for single studies. There was no significant difference in postoperative temperatures at any time, and there was no significant heterogeneity in the meta-analyses.

Figure 4: Clonidine given at the end of surgery; postoperative temperatures



2. Benzodiazepines versus placebo/no intervention

2.1 Intervention given in the preoperative phase

Three studies compared midazolam and placebo or no premedication in the preoperative phase; two of these gave midazolam in addition to other interventions (Kimberger 2007; Matsukawa 2001).

Toyota (2004) compared intramuscular midazolam versus no premedication. Room temperature was 24 to 25ºC; patients were covered with a single surgical drape.

Kimberger (2007) compared intravenous midazolam versus usual care and midazolam plus active warming versus active warming alone, with an outcome of core temperature preoperatively. Ambient temperatures at the start and end were around 19ºC.

Matsukawa (2001) compared midazolam plus atropine versus atropine alone with an outcome of change in core temperature preoperatively. Patients were 'minimally clothed' and covered with single layer cotton blanket; ambient temperature was 23 to 24ºC.

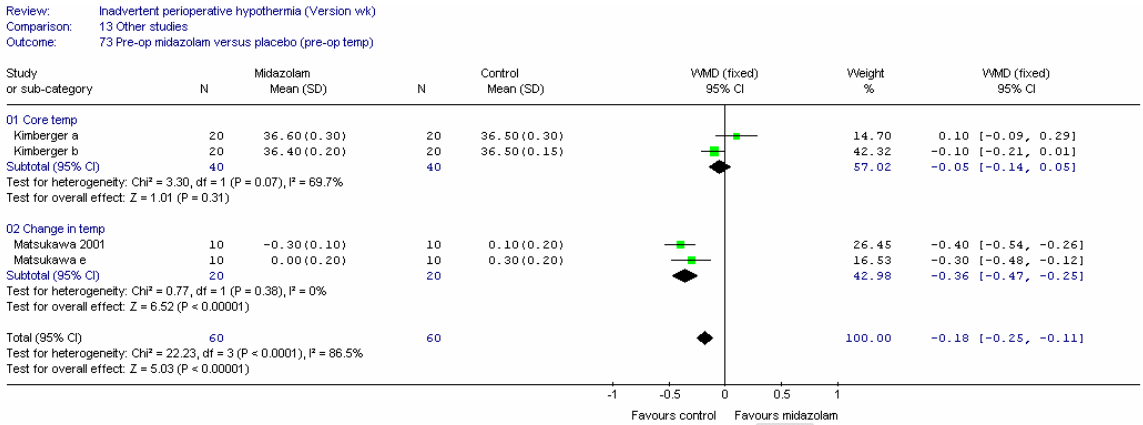
a) Core temperature preoperatively.

Kimberger (2007) compared (a) midazolam 30µg/kg plus usual care versus usual care alone. This study also compared (b) midazolam 30µg/kg plus forced-air warming device versus forced air warming alone. Meta-analysis of the two comparisons in 40 patients showed no significant differences between groups, but heterogeneity across comparisons (I^2=70%, p=0.07).

Matsukawa (2001) compared (a) 50µg/kg midazolam versus saline placebo and (b) 50µg/kg midazolam plus 10µg/kg atropine versus atropine alone, recording an outcome of change in core temperature preoperatively. Meta-analysis of the two comparisons in 40 patients showed a significantly lower mean core temperature for the midazolam group; WMD -0.36 (95% CI -0.47, -0.25).

Meta-analysis across the two subgroups showed significant heterogeneity between Matsukawa (2001) and Kimberger (2007) (I^2=87%, p<0.0001), which may be a dose effect. This conclusion is supported by another Matsukawa (2001) RCT in volunteers [Matsukawa 1997 BJA 78: 396-399], which showed a dose effect: there was no significant difference in core temperatures at 30 minutes for 25µg/kg IM compared with no midazolam, but a significant difference for 75µg/kg IM when compared with either the 25µg/kg dose or the control group.

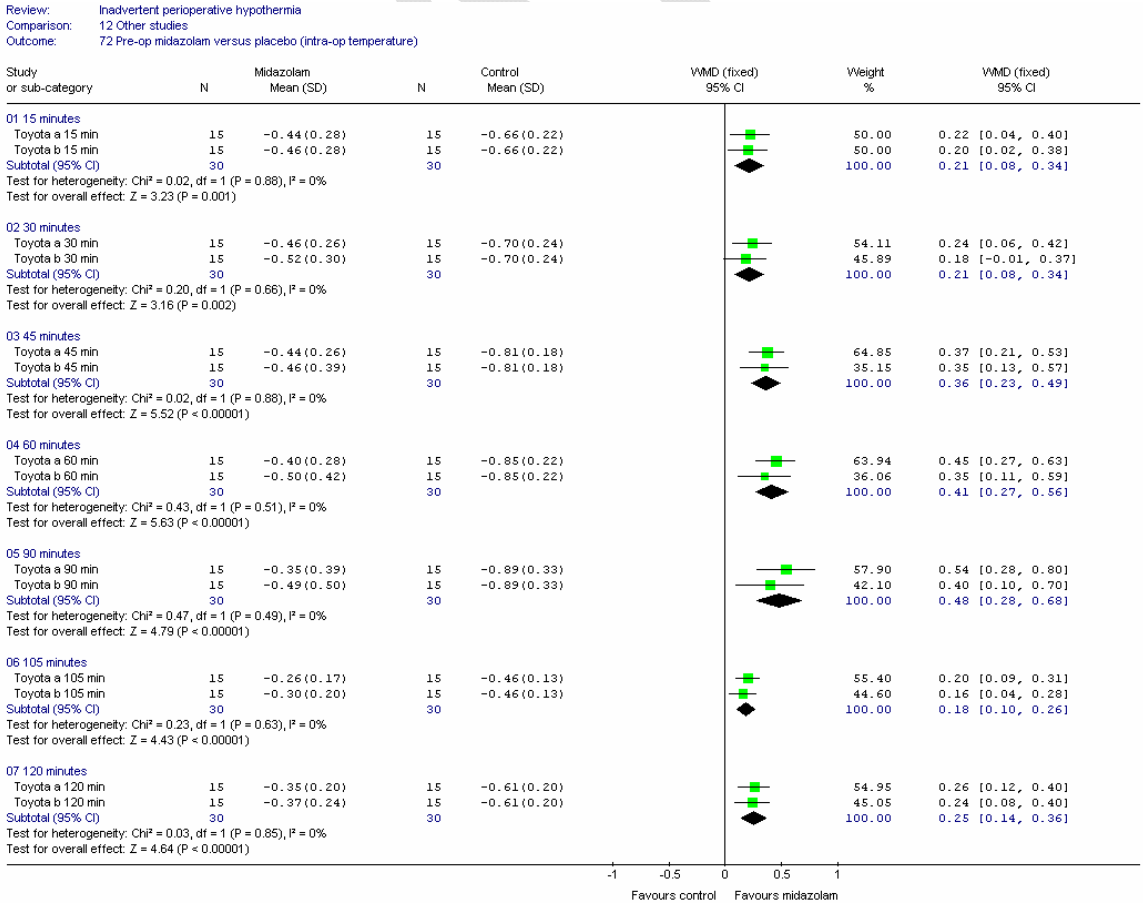
Figure 5: Midazolam in the preoperative phase



b) Core temperature intraoperatively

Toyota (2004) compared midazolam, either (a) 40µg/kg or (b) 80µg/kg IM, as premedication 30 minutes before induction of anaesthesia versus no premedication. Meta-analysis of the two comparisons in 60 patients showed a significantly higher mean core temperature at all times for the midazolam group, from 15 minutes intraoperatively (Figure 6).

Figure 6: Midazolam in preoperative phase, temperatures recorded intraoperatively



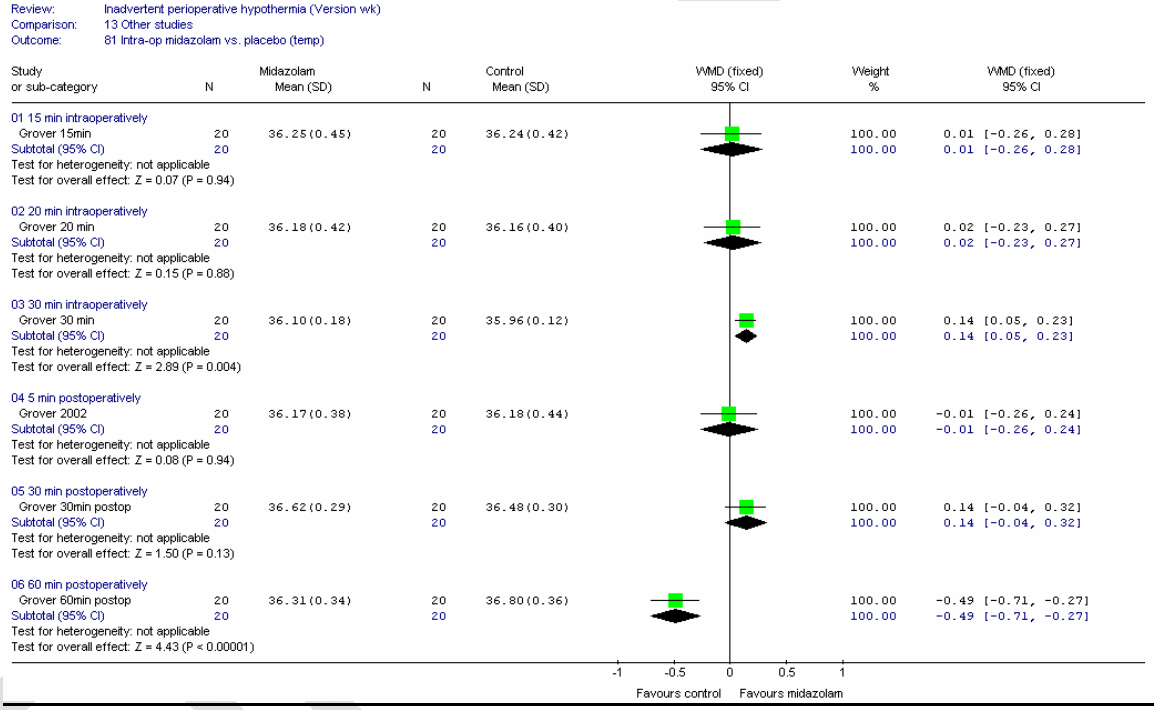
2.2 Intervention given in the intraoperative phase

Grover (2002) compared 30µg/kg IV midazolam versus placebo, given at the end of the procedure (one minute before switching off halothane) in 40 women having brachytherapy for cervical cancer. The outcomes studied were the core temperature intraoperatively (i.e. before the intervention) and postoperatively.

a) Core temperature intraoperatively

There was no significant difference in core temperature at 15 and 20 minutes intraoperatively, but at 30 minutes, there was a small, significant difference, with a higher mean core temperature in the midazolam group (Figure 7).

Figure 7: Midazolam in the intraoperative phase



b) Core temperature postoperatively

At 60 minutes postoperatively, there were significantly lower temperatures for the midazolam group (Figure 7).

B. Reversal of benzodiazepines versus placebo

1. Benzodiazepine antagonists

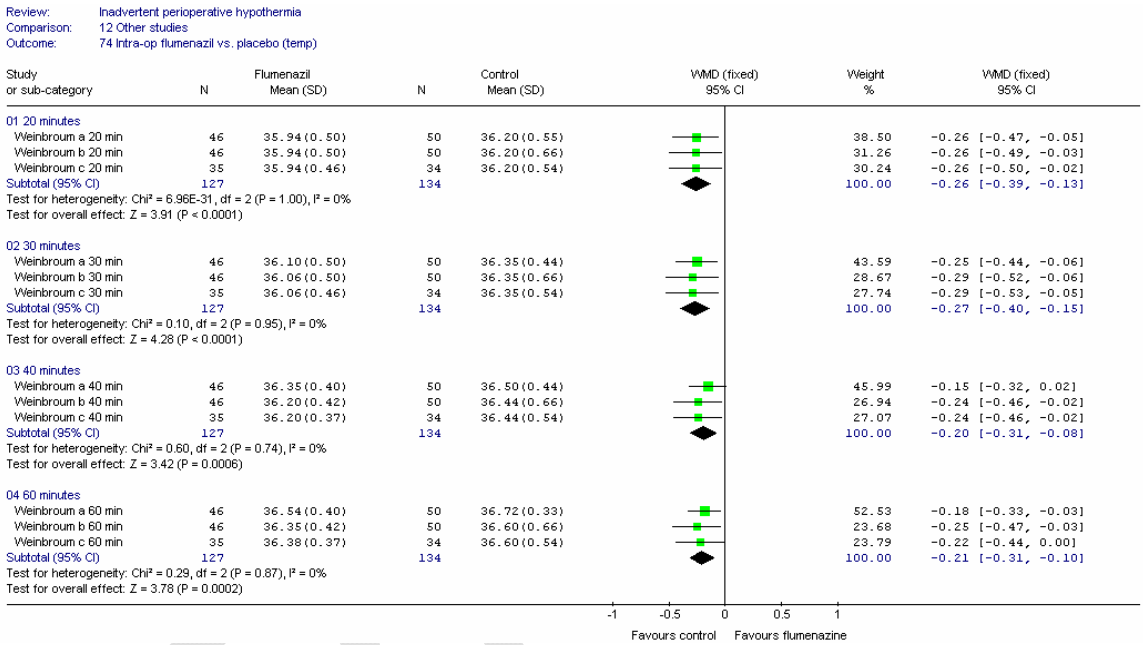
1.1 Intervention given in postoperative phase

Weinbroum (2001) compared flumenazil versus placebo IV (in 10ml volume, at a rate of 2ml/10sec) when the patients began to awaken, in three comparisons: a) using halothane; b) using enflurane and c) using isoflurane as the anaesthesia drug.

a) Postoperative temperatures

Outcomes measured were temperatures at 20, 30, 40 and 60 minutes postoperatively. Meta-analysis of the three comparisons in 261 patients showed significantly higher mean temperatures for the flumenazil group at all times postoperatively. The WMD ranged from -0.20 (95%CI -0.31, -0.08) for a control group temperature of 36.4 to 36.5°C at 40 minutes, to -0.27 (95%C -0.40, -0.15) for a control group temperature of 36.4°C at 30 minutes (Figure 8). There was no heterogeneity for any of the meta-analyses.

Figure 8: Flumenazil



C. Muscle relaxants

1. Anti-muscarinic drugs versus placebo

1.1 Intervention given in the preoperative phase

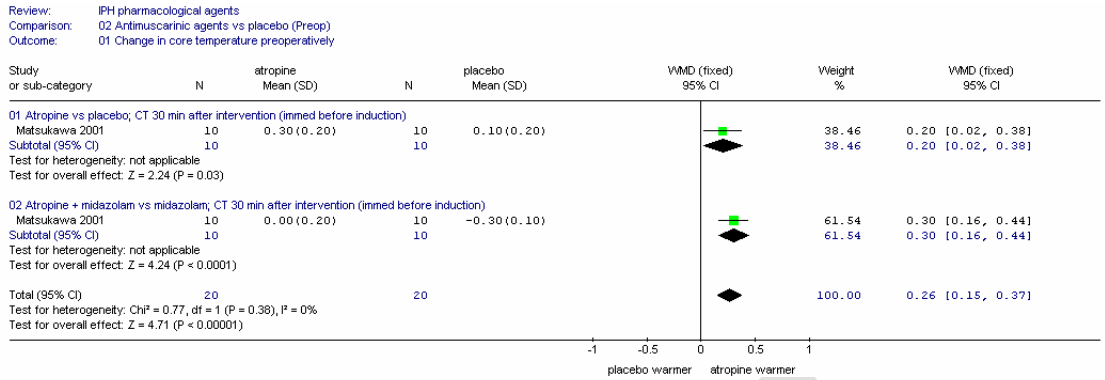
Matsukawa (2001) compared (a) IM atropine (0.01mg/kg) versus saline placebo and (b) atropine (0.01mg/kg) plus midazolam (0.05mg/kg) versus midazolam (0.05mg/kg) in 40 patients. The outcome was the change in core temperature, compared with baseline, 30 minutes later, just before induction of anaesthesia.

a) Change in core temperature preoperatively

Meta-analysis of the two comparisons gave a significantly higher mean temperature for the atropine group, 30 minutes after the intervention was given. There was no heterogeneity (I^2=0%, p=0.38). The WMD was 0.26°C (95%CI 0.15, 0.37).

The lack of heterogeneity suggested it was valid to combine the two types of comparison. In the absence of midazolam, the core temperature of patients given both atropine and placebo increased, and it is assumed that atropine is actively increasing the temperature rather than just preventing cooling.

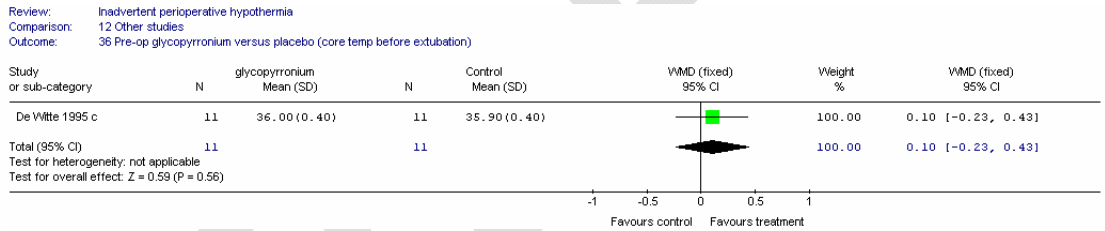
Figure 9: Atropine



b) Intraoperative core temperature (before extubation)

De Witte (1995) compared glycopyrronium versus placebo in 22 patients, as premedication 60 minutes before induction of anaesthesia. There was no significant difference between interventions, although the confidence interval is fairly wide.

Figure 10: Glycopyrronium



D. Reversal of muscle relaxants

1. Cholinesterase inhibitor versus placebo

1.1 Intervention given in the preoperative phase

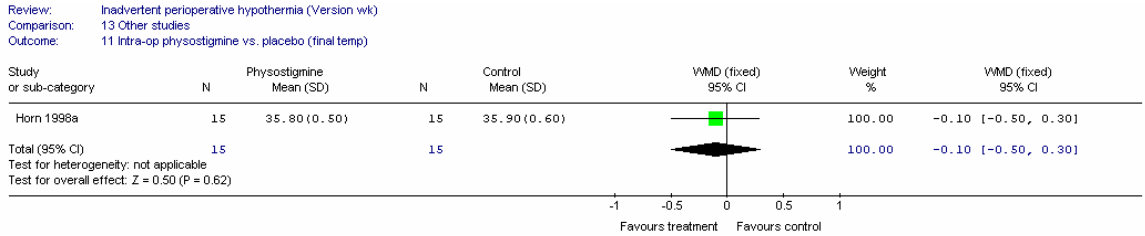
Horn (1998) compared physostigmine versus placebo (saline), given at the end of anaesthesia; patients were extubated 5 minutes later and core temperature measured 15 minutes after that. The ambient temperature was 23ºC.

Röhm (2005) compared physostigmine versus placebo, given intravenously over 15 minutes at the start of skin closure. Patients were covered with sheets during anaesthesia. Outcomes were temperatures 15 and 60 minutes after arrival in PACU.

a) Core temperature postoperatively

The Röhm (2005) study had a large baseline difference (0.4°C), which was larger than the effect size, so this study was not included in the analysis. The remaining study (Horn 1998a) in 30 patients showed no significant difference between interventions, but the confidence interval was fairly wide.

Figure 11: Physostigmine postoperatively



E. Induction of anaesthesia

1. N-methyl-D-aspartate (NMDA) receptor antagonist versus placebo

1.1 Intervention given in the preoperative phase

Two studies compared the effects of ketamine and placebo:

Sagir (2007) compared 0.5mg ketamine versus saline placebo during regional anaesthesia, in 80 patients. The theatre temperature was 24ºC; irrigation and IV fluids were pre-heated to 37ºC; patients were covered with 1 layer of cotton blanket. The outcome was the final core temperature at 60 minutes.

Kinoshita (2004) compared ketamine and saline in 20 patients, at a rate of 0.3mg/kg/h, given at induction, together with propofol. The theatre temperature was 25°C and warmed IV fluids were also given.

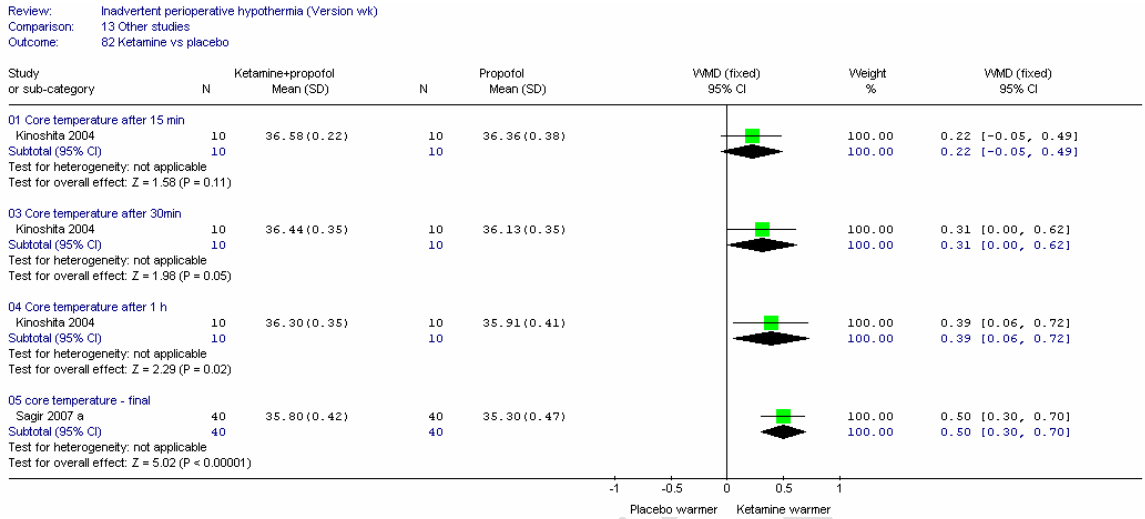
Sagir (2007) also compared 0.25mg ketamine plus 1.5mg granisetron versus 3mg granisetron during regional anaesthesia. This comparison did not correspond to an investigation of the added effect of ketamine because the amounts of granisetron were not the same in the two groups. This comparison was therefore not included.

a) Core temperatures intraoperatively

Figure 12 shows the two studies at different intraoperative times. There was a significant difference in core temperature from about 30 minutes, with the placebo group being warmer. The confidence intervals were fairly wide, apart from at the final temperature in the Sagir (2007) study.

DRAFT

Figure 12: Ketamine



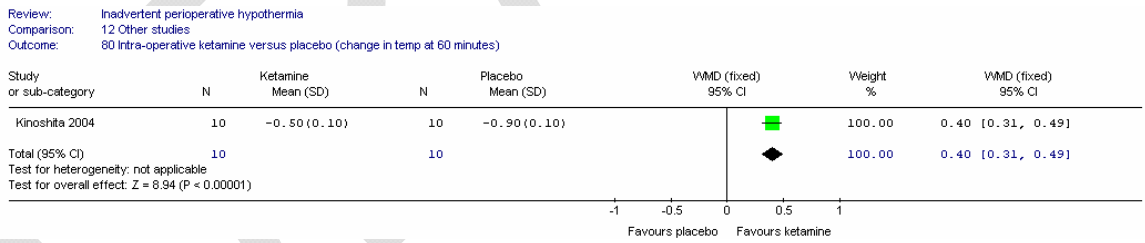
1.2 Intervention given in the intraoperative phase

Ikeda (2001) compared ketamine plus propofol versus propofol alone during general anaesthesia in 20 patients.

a) Core temperature intraoperatively

The core temperature decreased significantly less in the ketamine group (0.5ºC versus 0.9ºC) at 60 minutes after the start of the infusion.

Figure 13: Ketamine in the intraoperative phase



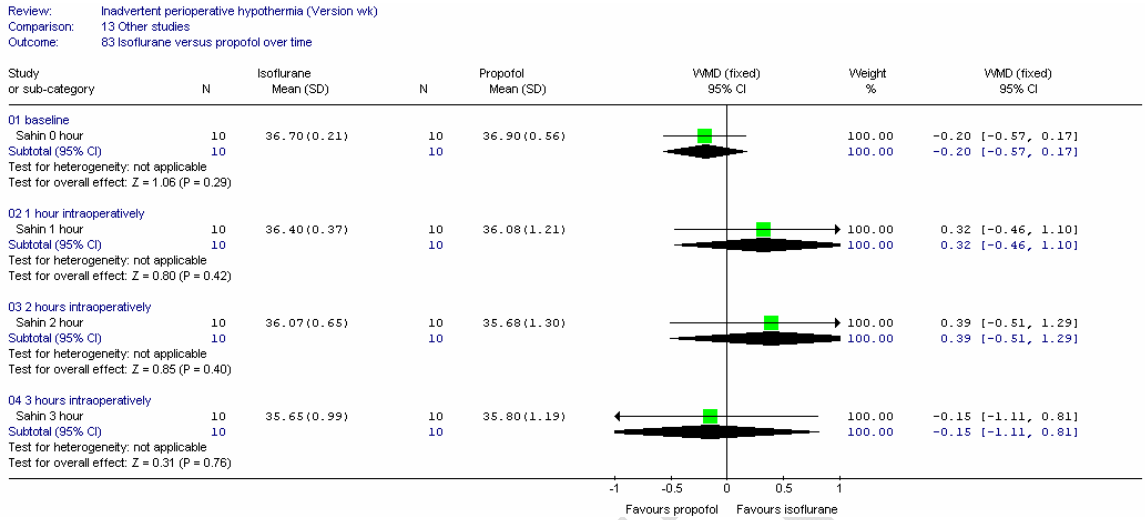
F. General anaesthesia drugs

1. Anaesthesia drug 1 versus drug 2

1.1 Intervention given in the preoperative phase

Sahin (2002) compared isoflurane versus propofol in 20 patients. The confidence intervals were too wide at all time points to determine if there was a difference between isoflurane and propofol (Figure 14). All patients received dextrose-free crystalloids and colloids at room temperature; ambient temperature was 21ºC (SD 1).

Figure 14: General anaesthesia drugs given in the preoperative phase



NB: Scale -4 to +4

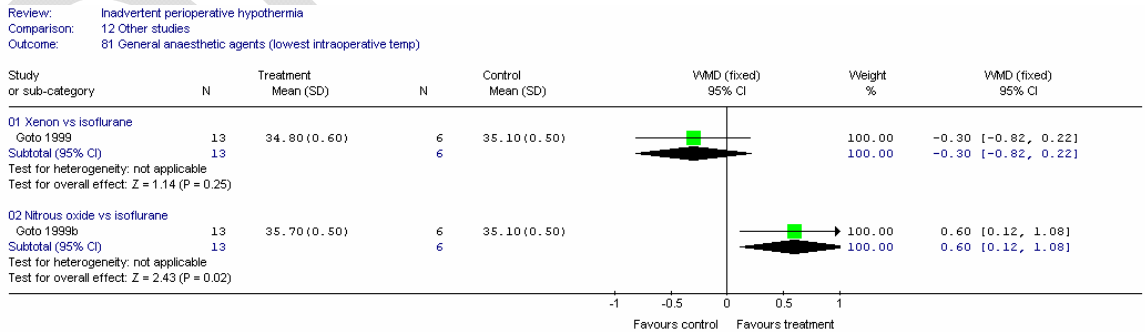
1.2 Intervention given in the intraoperative phase

Goto (1999) compared (a) xenon 43% plus isoflurane 0.5% (n=13) versus isoflurane 1.2% (n=13), and (b) nitrous oxide 63% plus isoflurane 0.5% (n=12) versus the same control group of isoflurane 1.2%. The outcome was the lowest core temperature intraoperatively.

a) Lowest core temperature intraoperatively

There was no significant difference in the lowest core temperature between xenon plus isoflurane and isoflurane, but the lowest core temperature for nitrous oxide plus isoflurane was higher than for isoflurane alone.

Figure 15: General anaesthesia drugs given in the intraoperative phase



2. Different doses of halothane

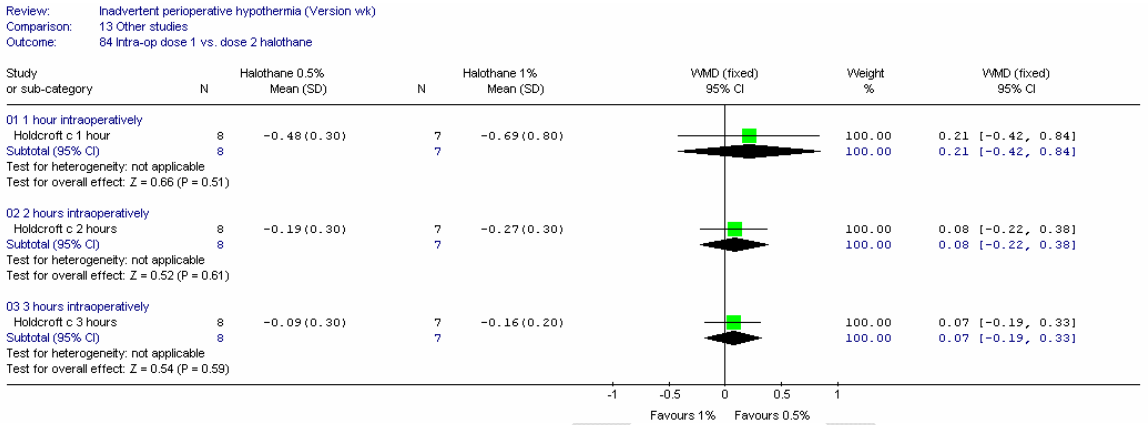
2.1 Intervention given in the preoperative phase

Holdcroft (1978) assessed halothane 0.5% versus halothane 1% in 15 patients, given preoperatively.

a) Core temperature intraoperatively

There was no significant difference in core temperature at 1, 2 or 3 hours, although the confidence interval was wide at one hour and fairly wide at two hours.

Figure 16: Doses of halothane



G. Analgesia

1. Opioid versus placebo

Two studies compared pethidine and placebo for patients given general anaesthesia (Horn 1998; Piper 2000), and two received regional anaesthesia (Kelsaka 2006; Hong 2005). These studies were combined where appropriate.

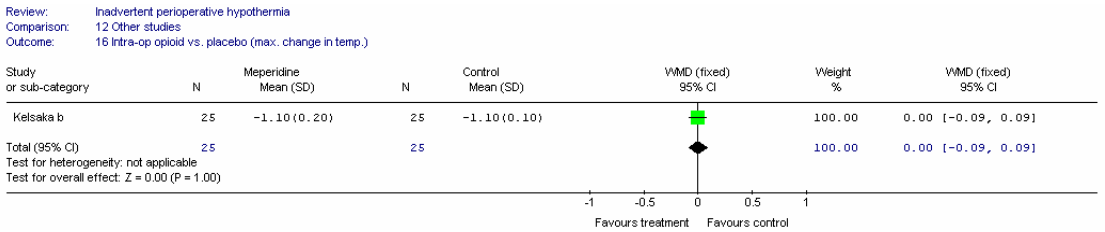
1.1 Interventions given in the preoperative phase

Kelsaka (2006) compared pethidine with saline placebo in 50 patients, given immediately before spinal anaesthesia for patients undergoing elective orthopaedic surgery. Lactated Ringer's solution, warmed to 37ºC, was infused at 10ml/kg/hr for 30 min before surgery; ambient temperature was 21 to 22ºC; patients were covered with one layer of surgical drape intraoperatively and one cotton blanket post-operatively.

a) Lowest intraoperative temperature

The outcome was the change in rectal temperature (i.e. the lowest rectal temperature minus the preoperative rectal temperature). There was no significant difference between groups.

Figure 17: Pethidine preoperatively



1.2 Interventions given in the intraoperative phase

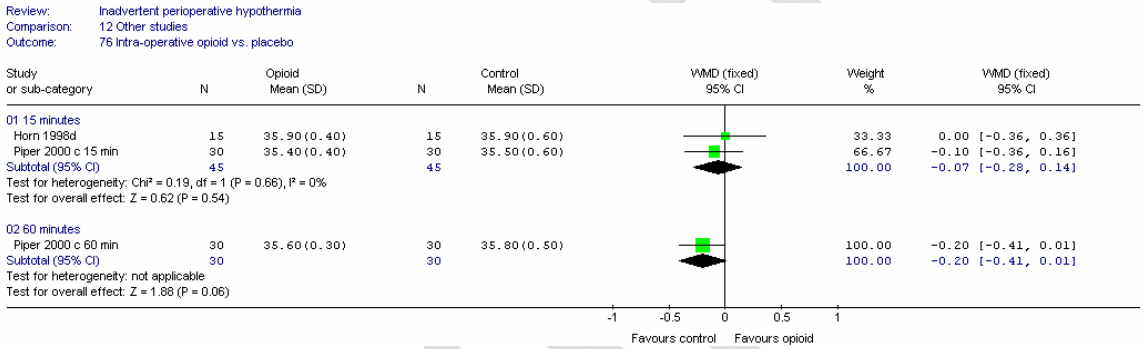
1.2.1 Pethidine

Two studies compared pethidine versus control (saline), given at the end of surgery (Horn 1998; Piper 2000) in 90 patients. Patients were extubated and the core temperature measured 15 and 60 minutes after that. One additional study (Hong 2005) compared 10mg pethidine plus 0.5% bupivacaine versus bupivacaine alone for regional anaesthesia for elective Caesarean section. This indirect study was not considered further.

a) Postoperative core temperatures

Meta-analysis of Horn (1998) and Piper (2000) in 90 patients at 15 minutes, and results from the Piper (2000) study of 60 patients at 60 minutes post-extubation, showed no significant differences in core temperature, between pethidine and placebo. There was no heterogeneity.

Figure 18: Pethidine – core temperatures postoperatively



1.2.2 Morphine

Hong (2005) compared three groups in women undergoing combined spinal-epidural anaesthesia for elective Caesarean sections: the women received 0.1mg morphine (Hong a), or 0.2mg morphine (Hong b), each in addition to 0.5% bupivacaine versus bupivacaine alone. This is an indirect population, and there was a baseline difference for each of these comparisons, which was not small compared with the effect size. Therefore the results are not reported.

2. Opioid dose 1 versus dose 2

2.1 Intervention given in the intraoperative phase

Hong (2005) compared 0.1mg morphine with 0.2mg morphine, each in addition to 0.5% bupivacaine, for combined spinal-epidural anaesthesia for elective Caesarean section (indirect population). This comparison had a large difference in baseline, so results were not considered further.

3. Opioid type 1 versus type 2

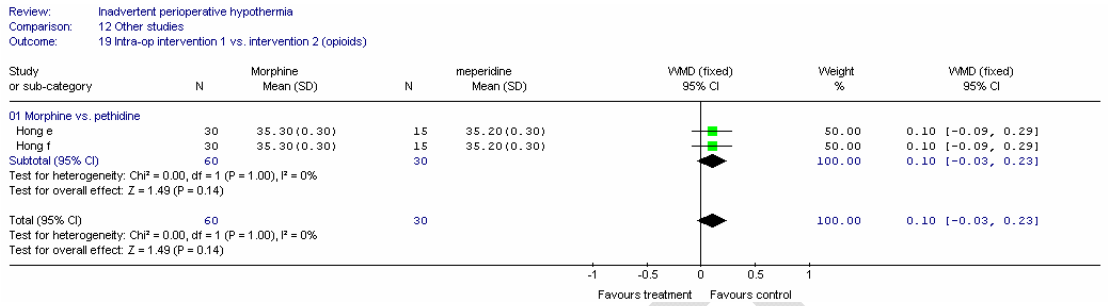
3.1 Intervention given in the intraoperative phase

3.1.1 Morphine versus pethidine

Hong (2005) compared 0.1mg morphine (Hong e), or 0.2mg morphine (Hong f), with 10mg pethidine, each in addition to 0.5% bupivacaine, for combined spinal-epidural anaesthesia for

elective Caesarean section (indirect population), measured at 60 minutes. Meta-analysis of the two comparisons in 90 patients showed no significant differences in temperatures between the groups.

Figure 19: Morphine versus pethidine in indirect population



3.1.2 Remifentanil versus alfentanil

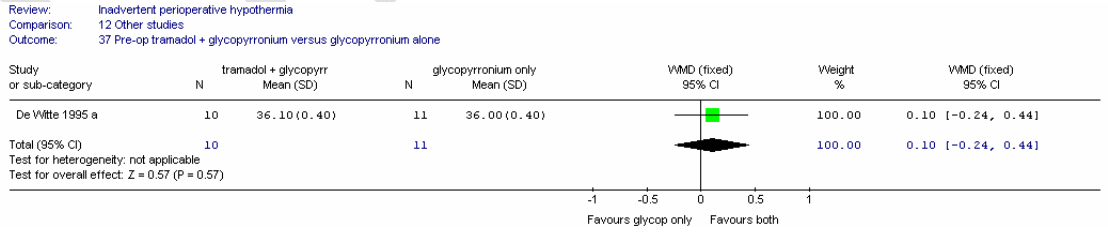
Crozier (2004) compared remifentanil versus alfentanil during elective ENT surgery in 98 patients. All patients were actively warmed during the procedure with forced air warming; the opioid infusion rate could be varied according to clinical need. The study had a baseline difference of -0.1°C and this was comparable with the difference in effect size, so conclusions were not drawn.

4. Other centrally-acting analgesics (for pain control) versus placebo / no intervention

4.1 Intervention given in the preoperative phase

De Witte (1995) compared tramadol plus glycopyrronium versus glycopyrronium alone in 21 patients, given as premedication 60 minutes before induction of anaesthesia. The outcome was the core temperature before extubation. There was no significant difference between interventions, although the confidence interval was fairly wide.

Figure 20: Tramadol given preoperatively



4.2 Intervention given at the start of the intraoperative phase

4.2.1 Nefopam

Bilotta (2002) compared nefopam with placebo in 60 patients, given immediately before epidural or subarachnoid anaesthesia. The theatre temperature was 22ºC (SD 1).

a) Core temperatures intraoperatively

The outcomes studied were the core temperature at 15, 30, 60 and 90 minutes intraoperatively. There was no significant difference between interventions until 90 minutes, after which time the placebo group was warmer by 0.30°C (MD -0.30°C (95%CI -0.57, -0.03); the confidence interval was fairly wide at 90 minutes. This is shown in Figure 21.

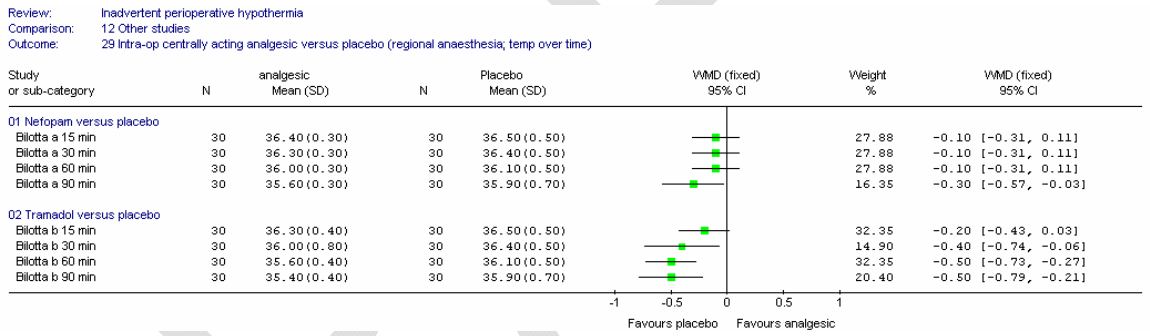
4.2.2 Tramadol

Bilotta (2002) compared tramadol with placebo in 60 patients, given immediately before epidural or subarachnoid anaesthesia. The theatre temperature was 22ºC (SD 1).

a) Core temperatures intraoperatively

The outcomes studied were the core temperature at 15, 30, 60 and 90 minutes intraoperatively. There was a significant difference from 30 minutes intraoperatively, with the placebo group being warmer by up to 0.50°C. The confidence intervals were fairly wide at 30 and 90 minutes (Figure 21).

Figure 21: Nefopam and tramadol



4.3 Intervention given at the end of the intraoperative phase

4.3.1 Nefopam

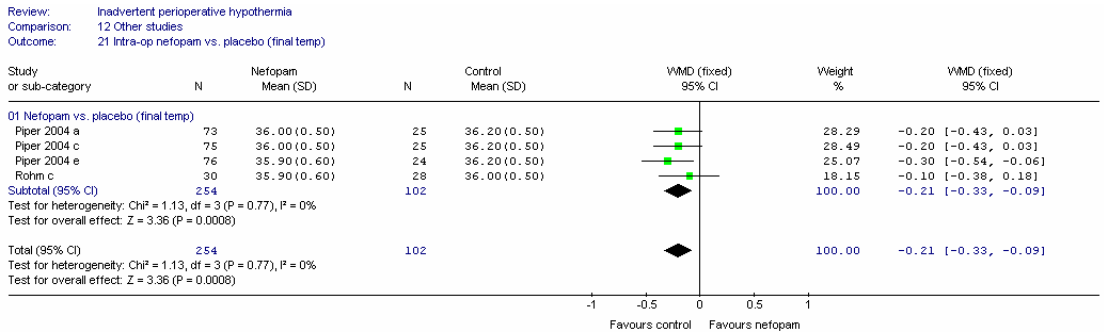
Piper (2004) compared nefopam at doses of 0.2mg/kg, 0.1mg/kg, and 0.05mg/kg with placebo, given at the end of surgery. The outcomes studied were the core temperature at 15 and 60 minutes after extubation.

Röhm (2005) compared nefopam with placebo, given intravenously over 15 minutes at the start of skin closure. Outcomes were temperatures at 15 and 60 minutes after arrival in PACU.

a) Core temperatures postoperatively

Meta-analysis of the four comparisons in 356 patients showed a significantly higher mean core temperature for the placebo group at 60 minutes after arrival in PACU: WMD -0.21 (95%CI -0.33, -0.09), for a control group temperature range of 36.0 to 36.2°C. There was no heterogeneity.

Figure 22: Nefopam



4.3.2 Tramadol

Two studies compared the effects of tramadol and placebo, given at the beginning of wound closure (Matthews 2002; de Witte 1998).

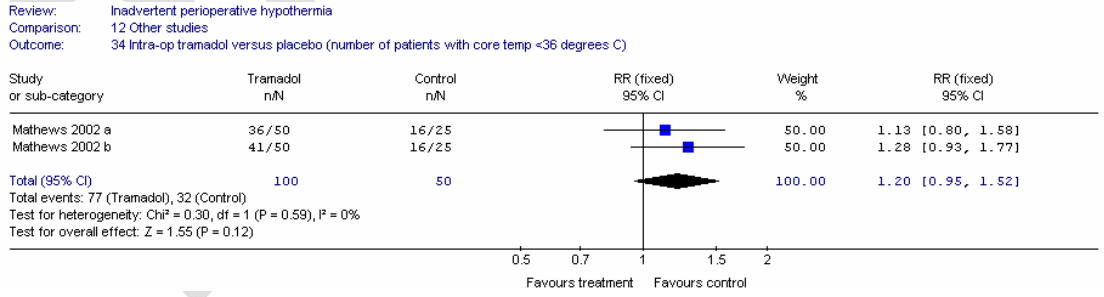
Mathews (2002) compared tramadol at either 2mg/kg or 1mg/kg versus saline control in 100 patients. The ambient temperature was 21.2 to 24.9ºC.

De Witte (1998) compared tramadol and placebo. The mean duration of surgery was 56 (SD 16) minutes in the tramadol group and 61 (SD 16) minutes for placebo.

a) Incidence of IPH postoperatively

Meta-analysis of the two comparisons in the Mathews (2002) study, in 100 patients, showed no significant difference in the incidence of IPH (less than 36.0°C), but the confidence interval is fairly wide.

Figure 23: Tramadol – incidence of IPH



b) Core temperature at extubation

One study (de Witte 1998) recorded the core temperature at extubation in 40 patients. There was no significant difference between interventions, but the confidence interval is fairly wide.

Figure 24: Tramadol – core temperature

5. Centrally acting analgesia dose 1 versus dose 2

5.1 Intervention given in the intraoperative phase

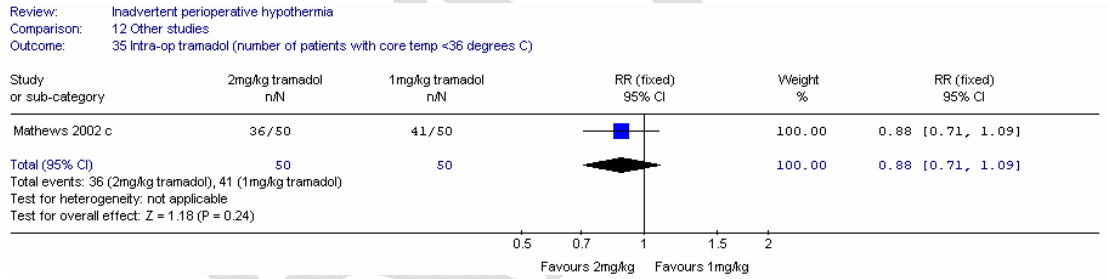
5.1.1 Nefopam

Mathews (2002) compared tramadol 2mg/kg with 1mg/kg, given at the beginning of wound closure, in 100 patients.

a) Incidence of hypothermia

The outcome recorded was the number of patients with a core temperature below 36ºC. There was no significant difference between doses.

Figure 25: Tramadol dose comparison



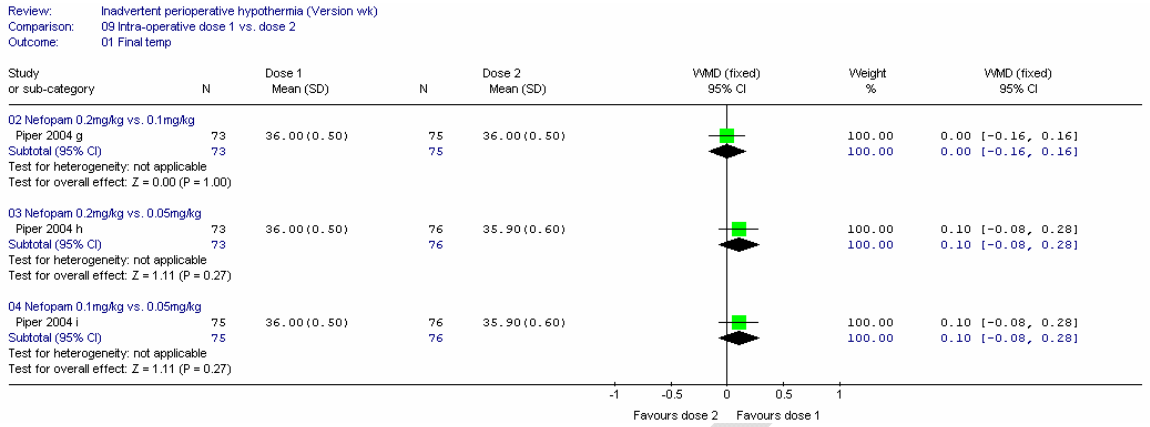
5.1.2 Nefopam

Piper (2004) compared nefopam at doses of 0.2mg/kg, 0.1mg/kg, and 0.05mg/kg, given at the end of surgery, with about 75 patients in each arm.

a) Core temperatures postoperatively

Piper (2004) recorded the core temperatures at 15 and 60 minutes post extubation. There were no significant differences between doses (Figure 26).

Figure 26: Nefopam dose comparison



6. Centrally acting analgesia type 1 versus type 2

6.1 Intervention given at the start of the intraoperative phase

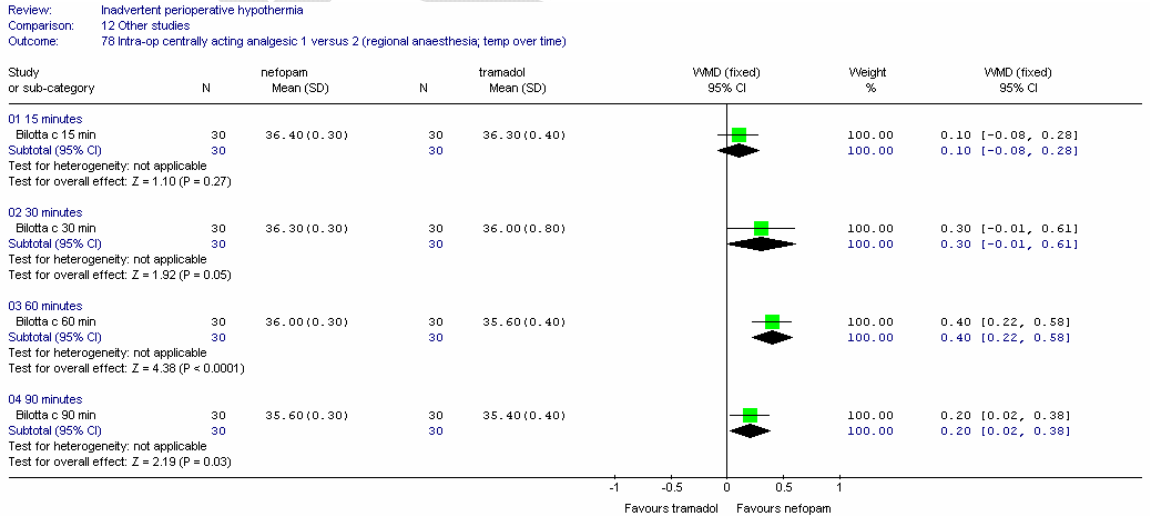
6.1.1 Nefopam versus tramadol

Bilotta (2002) compared nefopam with tramadol, given immediately before epidural or subarachnoid anaesthesia in 60 patients.

a) Core temperatures intraoperatively

The outcomes studied were the core temperature at 15, 30, 60 and 90 minutes intraoperatively. Patients receiving nefopam were significantly warmer than those receiving tramadol after 60 and 90 minutes; mean difference at 60 minutes: 0.40°C (95%CI 0.22, 0.58), for a tramadol temperature of 35.6°C.

Figure 27: Nefopam versus tramadol



H. Control of nausea

1. Serotonin receptor antagonists versus placebo

Two studies examined these drugs during general anaesthesia (Powell 2000; Piper 2002) and two during regional anaesthesia (Sagir 2007; Kelsaka 2006). We combined the studies across types of anaesthesia.

Piper (2002) compared 12.5mg dolasetron versus placebo, given after induction of general anaesthesia, in 60 patients, and recorded the temperature at the end of surgery (mean duration of surgery 70.2 (SD 32.5) minutes for dolasetron group and 74.3 (SD 34.4) for controls) and 15 and 60 minutes after extubation.

Powell (2000) compared ondansetron 4mg or 8mg, given at induction, versus saline control, in 55 patients, and recorded the temperature at 30, 60 and 90 minutes after induction. The duration of anaesthesia administration was 38 minutes (SD 12 to 18).

Kelsaka (2006) compared 8mg IV ondansetron with saline placebo, given immediately before spinal anaesthesia in 50 patients undergoing elective orthopaedic surgery. The outcome was the change in rectal temperature (i.e. the lowest rectal temperature recorded during the operation minus the preoperative rectal temperature). Patients received warmed IV fluids.

Sagir (2007) compared (a) granisetron (3mg) versus placebo and (b) granisetron (1.5mg) plus ketamine (0.25mg) versus ketamine (0.5 mg) alone during regional anaesthesia, in 120 patients. The duration of anaesthesia/surgery was not stated. The comparison of the combination versus ketamine alone was excluded from the analysis because it did not have the same amount of ketamine in each arm.

a) Core temperature intraoperatively

Two studies (Powell 2000, in 82 patients; Kelsaka 2006, in 50 patients) recorded the core temperature intraoperatively, at 30 minutes and lowest intraoperative temperatures respectively. There was no significant difference at either time or dose, although the confidence intervals are fairly wide.

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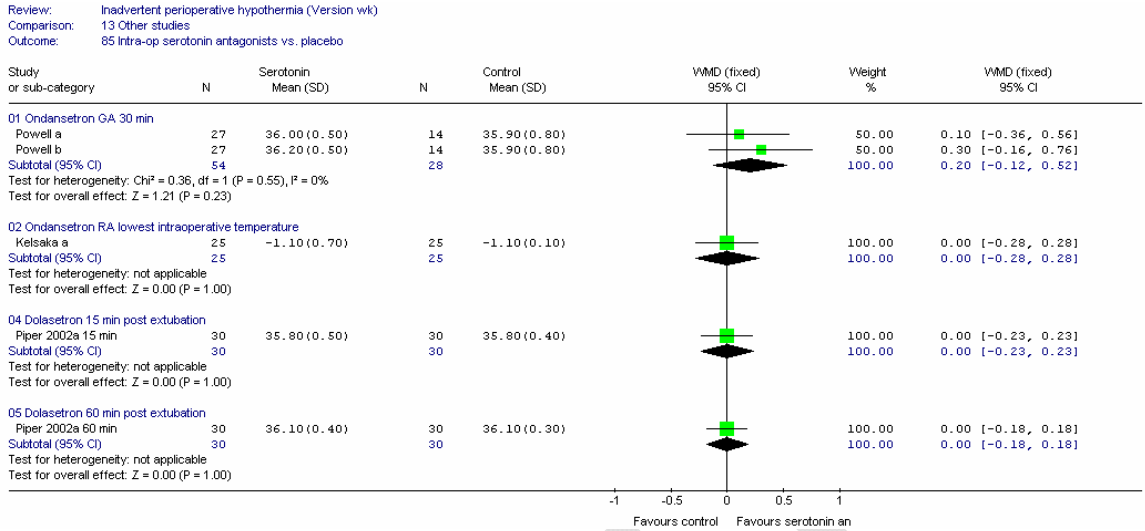
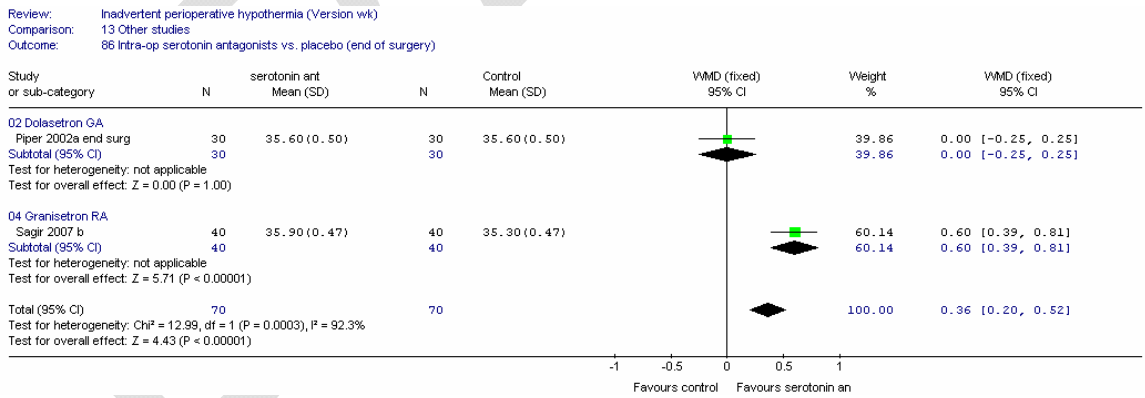
Figure 28: Serotonin receptor antagonists



b) Core temperature at the end of surgery

Two studies recorded the core temperature at the end of surgery. There was no significant difference for the Piper (2002) study comparing dolasetron with placebo in general anaesthesia, but there was a large effect for granisetron versus placebo in regional anaesthesia, with granisetron treated patients being warmer: MD 0.60°C (95%CI 0.36, 0.84) in 60 patients.

Figure 29: Serotonin receptor antagonists (end of surgery)



c) Core temperature postoperatively

One study reported postoperative temperatures (Piper 2002) (Figure 29) in 60 patients. There was no significant difference between dolasetron and placebo.

2. Serotonin receptor antagonist dose 1 versus dose 2

2.1 Intervention given in the preoperative phase

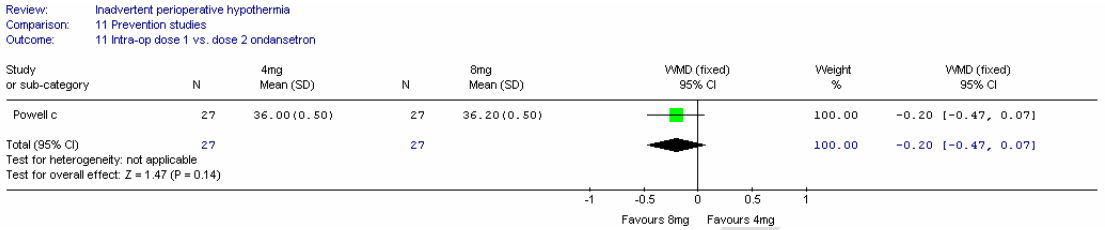
2.1.1 ondansetron dose comparison

Powell (2000) assessed ondansetron 4mg versus ondansetron 8mg in 54 patients.

a) Core temperatures intraoperatively

There was no significant difference between interventions at 30 minutes intraoperatively, but the confidence interval was fairly wide

Figure 30: Ondansetron dose comparison



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7.2 Risk factors for IPH – non-pharmacological

SELECTION CRITERIA

Selection criteria were as outlined in the general methods section apart from the types of risk factor and outcomes described below.

Types of risk factor

Any property reported to be a risk factor for IPH was to be considered, including the following *a-priori* ones predicted by the GDG:

- Age
- BMI
- Length of preoperative starvation
- Temperature of patient at the beginning of the preoperative phase
- Temperature of patient at first anaesthetic intervention
- ASA grade
- Pre-existing medical conditions (diabetes mellitus, thyroid disease, corticosteroid disease, cardiac disease)
- Type of surgery: according to the grade defined in the NICE Preoperative Test guideline
- Magnitude of surgery (major, intermediate, minor)
- Laparoscopic surgery
- Site of surgery: open body cavity or other
- Duration of anaesthesia
- Duration of surgery
- Urgency of operation: urgent, emergency, elective
- Environmental factors: temperature, humidity (pre-, intra-, and post-operative)
- Irrigation fluids: warmed/unwarmed
- Infused fluids: warmed/unwarmed, by volume infused.

Type of outcome measure

As noted in the general methods section, ideally, the incidence of hypothermia should be determined for patients who were not warmed, but studies in which some or all of the patients were warmed could also be included. The GDG considered that risk factors may be different in warmed patients. Preferably patient warming would be included as a variable in multivariate analyses.

SEARCH STRATEGY

Searches were performed on the following core databases: MEDLINE, EMBASE, CINAHL and *The Cochrane Library* (1966 to current day with guidance from the GDG). Additional databases were not searched for this review. The search strategies are given in Appendix B.

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Twenty-five studies met the inclusion criteria for the review. The reference lists of the retrieved studies were inspected for further potential papers.

METHODOLOGICAL QUALITY OF STUDIES

The methodological quality of studies was assessed according to the type of study design. In evaluating the literature, RCTs and cohort studies were selected to be the best available evidence source for this review, and were quality assessed separately.

Both RCTs and cohort studies were assessed according to the criteria given in the general methods section

CHARACTERISTICS OF CLINICAL STUDIES INCLUDED IN THE REVIEW (APPENDIX C)

We included 25 studies, for which full data extraction was carried out. Although there were additional studies available, we did not believe their results would materially affect the review and therefore decided to truncate it at this point. In most of the remaining studies multivariate analyses had not been carried out or the study design was inferior.

The 25 included studies examined had different study designs:

- Fifteen were prospective cohort studies (Abelha 2005; Baker 1995; Closs 1986; El-Gamal 2000; Flores Maldonado 1997; Frank 2000; Hind 1994; Kitamura 2000; Kongsayreepong 2003; Kurz 1995; Lau 2001; Morris 1971; Stewart 1998; Vorrakitpokatorn 2006; Yamakage 2000)
- Eight were RCTs (Danelli 2002; Frank 1992; Frank 1994; Hendolin 1982; Mizobe 2005; Nakajima 2002; Nguyen 2000; Steinbrook 1997)
- One was a retrospective cohort study (Roberts 1994, which did not use a multivariate analysis)
- One was a case-control study (Kasai 2002).

One of the RCTs had an ANCOVA multivariate analysis that covered risk factors other than the randomised comparison (Frank 1992).

The study sizes ranged from 13 (Steinbrook 1997) to 101 for the RCTs, and 22 (Morris 1971) to 18,759 (Lau 2001) for the cohort studies. The case-control study included 400 patients, 200 cases of patients with core temperatures less than 35.0°C and 200 with temperatures over 36.0°C.

Two studies were carried out in the UK (Closs 1986; Hind 1994); one in each of Austria, Italy, Finland and Portugal; eight were in North America; one in Mexico; five in Japan; two in Thailand; one in China (Hong Kong); one in Egypt and one in Australia.

A range of procedures was undertaken.

- Eleven studies included patients undergoing abdominal surgery (Danelli 2002, colonic resection; Hind 1994, gynaecological; Kasai 2002, general abdominal; Kitamura 2000 and Kurz 1995, colon surgery; Mizobe 2005, lower abdomen; Morris 1971 and Nakajima 2002, colorectal or gynaecological; Nguyen 2000, gastric bypass; Steinbrook 1997; Stewart 1998, general abdominal)
- One study in abdominal and orthopaedic surgery (Closs 1986, cholecystectomy and fractured femur)
- Two in orthopaedics (El-Gamal 2000 and Yamakage 2000, surgery on lumbar vertebrae (e.g. disk herniation, spondylolisthesis))
- Five in urology (Frank 2000; Frank 1994 and Hendolin 1982, prostatectomy; Roberts 1994 and Vorrakitpokatorn 2006, percutaneous nephrolithotomy)
- Two in mixed, non cardiac surgery (Abelha 2005; Kongsayreepong 2003)
- Two in mixed surgery (Lau 2001; Flores Maldonado 1997)
- One in cardiac surgery carried out under bypass under normothermia (Baker 1995)
- One was in vascular surgery (Frank 1992).

Three studies stated they included patients receiving emergency surgery (Baker 1995; Lau 2001 (31% elective); Flores Maldonado 1997 (35%)). Two studies had patients with elective surgery only (Hind 1994; Kurz 1995). The rest did not state if the surgery was elective or emergency.

The studies covered a range of types of anaesthesia:

- Ten had general anaesthesia only (Baker 1995; El-Gamal 2000; Hind 1994; Kitamura 2000; Kurz 1995; Morris 1971; Nguyen 2000; Roberts 1994; Vorrakitpokatorn 2006; Yamakage 2000). Five had combined general and regional anaesthesia (Danelli 2002; Frank 1992; Kasai 2002 case-control; Mizobe 2005; Nakajima 2002)
- One had spinal anaesthesia only (Frank 2000)
- One study had patients having either general or regional anaesthesia (Flores Maldonado 1997)
- One study had patients having either general or combined general/epidural anaesthesia (Stewart 1998)
- Three included patients having general, regional or combined general/regional anaesthesia (Abelha 2005; Kongsayreepong 2003; Lau 2001)
- Two were randomised comparisons of general and regional anaesthesia (Frank 1994; Hendolin 1982)
- One was a randomised comparison of combined general/epidural and general anaesthesia (Steinbrook 1997).

All studies but four (Baker 1995; Closs 1986; Kasai 2002, case control; Steinbrook 1997)

reported the duration of surgery and/or anaesthesia. Full details are given in Table 1.

- Two studies reported a wide range of surgery/anaesthesia durations, e.g. 0.5 to 11h anaesthesia (Abelha 2005; Kongsayreepong 2003)
- Five studies had a mean duration between 1 and 2 hours (El-Gamal 2000; Hind 1994; Flores Maldonado 1997; Frank 2000; Vorrakitpokatorn 2006)
- Two studies restricted the sample to patients having operations longer than 2 hours (Lau 2001; Morris 1971)
- The other studies had surgical times longer than 3 hours (Danelli 2002; Frank 1992; Frank 1994; Hendolin 1982; Kitamura 2000; Kurz 1995; Mizobe 2005; Nakajima 2002; Nguyen 2000; Roberts 1994; Yamakage 2000).

Table 1: Duration of surgery/anaesthesia

Study name	Duration of anaesthesia/surgery
Abelha 2005	Anaesthesia duration: 3.6h (SD 1.8) range 0.7 to 11h; 51% >3h.
Baker 1995	Not stated, but mean time on CP bypass was 1.5h (SD 0.6).
Closs 1986	Cholecystectomy and duration of surgery not stated, but significantly longer for FNF patients.
Danelli 2002 (RCT)	Duration of surgery median 4.1h (range 3-5h) and 3 h (2-6h).
El-Gamal 2000	Duration of surgery 1.7-1.8 h (SEM 0.08).
Flores Maldonado 1997	Mean surgical time 1.1h (SD 0.9) and 1.8 (SD 1.0).
Frank 1992 (RCT)	Duration in theatre: general warm 6.6h (SD 0.5); general cold 4.4h (0.3); epidural warm 5.1h (0.3); epidural cold 5.5h (0.4).
Frank 1994 (RCT)	Duration of surgery: GA 3.4h (SD 0.2); EA 3.5h (SD 0.2).
Frank 2000 (RCT)	Duration of surgery: mean 1.5h (SD 0.9) range 1.1 to 2.6.
Hendolin 1982	Duration of anaesthesia around 24 h; duration of surgery about 14h.
Hind 1994	Duration of surgery 1-2h.
Kasai 2002	Not stated.
Kitamura 2000	Duration of surgery 3.2h (SD 0.6); 3.5h (SD 1.0) h; 3.1h (0.8); 3.3h (0.7).
Kongsayreepong 2003	Surgery duration 0.25 to 10.75h. Mean 3.80h (SD 2.28); 27% had ≤ 2h. Anaesthesia duration 0.5 to 11.50h; mean 4.25h (SD 2.33) 19% ≤ 2h.
Kurz 1995	Mean duration of surgery 3.8h (SD 1.3).
Lau 2001	Surgery duration for all patients >2h, but no details.
Mizobe 2005 (RCT)	Anaesthesia maintained for 3h.
Morris 1971	All operations lasted >2h and evaluated during 0-2h.
Nakajima 2002 (RCT)	Duration of anaesthesia about 3h.
Nguyen 2000 (RCT)	Duration surgery: laparoscopy 3.9h (SD 0.7); open 3.4h (SD

	0.6).
Roberts 1994	Mean 2.6h (SD 0.9).
Steinbrook 1997 (RCT)	Not stated.
Vorrakitpokatorn 2006	Duration of surgery 2h (SD 0.8); 44% had >2h.
Yamakage 2000	Approximately 3h.

Three studies included some children: Flores Maldonado (1997) ranged from 5 to 90 years (mean 42); Lau (2001) had 13% of the patients under 15 years; and Kongsayreepong (2003) had a range of 15 to 93 years (children ≤ 14 years were excluded from the analysis for this study). The GDG was concerned that large numbers of children may have been included in the Flores Maldonado (1997) study.

All studies but five (Baker 1995; Closs 1986; Lau 2001; Roberts 1994; Vorrakitpokatorn 2006) reported the theatre temperature.

- Eight studies had a mean or range around 20 to 21°C (Abelha 2005; Frank 1992; Frank 2000; Hind 1994; Kongsayreepong 2003; Kurz 1995; Nguyen 2000; Steinbrook 1997)
- Eight studies were around 22 to 24°C (Danelli 2002; Flores Maldonado 1997; Hendolin 1982; Kasai 2002, case-control; Kitamura 2000; Mizobe 2005; Stewart 1998; Yamakage 2000)
- Two studies were around 24 to 26°C (El-Gamal 2000; Nakajima 2002)
- One study had two groups at different temperatures: cool theatre 18 to 21°C; warm theatre 21 to 24°C (Morris 1971).

Eleven of the studies recorded the core temperature using a tympanic membrane thermometer (Abelha 2005; El Gamal 2000; Flores Maldonado 2007; Frank 1994; Frank 2000; Kasai 2002; Kitamura 2000; Kongsayreepong 2003; Nakajima 2002; Nguyen 2000; Vorrakitpokatorn 2006); one recorded temperature in the pulmonary artery (Baker 1995); two in the bladder (Danelli 2002; Stewart 1998); six in the oesophagus (Hind 1994; Kurz 1995; Mizobe 2005; Morris 1971; Roberts 1994; Steinbrook 1997); one in the rectum (Yamakage 2000); one sublingually using a reliable method (Frank 1992); one recorded aural or nasopharyngeal temperatures (Hendolin 1982) and one recorded aural temperatures, but not in the intra and immediate postoperative phases (Closs 1986). One study (Lau 2001) did not state the measurement site.

The studies varied in their use of warming mechanisms:

- Three stated that they did not warm the patients (Kitamura 2000; Roberts 1994; Steinbrook 1997)
- Eight did not state if there was a warming mechanism (Closs 1986; El-Gamal 2000; Flores Maldonado 1997; Hind 1994; Lau 2001; Mizobe 2005; Morris 1971; Nakajima 2002)
- One implied that some patients had forced air warming, but the number was not given

(Vorrakitpokatorn 2006)

- Six had no warming devices but fluids were warmed (Danelli 2002; Frank 1992; Frank 1994; Frank 2000; Kurz 1995; Yamakage 2000)
- One did not use warming devices, but gave the patients warmed blankets, and the blood temperature was maintained at 37°C (Baker 1995)
- One did not use warming devices but warmed the blood (Hendolin 1982)
- One study reported that all the patients had forced air warming (Stewart 1998)
- One RCT stated that all patients had forced air warming, but fluids were not warmed (Nguyen 2000)
- One study reported that 44% of patients were given 'warming techniques' intraoperatively and this was taken into account in the multivariate analysis (Abelha 2005)
- One study reported that 49% of patients were given forced air warming devices intraoperatively and this was assessed by univariate analysis and then not included in the multivariate analysis (Kongsayreepong 2003)
- One had a circulating water mattress and warmed fluids (Kasai 2002, case-control).

Risk factors investigated by the cohort studies (multivariate analyses) or RCTs

The following risk factors have been investigated in the included studies:

Patient characteristics

- Age
- Blood pressure (1 case control study)
- BMI (no studies; but body fat, body weight, 1 body weight/surface area reported)
- Gender
- Height
- Heart rate (1 case control study)
- Length of preoperative starvation (no studies)
- Temperature in the preoperative phase
- Temperature at first anaesthetic intervention
- ASA grade
- Score of Acute physiologic system (SAPS II)
- Pre-existing medical conditions (diabetes mellitus, thyroid disease, corticosteroid disease, cardiac disease).

Anaesthesia factors

- Duration of anaesthesia
- Type of anaesthesia
- Anaesthesia: end expiratory pressure
- Height of spinal block

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Surgery factors

- Urgency of operation: urgent, emergency, elective
- Type of surgery: according to NICE preoperative test guideline grade (none classified in this way)
- Magnitude of surgery (major, intermediate, minor)
- Laparoscopic/open surgery
- Duration of surgery
- Patient position intraoperatively

Other risk factors

- Irrigation fluids volume
- IV fluids volume
- Blood transfusion
- Blood loss
- Packed erythrocytes
- Forced air warming
- Temperature monitoring
- Particular hospital

Environmental factors

- Theatre temperature.

Outcomes

The studies measured the following outcomes:

Seven studies measured the incidence of IPH. The studies differed in their definitions of hypothermia:

- Three recorded the incidence of a core temperature less than 35.0°C (Abelha 2005; Lau 2001; Vorrakitpokatorn 2006)
- Four defined it as temperatures less than 36.0°C (El-Gamal 2000; Kongsayreepong 2003; Flores Maldonado 1997; Kasai 2002, case control)

Kongsayreepong (2003) also recorded the incidence of core temperatures less than 35.5°C and less than 35.0°C, and noted that multivariate analyses using these alternative definitions gave results consistent with those for a definition of less than 36.0°C.

The studies also differed in the phase of measurement: all but two (Flores Maldonado 1997; Kasai 2002, case control) measured the incidence in PACU or ICU; these exceptions measured the occurrence intraoperatively.

Three studies (El-Gamal 2000; Frank 2000; Morris 1971) carried out multivariate analyses for the core temperature and five RCTs (Frank 1994; Mizobe 2005; Nakajima 2002; Nguyen 2000; Steinbrook 1997) recorded the mean difference between interventions, in core temperature at different times.

METHODOLOGICAL QUALITY OF INCLUDED STUDIES

The methodological quality was assessed separately for the cohort studies and RCTs and details for each study design are given in Appendices C and D. Further details of the criteria are given in the general section.

RCTs

Three studies reported the method of randomisation and this was adequate in each case (Danelli 2002, random number sequence; Mizobe 2005, computer generated; Steinbrook 1997, coin toss). The other studies did not state the method.

Two studies reported a method of allocation concealment, in each case the method was partially adequate (Mizobe 2005, sequentially numbered envelopes; Nguyen 2000, sealed envelopes). The other studies did not state the method.

Blinding of the outcome assessors was carried out in two studies (Kinoshita 2004; Mizobe 2005), possibly carried out in two studies (Danelli 2002; Frank 1994) and definitely not carried out, or highly unlikely, in one study (Nguyen 2000). The other studies did not state the blinding.

All studies but one (Mizobe 2005) reported that all the patients were analysed. For these other studies there was less than 20% missing data. There was no difference in the extent of missing data between groups (where reported). Two studies carried out a power calculation (Danelli 2002; Nguyen 2000).

Baseline comparability was demonstrated in most of the studies. Two studies (Frank 1992; Frank 1994) were not comparable for the volume of crystalloid used (greater for general anaesthesia). However, this factor was taken into account in the analysis in the former. One other study (Steinbrook 1997) was not comparable at baseline for age, weight, intraoperative fluids (may not be significant difference). One study (Danelli 2002) had a significantly longer duration of surgery in the laparoscopic group (mean difference 1.1h). The GDG regarded the Steinbrook (1997) study to have potential for bias, but the other studies were considered acceptable.

Overall, only one study (Steinbrook 1997) was considered to have potential for bias on the basis of conventional quality assessment.

However, in terms of possible confounders, there are some features that may influence the results of the risk factors analyses even though these features were held constant or were likely to be distributed equally across groups:

- In one study all patients had forced air warming (Nguyen 2000). The GDG considered that other risk factors may depend on whether the patient is warmed. In another study (Steinbrook 1997) patients were selectively warmed if their temperatures fell below 35.0°C, which may have confounded the study
- One RCT had a high theatre temperature, 24 to 26°C (Nakajima 2002).

The Frank (1994) study, which randomised patients to general and epidural anaesthesia, reported non-randomised within-trial subgroups of older and younger patients (cut at 62 years, the median). We decided not to consider the subgroup comparison of older and younger patients, but the post-hoc subgroup analysis of general versus epidural for each of the age groups was considered acceptable. This is not ideal, because we are unclear about the distribution of baseline characteristics across the general and epidural groups within the two age subgroups, but the randomisation was at least partly retained.

Cohort studies

No study was considered to be truly representative of the population (i.e. all procedures under general or regional anaesthesia in adults).

Fifteen studies were considered to be somewhat representative of the community:

- Two studies (Abelha 2005; Kongsayreepong 2003) restricted the population to non-cardiac patients in ICU
- Closs (1986) was restricted to cholecystectomy and fractured femur operations
- Two studies (Kurz 1995; Stewart 1998) were restricted to colorectal surgery
- Lau (2001) was a study of all surgery carried out in Hong Kong public hospitals, but was limited to procedures lasting more than 2 hours; this study also had 13% patients under 15 years
- Two studies (Roberts 1994; Vorrakitpokatorn 2006) had percutaneous nephrolithotomy
- Morris (1971) was restricted to procedures over 2 hours
- The patients in El-Gamal (2000) all had orthopaedic surgery
- Flores Maldonado (1997) included some children
- The patients in Frank (1992) all had lower extremity vascular bypass grafting
- Frank (2000) had spinal anaesthesia for prostate surgery
- Hind (1994) had elective gynaecological surgery
- Kitamura (2000) examined a diabetes subgroup
- Yamakage (2000) had surgery on lumbar vertebrae.

Two studies were considered to be a selected group:

- Baker (1995): the patients were undergoing normothermic cardiopulmonary bypass. The GDG did not regard this as generalisable

In all studies, the non exposed cohort was drawn from the same community as the exposed cohort. All studies but two recorded the temperature at an adequate site. Closs (1986) recorded aural temperatures on the ward and Frank (1992) used a sublingual recording, but the method was detailed. All studies were prospective apart from Roberts (1994) and the case-control study.

All studies but three reported that all the patients were followed up. One (Closs 1986) did not say; Lau (2001) reported that 2159/20918 (10%) of patients had missing data; Kongsayreepong (2003) reported that 10/194 (5%) patients were deliberately excluded from analysis because they were children under 14 years or they were hyperthermic.

Five studies stated that the patients were not hypothermic preoperatively (El-Gamal 2000; Frank 1992; Morris 1971; Roberts 1994; Yamakage 2000); in two studies (Abelha 2005; Kongsayreepong 2003) some of the patients were hypothermic (<36.0°C by GDG definition) at the start of surgery: the patients in Abelha (2005) had a range of 35.0 to 38.6°C and mean 36.37°C; however these patients were not hypothermic according to the authors' definition (less than 35.0°C). The patients in Kongsayreepong (2003) had a range of 34.5 to 39.3°C (although hyperthermic patients were excluded from the analysis) and mean 37.0°C (authors' definition less than 36.0°C); 49% patients were warmed intraoperatively however. The rest of the studies did not say if the patients were hypothermic at the start of the intraoperative phase.

Confounders taken into account

We considered whether the studies took account of particular confounders, either in the study design or the multivariate analysis. The GDG had identified, by consensus, four risk factors to be important: age, ASA grade, type of anaesthesia, and duration of anaesthesia/surgery or magnitude of surgery.

Three studies were comparable at baseline apart from the study risk factor (El-Gamal 2000; Kitamura 2000; Morris 1971).

- El-Gamal (2000) (n=40) selected two cohorts of different ages, and held constant the ASA grade (I-II), the type of surgery (lower extremity orthopaedic) and the type of anaesthesia (general). The groups were also comparable at baseline for BMI, duration of surgery, IV fluid volume and preoperative core temperature. Overall 4/4 important confounders were taken into account. It is noted that the ratio of events:covariates is too small (4) for the dichotomous outcome.

- Kitamura (2000) (n=27) investigated the effect of diabetes, in older and younger age groups. The four groups were comparable for BMI, IV fluid rate, duration of surgery, ambient temperature. The type of anaesthesia was constant (general). However, the diastolic arterial blood pressure was significantly different for diabetes with and without neuropathy. The GDG did not consider this to be an important difference. Overall 3/4 important confounders were taken into account.
- Morris (1971) (n=22) investigated the effect of theatre temperature in subgroup analyses. There was no significant difference in age or site of operation between lower and higher temperature theatres. Duration of surgery was constant (all over 2 hours) as was the type of anaesthesia (general). Overall 2 to 3 of 4 important confounders were taken into account.

Four studies had all or most of the important confounders taken into account in the multivariate analysis (Abelha 2005; Frank 1992; Lau 2001; Vorrakitpokatorn 2006).

- In Lau (2001) (n=18,759), the multivariate analysis included age, ASA grade and type of anaesthesia. The duration of surgery was held partially constant – operations were selected if they lasted longer than 2 hours. Overall 3 or 4/4 important confounders were taken into account. There were 111 events for 4 covariates, i.e. ratio of 28, which is acceptable.
- In Vorrakitpokatorn (2006) (n=128), the multivariate analysis included age and duration of surgery. The type of anaesthesia was held constant (general). Overall 3/4 important confounders were taken into account (ASA grade was missing). There were 72 events for 4 covariates, i.e. a ratio of 18, which is acceptable.
- In Abelha (2005) (n=185), the multivariate analysis reported results for magnitude of surgery and SAPS II. It was also adjusted for anaesthesia type and anaesthesia duration. The SAPS II score (Simplified Acute Physiology Score) is used to predict death and is assigned after 24 hours of ICU admission. The score is derived from 12 physiologic variables, age and underlying disease variables (AIDS, metastatic cancer and haematologic malignancy). Thus, at least indirectly, this study does include all 4 important variables.
- Frank (1992) (n=97) was an RCT that also had multivariate analysis. This study had different types of analgesia for the two types of anaesthesia: the general anaesthesia group had morphine PCA and the epidural group had fentanyl. The GDG considered this difference to be acceptable. The study had 3/4 important risk factors.

Two studies were considered to be fairly acceptable - the multivariate analysis only had between 8 and 10 events per covariate (Kongsayreepong 2003; Flores Maldonado 1997).

- Kongsayreepong (2003) (n=184) included in the multivariate analysis: age, ASA grade, magnitude of surgery, type of anaesthesia and duration of surgery, i.e. 4/4 important confounders taken into account, but the ratio of events to covariates was 105/12 = 9

- Flores Maldonado (1997) (n=130) included in their multivariate analysis age, duration of surgery, magnitude of surgery, and type of anaesthesia, i.e. 3/4 important confounders taken into account, but the ratio of events to covariates was 53/7 = 8.

Five studies were considered to be possibly confounded because not enough of the important factors were included in the analysis (Baker 1995; Hind 1994; Kurz 1995; Closs 1986; Yamakage 2000).

- Hind (1994) (n=30) carried out two multivariate analyses on the same data.
- The first of these analyses (Hind 1994a) included age and kept constant the type of anaesthesia (general). Surgery duration was excluded from the analysis on the basis of univariate analysis. This meant that only 2/4 important confounders were taken into account. This study also had too many variables in total for the number of patients (30/6 = 5).
- The second analysis (Hind 1994b) included none of the important factors, but kept constant the type of anaesthesia (general). Surgery duration was excluded from the analysis on the basis of univariate analysis. This meant that only 1/4 important confounders were taken into account.
- In addition, the Hind (1994) study reported many correlations between 'independent' variables, i.e. confounding. For example, between age and theatre temperature or body fat or IV fluids or blood loss. Body fat also correlated with theatre temperature. The authors commented that the age-theatre temperature correlation was possibly due to the fact that older patients were put first on the operating list, which was when the theatre was colder.
- Baker (1995) (n=56) included age and type of surgery of the important factors (i.e. 2/4 confounders taken into account). This study also had a large number of other variables in the multivariate analysis, so that the number of patients per covariate was 56/13 = 4.
- Closs (1986) (n=31) was only adjusted for age in the analysis, i.e. 1/4 important risk factors. In addition, no data were recorded during the intraoperative and immediate postoperative periods.
- In Kurz (1995) (n=40), the multivariate analysis included none of the important variables. The type of anaesthesia was constant (general); the patients had colon surgery and the mean duration was 3.8 hours (SD 1.3). The type of surgery was reported to be comparable for different size patients. Thus, account was taken of 2 of 4 important factors.
- In Yamakage (2000) (n=60), the type of anaesthesia was held constant (general) and the surgery type was fairly specific (on lumbar vertebrae) and had a duration of approximately 3 hours. Age was partly adjusted in the body fat calculator. Thus account was taken of 2 to 3 of 4 important factors.

Three studies did not have enough events or patients for the number of variables included in the multivariate analysis (Hind 1994a, see above; Baker 1995, see above; Frank 2000). The

Frank (2000) study had 44 patients for 6 covariates, i.e. 7 patients per covariate, which is slightly low.

The remaining two cohort studies were considered to be confounded: Roberts (1994) used a subgroup analysis, but confounders were not allowed for and were not comparable at baseline for duration of surgery. In Stewart (1998), all patients having open surgery had combined general/epidural anaesthesia, but all receiving laparoscopic surgery had general anaesthesia, leading to confounding.

Other factors:

- The Stewart (1998) study reported that all the patients were given forced air warming; Abelha (2005) reported that 44% of patients were given forced air warming devices, but this was taken into account in the multivariate analysis; Kongsayreepong (2003) reported that 49% of patients were given forced air warming devices and this was assessed by univariate analysis and then not included in the multivariate analysis; the case control study gave the patients a circulating water mattress and warmed fluids (Kasai 2002).
- As mentioned earlier, the GDG was concerned that large numbers of children may have been included in the Flores Maldonado (1997) study.
- One study (El-Gamal 2000) had high theatre temperatures (24 to 26°C).

Overall the GDG decided that five studies were confounded: Roberts (1994), Stewart (1998), as above; Baker (1995), because of the type of surgery and low ratio of events to covariates; and the Closs (1986) and Hind (1994b) studies, each of which had only one of the four important factors. These studies were not considered in the analyses. The case control study was also considered to have greater potential for bias, and was not included further.

Four studies were treated cautiously, three because there were only 2/4 important factors included (Hind 1994a; Kurz 1995; Yamakage 2000). The Hind (1994a) study also had too many variables in total for the number of patients (30/6 = 5) and the Frank (2000) study had a ratio of 44/6 (=7). The presence of warming devices in about half of the patients in Kongsayreepong (2003) study without adjustment in the multivariate analysis was also taken into consideration, as was the Flores Maldonado (1997) study because it included children. All these studies at higher risk of bias were considered in sensitivity analyses.

RESULTS (see Appendix F for more details)

The results for the different risk factors are given in Appendix F. We consider below the effects of different risk factors on the incidence of hypothermia or the core temperature.

A. PATIENT RELATED RISK FACTORS

1. Age

Meta-analysis was not possible in many instances because the risk factor comparators were different (Figure 1). However, it was possible to combine two studies that had less than 40 years as a comparator (Kongsayreepong 2003; El-Gamal 2000) (Figure 2).

a) Incidence of IPH intraoperatively

One study (Flores Maldonado 1997) reported the effect of age on the incidence of IPH (temperature less than 36.0°C) intraoperatively. The multivariate analysis in 130 patients gave no numerical data for this risk factor, simply reporting that the effect was non significant for age as a continuous variable (mean 42 years, SD 20 years). Anaesthesia was general or regional and the theatre temperature was 22.9°C.

b) Incidence of IPH in PACU or ICU

Four cohort studies (Kongsayreepong 2003 (n=184; temperature less than 36.0°C); El-Gamal 2000 (n=40; temperature less than 36.0°C); Lau 2001 (n=18,759; temperature less than 35.0°C); Vorrakitpokatorn 2006 (n=128; temperature less than 35.0°C)) investigated the effect of age on the incidence of IPH postoperatively. Each study considered age as a categorical variable. The incidence of IPH did not appear to be affected by adult age, but, in the large Lau 2001 study (18,758 patients), older adults (over 65 years), in comparison with children under 15, had significantly more patients with a core temperature below 35°C. The meta-analysis (Figure 2) of two studies in 224 patients compared older cohorts (over 65 or over 70 years) with a younger cohort (under 40). There was no statistically significant difference between cohorts in the number of patients with temperatures below 36.0°C, but the younger group was favoured. There was no heterogeneity (I^2 = 0%).

El-Gamal (2000) had a theatre temperature greater than 24°C; Kongsayreepong (2003) had a temperature of 20 to 21°C and the others did not say. The confidence intervals are generally wide, which gives uncertainty to the results.

Figure 1: Age – incidence of IPH in ICU/PACU

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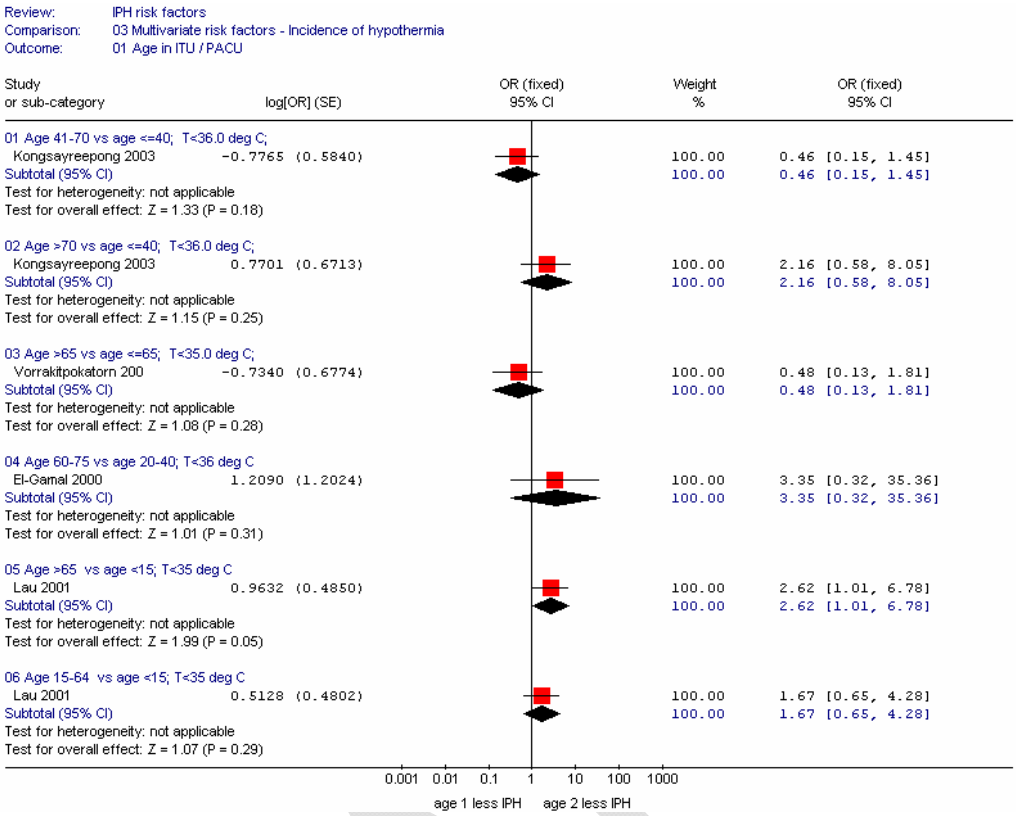
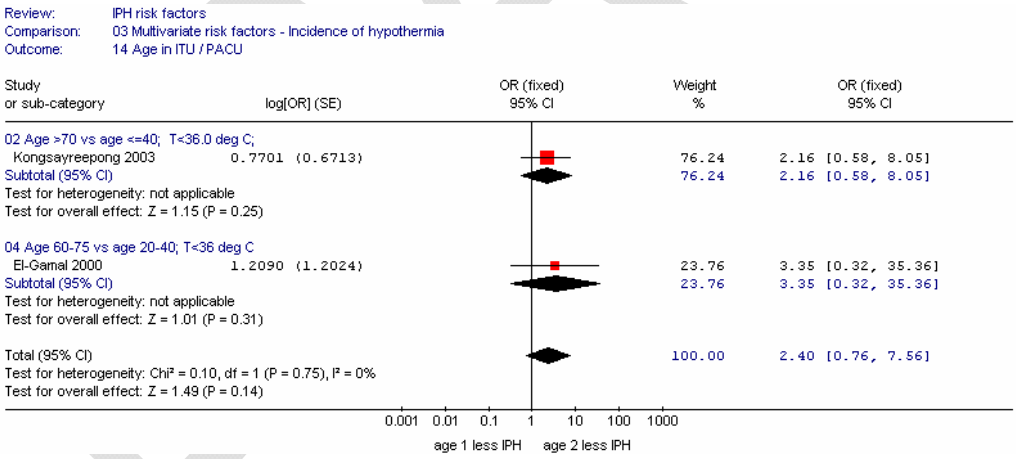


Figure 2: Age older cohort versus younger (under 40 years) cohort (not overlapping) – incidence of IPH in ICU/PACU



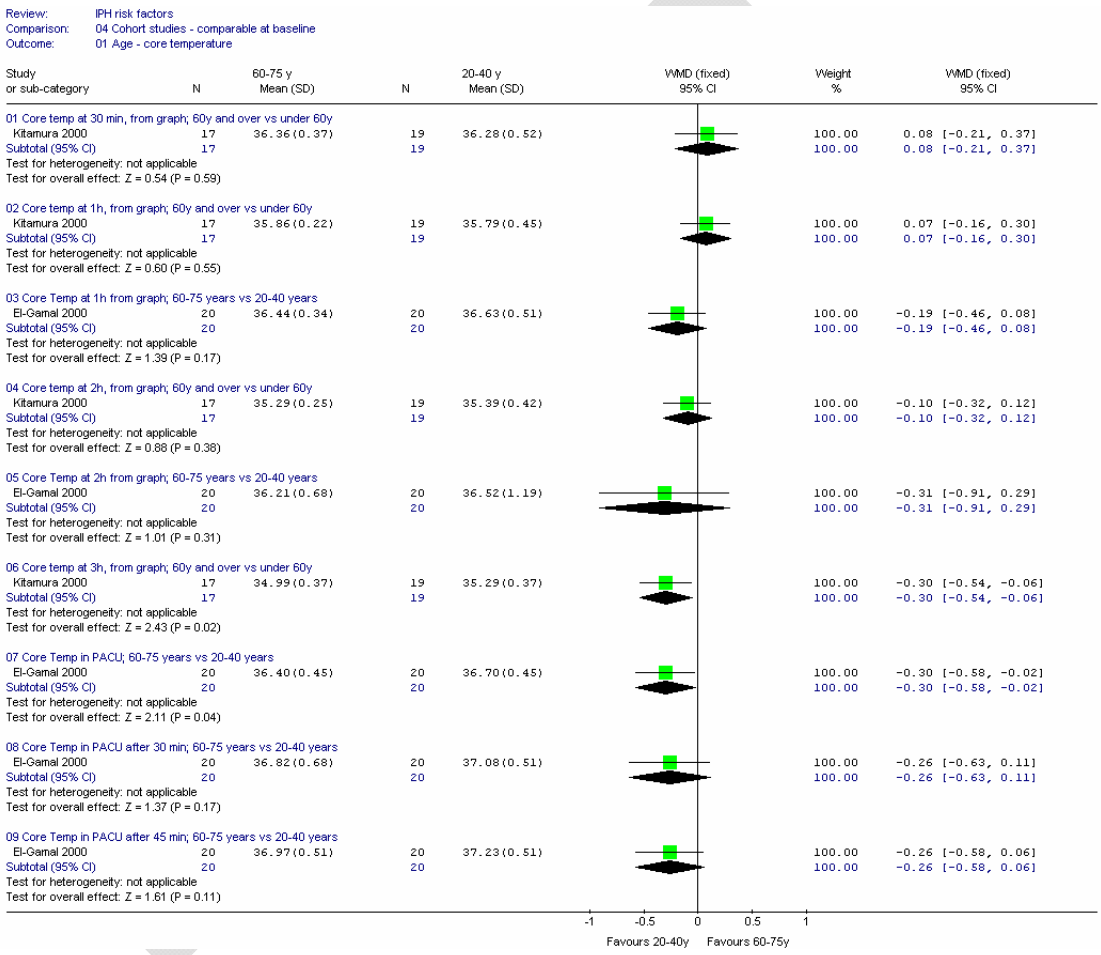
c) Core temperature

Two cohort studies, El-Gamal (2000) in 40 patients and Kitamura (2000) in 36 patients reported the effect of age on core temperature at various times after the start of general anaesthesia (the mean duration of surgery was 1.7 to 1.8 h and 3.1 to 3.3 h respectively). The El-Gamal (2000) study included two cohorts of patients aged 60 to 75 years and 20 to 40 years, and the Kitamura (2000) study divided the cohort into older (60 years and older) and younger (less than 60 years) patients. The results are shown in Figure 3. There is no significant difference between age groups, until 3 hours after the start of surgery and on arrival in PACU, where the younger group had significantly higher temperatures (WMD: 3

hours: -0.30°C (95%CI -0.54, -0.06); PACU: -0.30°C (95%CI -0.58, -0.02)), however, the confidence intervals are fairly wide or wide. At shorter durations, the younger cohort is favoured.

A third study (RCT with multivariate analysis), Frank (2000), reported that, for patients aged 47 to 67 years, age had a statistically significant effect on core temperature in PACU. Treating age as a continuous variable, gave a 'b' coefficient of 0.03°C/year (p=0.01). The mean duration of surgery was 1.5 hours.

Figure 3: Age - older cohort versus younger (under 40 years) cohort (not overlapping) – core temperatures

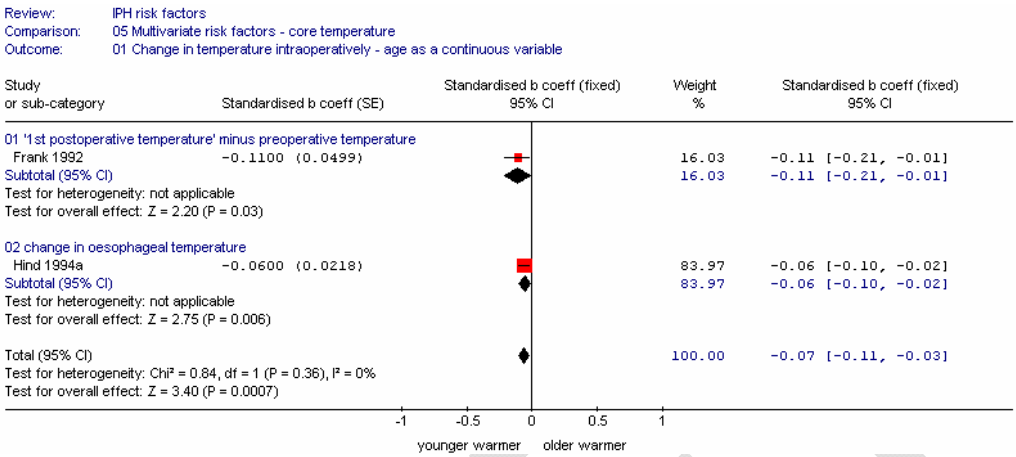


d) Change in core temperature

Two cohort studies (Frank 1992; Hind 1994a), in 97 and 30 patients respectively, carried out multivariate analyses for the change in core temperature intraoperatively. For Frank (1992), this was the difference between the 'first postoperative temperature' and the preoperative temperature. For Hind (1994), the change in oesophageal temperature was reported but it was not stated when this was measured. The durations of surgery were over 4 hours for Frank (1992) and 1 to 2 hours for Hind (1994). Both studies reported the unstandardised 'b' coefficients and Hind (1994) also reported the standardised ß coefficient. Meta-analysis

showed a statistically significantly larger decrease in temperature for older patients, with no heterogeneity (I^2=0%); mean -0.07°C/year (95%CI -0.11, -0.03) (Figure 4). We note, however, that the Hind (1994) study had methodological imperfections.

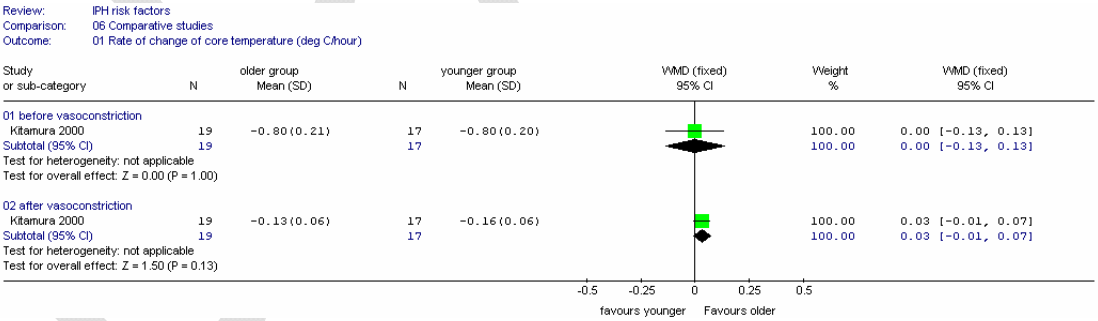
Figure 4: Age – continuous variable – change in core temperature



e) Rate of change of temperature in intraoperative phase

One cohort study (Kitamura 2000), in 36 patients, recorded the rate of change of core temperature before and after vasoconstriction and found no significant difference between older (≥60 years) and younger (less than 60) patients at either time.

Figure 5: Age over or equal to 60 years versus under 60 years – rate of change of temperature



f) Time for rewarming to 36.0°C

One study (Frank 1992) reported a borderline significant decrease in the time for rewarming to 36°C for younger patients. The standardised ß coefficient was 0.111 hours per year ($p \leq 0.05$).

Conclusions for age as a risk factor

The evidence suggests that age is not an important risk factor for the incidence of hypothermia either intraoperatively or postoperatively, although the data on core temperature suggests that older people (over 60 years) have lower temperatures after 3 hours of surgery and in PACU. There does not appear to be a sensible cut-off point above

which adult patients are at higher risk of perioperative hypothermia, although 60 years is a possibility.

There is some evidence that older patients take longer to rewarm to 36°C postoperatively.

The GDG noted that some consequences of hypothermia are more severe for older people, especially morbid cardiac events.

2. Gender

a) Incidence of IPH intraoperatively

One cohort study (Flores Maldonado 1997) in 130 patients showed no significant effect of gender on the incidence of IPH (temperature less than 36.0°C) using multivariate analysis, but no numerical data were given (see Appendix F). This study may have had a less representative population (some children included).

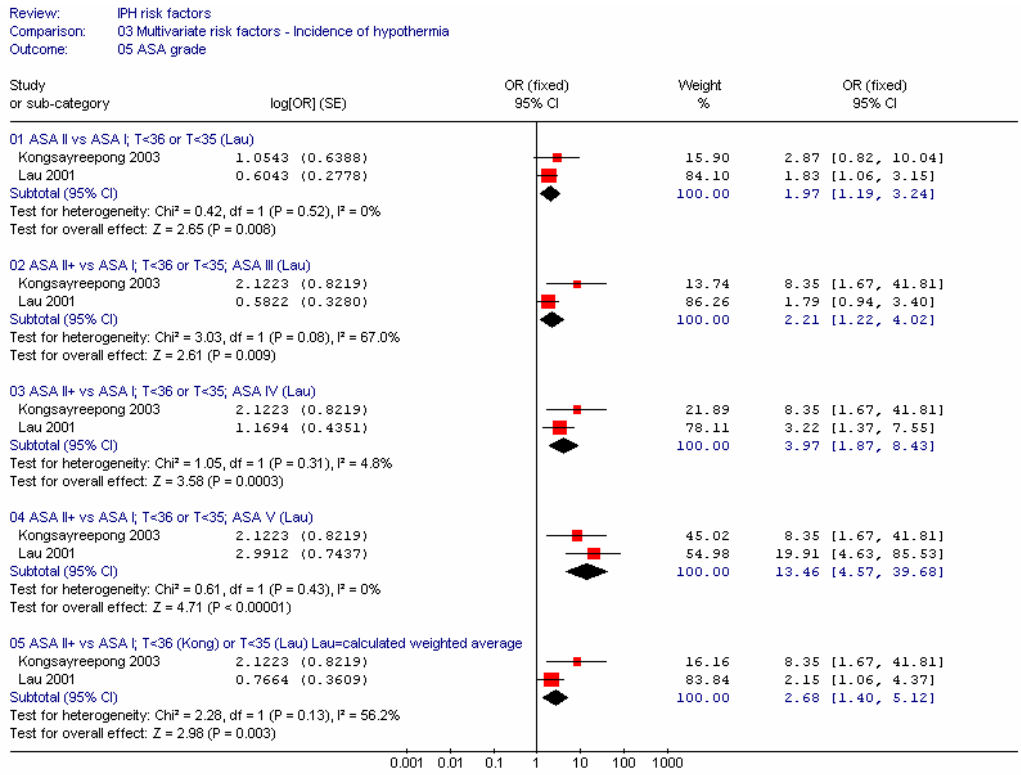
3. ASA grade

a) Incidence of IPH in PACU or ICU

Two cohort studies (Kongsayreepong 2003; Lau 2001), in 184 and 18,759 patients respectively, investigated the effect of ASA grade on the incidence of IPH in PACU or ICU, using multivariate analysis. Lau (2001) subdivided the patients into categories I, II, III, IV, V and Kongsayreepong (2003) into I, II and higher than II. We carried out meta-analyses using either ASA III versus ASA I, ASA IV versus ASA I, or ASA V versus ASA I for the Lau (2001) study in combination with the Kongsayreepong (2003) comparison, ASA above II versus ASA I (Figure 6). The proportion of patients in the Kongsayreepong (2003) study in the higher ASA groups was not given. We note that the Kongsayreepong (2003) study defined IPH as temperature below 36.0°C, whereas the Lau (2001) study used below 35.0°C. The former also reported that 49% of the patients had forced air warming, which was not taken into account in the multivariate analysis.

Meta-analysis of ASA II versus ASA I showed a statistically significant difference favouring ASA I (OR 1.97 (95%CI 1.19, 3.24) with no heterogeneity (I^2=0%), which suggests the difference in the definition of hypothermia may not be important (and the Kongsayreepong (2003) study suggested that the results in their study were consistent regardless of the definition). There are also statistically significant differences at higher ASA grades compared with ASA I, increasing, in the Lau (2001) study, with ASA grade. There is, however, some heterogeneity for the combination of ASA III versus ASA I with ASA II+ versus ASA I. This could be because the ASA II+ in Kongsayreepong (2003) was closer to ASA IV and V (although patients with these grades are rarer); it could possibly be related to the definition of hypothermia, or some other factor. It is notable that Lau (2001) shows a similar odds ratio for both ASA II and ASA III in comparison with ASA I.

Figure 6: Effect of ASA grade – incidence of IPH



To obtain an indication of the effect of any ASA grade above II for the Lau (2001) study, we calculated a weighted odds ratio (using log odds) and a weighted standard error, and combined these statistics in a meta-analysis with the Kongsayreepong (2003) study. This gave an odds ratio of 2.68 (95%CI 1.40, 5.12), with some heterogeneity (I^2=56%, p=0.13).

Conclusion for ASA as a risk factor

ASA grade greater than ASA I is a risk factor for perioperative hypothermia, and the risk increases with ASA grade.

4. Body fat/body weight/height

Five cohort studies (Frank 2000; Hind 1994a; Kongsayreepong 2003; Kurz 1995; Yamakage 2000) investigated the effect of body fat or body weight, either on the incidence of IPH or on core temperatures. Both body fat and body weight were treated as continuous variables. One study investigated the effect of height (Kurz 1995). No studies investigated body mass index (BMI).

Meta-analysis was not carried out, either because of a lack of data – some studies reported only whether or not the factor was significant (Kurz 1995; Frank 2000; Hind 1994a; Yamakage 2000 for some outcomes) – or because of different outcome measures. We note that the Kurz (1995), Hind (1994) and Yamakage (2000) studies are possibly confounded

because they used only 2 out of the 4 important risk factors in the multivariate analyses, and the Hind (1994) study also reported correlations between body fat and age (with an unexpected negative correlation), and body fat and theatre temperature.

Appendix F summarises all the results.

Kongsayreepong (2003) reported a mean weight of 57.2kg (SD 12) and a range of 30 to 91kg, which suggests children were included.

Kurz (1995) reported a mean height of 169 cm (SD 7), range 152 to 180 cm; and a mean weight of 73 kg (SD 20), range of 40 to 110 kg; the body fat ranged from 15 to 49%.

Frank (2000) reported a mean weight of 88kg (SD 20) and range 70 to 120 kg; the body fat mean was 27% (SD 7), with a range of 13 to 39%.

Hind (1994) reported a mean body fat content of 23.7% (SD 5.6); range 15 to 39.4%.

Yamakage (2000) reported a mean height of 159 cm (SD 7); and weight 63 kg (SD 8).

a) Incidence of IPH in ICU

One cohort study (Kongsayreepong) in 184 patients showed a small statistically significant effect of body weight on the incidence of IPH (temperature less than 36.0°C) in ICU, using multivariate analysis; OR 0.94 (95%CI 0.89, 0.98), with less hypothermia for a higher body weight.

b) Core temperature

The Kurz (1995) study in 40 patients reported no significant effect of body weight on change in core temperature over the first hour of surgery (no numerical data given), but there was a statistically significant effect identified with body fat (0.016°C/%, $p<0.01$) and with body weight divided by surface area (0.033°C.m^2/kg). Yamakage reported that there was no statistically significant effect of body fat on the change in core temperature at 1 hour ($p=0.054$), however no numerical data were given.

At 2 hours, the Yamakage (2000) study in 60 patients reported a statistically significant effect of body fat on change in core temperature (0.03°C/%; $p<0.0001$) but Hind (1994) (n=30) found no significant effect of body fat on the change in core temperature intraoperatively (time not stated or data given). The latter study also reported correlations between body fat and age, and body fat and theatre temperature, and had more than one methodological limitation.

Frank (2000) (n=44) reported no significant effect of body fat or body weight on the core temperature in PACU (p=0.14).

Kurz (1995) (n=40) reported no significant effect of height on change in core temperature over the first hour of surgery (data not given). This study was possibly confounded because the authors used only 2 out of the 4 important risk factors in the multivariate analysis.

Conclusions for body fat/weight and height as a risk factor

Increased body weight may have a small protective effect on the incidence of perioperative hypothermia in ICU. The evidence for body weight and body fat intraoperatively is inconsistent. There is no significant effect of height on IPH in a poorer quality study.

5. Comorbidities – diabetes

Two cohort studies investigated diabetes as a risk factor for IPH (Kongsayreepong 2003 (n=184); Kitamura 2000 (n=27)). The Kitamura (2000) study divided the cohort into diabetics (with and without neuropathy) and controls; the groups in the comparisons considered below were comparable at baseline for characteristics other than those under study. Kongsayreepong (2003) carried out a multivariate analysis which included the risk factor, history of diabetic neuropathy.

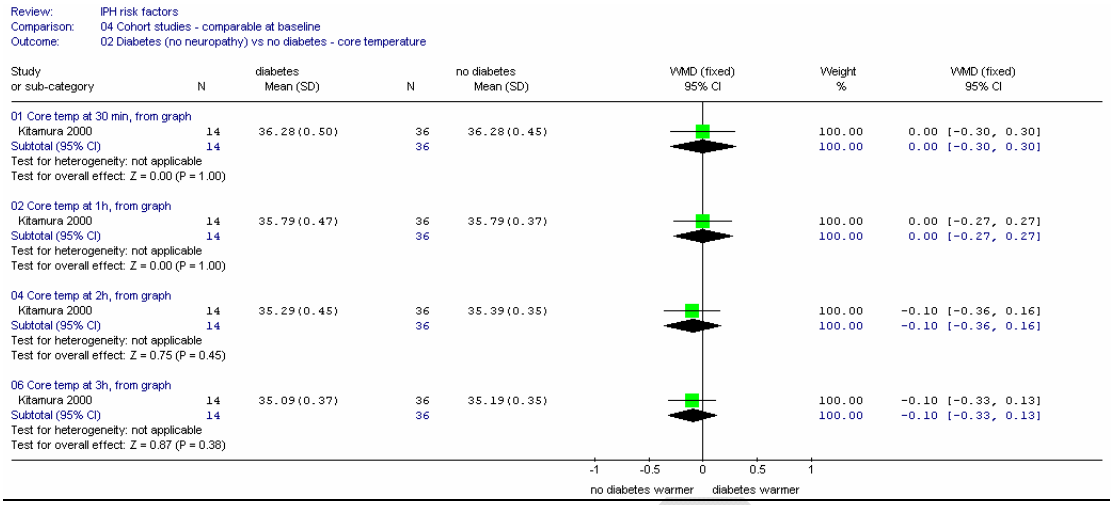
a) Incidence of IPH in ICU

Kongsayreepong (2003) investigated the effect of a history of diabetic neuropathy compared with no history on the incidence of IPH in ICU (temperature less than 36.0°C) and found no significant difference; OR 0.86 (95%CI 0.24, 3.14); 14% of patients were reported to have diabetic neuropathy.

b) Core temperature

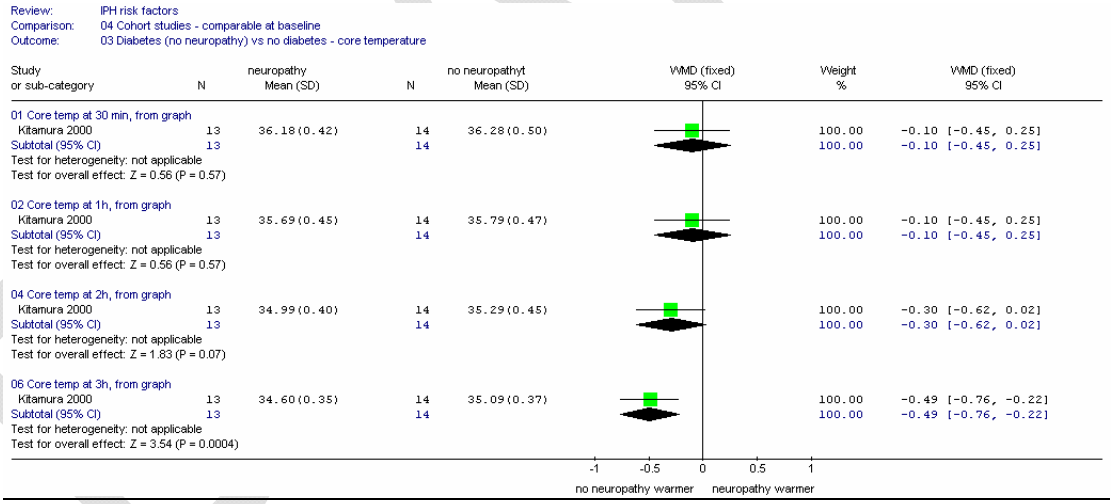
Kitamura (2000) reported the core temperature intraoperatively, for groups of patients with diabetes and no neuropathy versus those without diabetes. There were no significant differences between groups at any time, although the confidence intervals are fairly wide.

Figure 7: Effect of diabetes – core temperature



Kitamura (2000) reported the core temperature intraoperatively, for groups of patients with diabetes, with and without neuropathy. There were no significant differences between groups until three hours, at which time the neuropathy group had significantly lower core temperatures; mean difference: -0.49°C (95%CI -0.76, -0.22). The confidence intervals are fairly wide.

Figure 8: Effect of diabetic neuropathy – core temperature



Conclusion for diabetes

Diabetes without neuropathy is not a risk factor for IPH, but patients with diabetic neuropathy have significantly lower core temperatures than diabetic patients without neuropathy after three hours of surgery.

6. Patient temperature preoperatively

a) Incidence of IPH in ICU

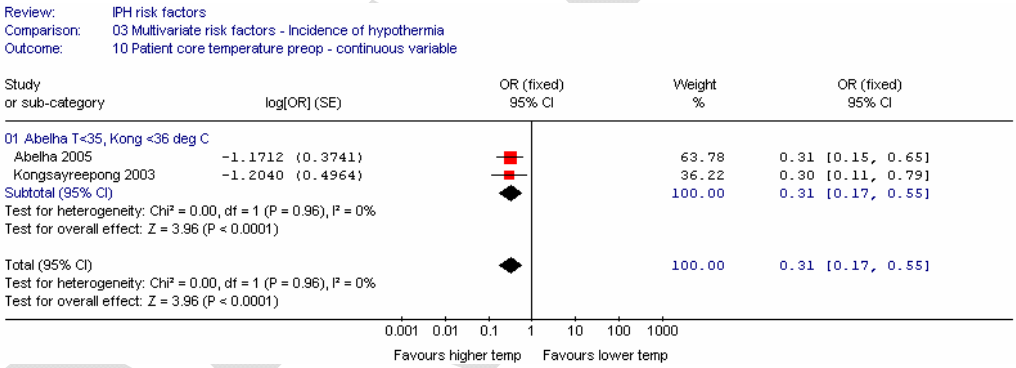
Two cohort studies (Kongsayreepong 2003; Abelha 2005) included patient preoperative temperature in the multivariate analyses of incidence of IPH in ICU (Abelha (2005) defined

hypothermia as temperatures below 35.0°C; Kongsayreepong (2003) used below 36.0°C). The mean core temperature initially in Abelha (2005) was 36.37°C (SD 0.49), range 35.00 to 38.60; in Kongsayreepong (2003) it was 37.0°C (SD 0.7) range 34.5 to 39.3 (although hyperthermic patients were excluded from the analysis). We note also that warming devices were used in both studies, but only Abelha (2005) took this into account in the multivariate regression analysis. The studies did not report the perioperative stage in which warming devices were used.

Meta-analysis of 369 patients found a statistically significant effect of preoperative temperature (Figure 9); OR 0.31 (95%CI 0.17, 0.55), with a remarkably high homogeneity (I^2=0%, p=0.96), despite differences in the definition of IPH.

GDG consensus was that patients arriving in the holding area with temperatures below 36.0°C should not undergo surgery until their temperature has been raised, except in an emergency.

Figure 9: Effect of patient preoperative temperature – incidence of IPH in ICU



Conclusion

A low preoperative temperature is a significant risk factor for IPH.

B. ANAESTHESIA RISK FACTORS

1. Type of anaesthesia

Eight studies investigated the effect of type of anaesthesia (Abelha 2005; Flores Maldonado 1997; Frank 1992; Frank 1994; Hendolin 1982; Kongsayreepong 2003; Lau 2001; Steinbrook 1997). Four of these were RCTs (Frank 1992; Frank 1994; Hendolin 1982; Steinbrook 1997) and the others were cohort studies. In the latter, different approaches were taken to the analysis: Lau (2001) compared, separately, regional anaesthesia or combined anaesthesia versus general anaesthesia (reference); Abelha (2005) compared, separately, general anaesthesia or combined anaesthesia versus regional anaesthesia (reference). Flores Maldonado (1997) considered spinal, epidural and general anaesthesia as separate categories and Kongsayreepong (2003) included categories of general, regional

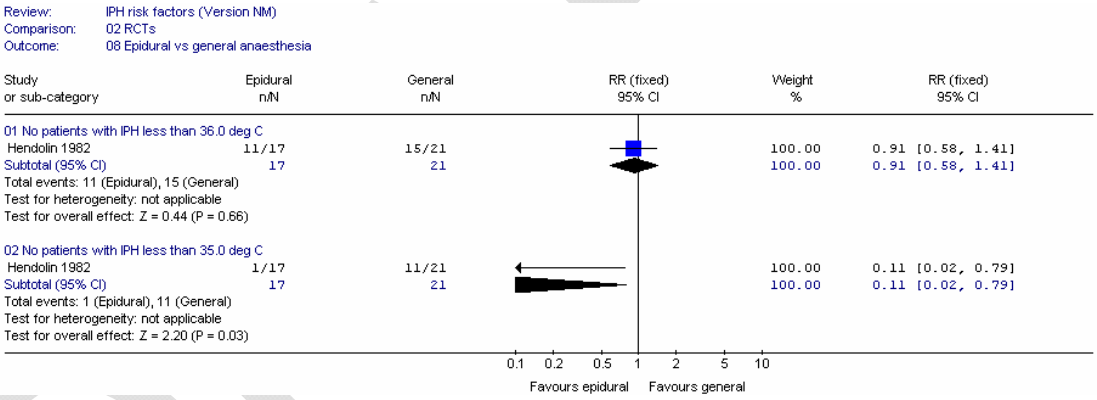
and combined anaesthesia. In the latter two studies, this meant that, for example, spinal was compared with the remaining categories (general and epidural).

1.1 Regional versus general anaesthesia

a) Incidence of IPH intraoperatively

Two studies compared regional and general anaesthesia as risk factors for the incidence of IPH intraoperatively (Flores Maldonado 1997 (n=130); Hendolin 1982 (n=38)). Flores Maldonado (1997) reported that there was no significant difference in the incidence of IPH (temperature below 36.0°C) between general anaesthesia and spinal or epidural anaesthesia, but no numerical data were given. Hendolin (1982) was a small RCT that compared general versus epidural anaesthesia in 38 patients, and recorded the incidence of hypothermia according to two definitions, less than 36.0°C and less than 35.0°C (figure 10). There was no significant difference when the definition less than 36.0°C was applied, but for a temperature below 35.0°C, there was a statistically significant difference favouring epidural anaesthesia, although the confidence interval is very wide.

Figure 10: Regional versus general anaesthesia

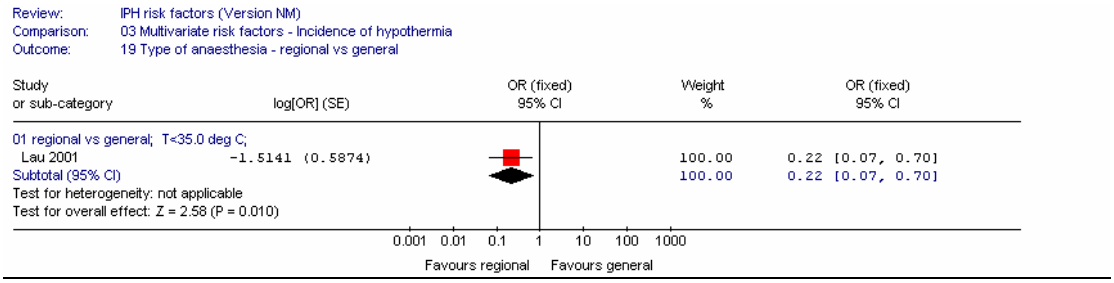


b) Incidence of IPH in PACU or ICU

Two studies compared regional versus general anaesthesia as risk factors for the incidence of IPH in PACU or ICU (Abelha 2005; Lau 2001). Both studies defined IPH as less than 35.0°C. Abelha (2005) reported that the type of anaesthesia was adjusted for in the multivariate analysis, but no results were given. It is assumed this was not significant.

The Lau (2001) study in 18,759 patients, however, found a statistically significant odds ratio for the incidence of IPH below 35.0°C, favouring regional anaesthesia; OR 0.22 (95%CI 0.07, 0.70), although the confidence interval is wide.

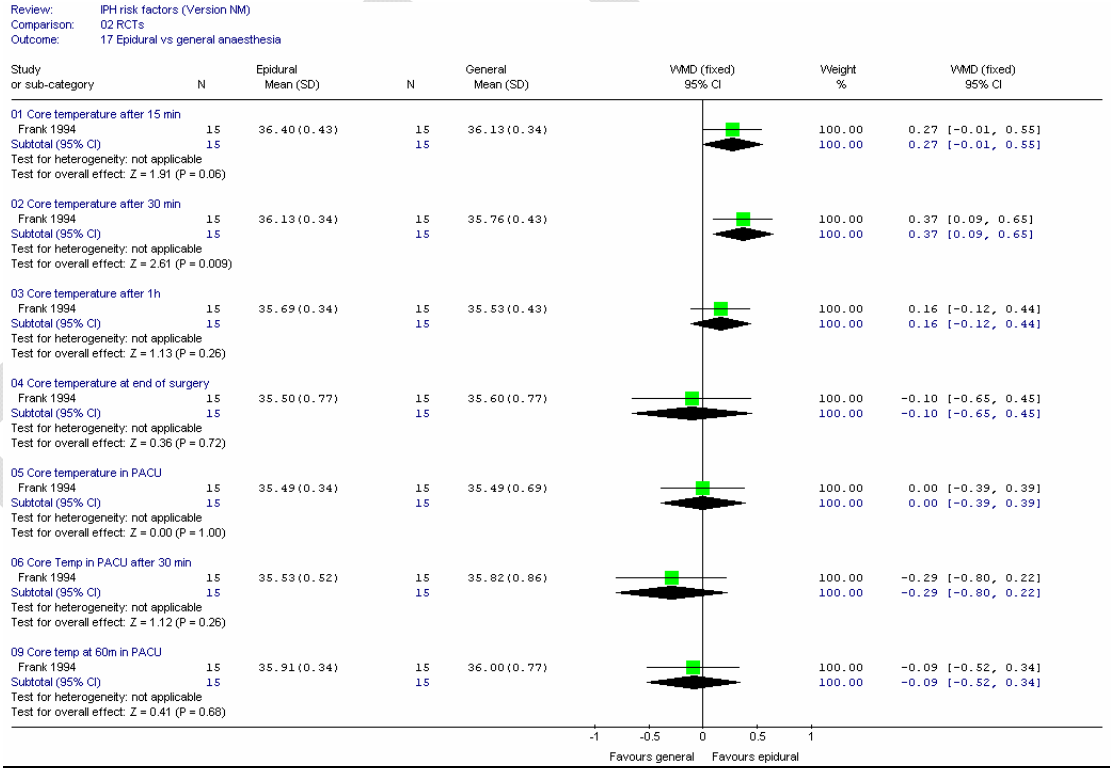
Figure 11: Regional versus general anaesthesia



c) Core temperature intraoperatively (Figure 14)

One RCT in 30 patients compared general with epidural anaesthesia and recorded core temperatures at various times intraoperatively (Frank 1994). Fluids were warmed for both groups. The study showed a statistically significant difference 30 minutes after induction of anaesthesia, with the epidural groups being warmer, but thereafter there was no significant difference between groups. The confidence intervals were fairly wide or wide. At 30 minutes the mean difference was 0.37°C (95%CI 0.09, 0.65), for a general anaesthesia group temperature of 35.8°C.

Figure 12: Regional versus general – core temperature intra- and postoperatively



Overall, it is unclear whether regional anaesthesia constitutes less of a risk than general anaesthesia. This is emphasised by the evidence from the small Hendolin (1982) study that indicates that conclusions depend on the definition of IPH. We were therefore reluctant to take the results from the Lau (2001) study for the incidence of IPH (temperature less than 35.0°C) in PACU, also taking into consideration the Abelha (2005) study (temperature less

than 35.0°C, not significant) and the intraoperative incidence of IPH (temperature less than 36.0°C, not significant) from the Flores Maldonado (1997) study. We have therefore erred on the side of caution and concluded that the risk of IPH has not been shown to differ between general and regional anaesthesia.

1.2 Combined versus not combined

Two studies analysed the effect of combined (both general and regional) anaesthesia versus not combined. Kongsayreepong (2003) compared combined anaesthesia with general and regional separately in 184 patients and Lau (2001) compared combined with general anaesthesia in 18,759 patients.

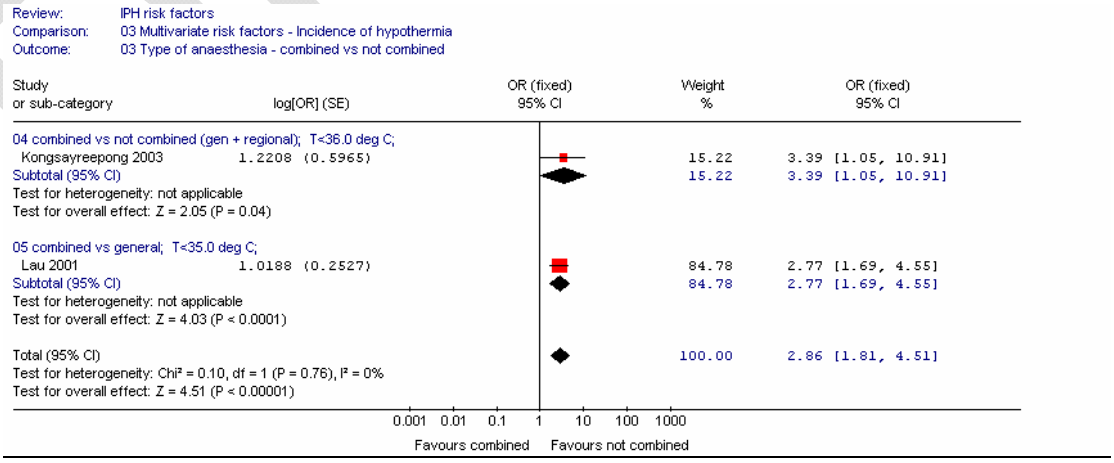
a) Incidence of IPH in PACU or ICU

Kongsayreepong (2003) found a statistically significant odds ratio for the incidence of IPH in ICU (temperature less than 36.0°C), favouring general and regional anaesthesia; OR 3.39 (95%CI 1.05, 10.91), although the confidence interval was wide.

Lau (2001) found a statistically significant odds ratio for the incidence of IPH in PACU (temperature less than 35.0°C), favouring regional anaesthesia; OR 2.77 (95%CI 1.69, 4.55).

Meta-analysis of the two studies in 18,943 patients gave a statistically significant odds ratio of 2.86 (95%CI 1.81, 4.51), favouring non-combined anaesthesia, with no heterogeneity (I^2=0%, p=0.76).

Figure 13: Combined versus not combined anaesthesia – core temperature intra- and postoperatively



Conclusions for type of anaesthesia

The following conclusions were drawn:

1. Two studies showed that there was no significant difference for general versus regional anaesthesia in the incidence of IPH (temperature less than 36.0°C) intraoperatively, but in a small study (n=38) there was a statistically significant difference favouring epidural anaesthesia for temperatures less than 35.0°C. The confidence interval was very wide in the latter.
2. One RCT in 30 patients showed a significant difference for general versus epidural anaesthesia in core temperature at 30 minutes intraoperatively, favouring epidural anaesthesia, but the confidence interval was fairly wide. There were no significant differences at 15 minutes or one hour or in PACU.
3. Two studies compared the incidence of IPH (temperature less than 35.0°C) in PACU for general versus regional anaesthesia. One of these appeared to report there was no significant difference, but the other, very large study reported significantly less IPH for regional anaesthesia.
4. Meta-analysis of two studies (one very large) showed the incidence of IPH in ICU or PACU was significantly higher for combined general and regional anaesthesia compared with general or regional anaesthesia separately. The definition of hypothermia did not seem to be important.

2. Duration of anaesthesia and duration of surgery

Six studies investigated the effect of the duration of anaesthesia or the duration of surgery on the incidence of hypothermia or changes in temperature (Abelha 2005 (n=185); Flores Maldonado 1999 (n=130); Frank 1992 (n=97); Frank 2000 (n=44); Kongsayreepong 2003 (n=184); Vorrakitpokatorn 2006 (n=128)). The studies investigated duration in different ways, either as a continuous variable, or as groups dichotomised at a threshold value. One study split the patients at 3 hours of anaesthesia (Abelha 2005) and two at 2 hours (Kongsayreepong 2003; Vorrakitpokatorn 2006). None of the studies considered 1 hour as a suitable cut-off point.

a) Incidence of hypothermia intraoperatively

One study (Flores Maldonado 1999) investigated the effect of duration of surgery as a continuous variable (mean duration 83 minutes, SD 59) for IPH (temperature less than 36.0°C) in 130 patients. The authors stated there was no significant effect, but numerical data were not given.

b) Incidence of hypothermia in ICU

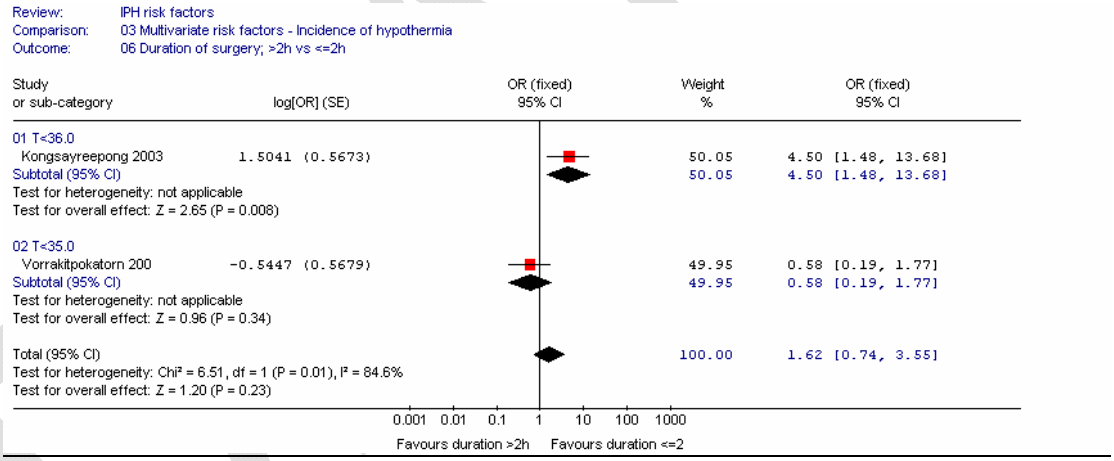
One study (Abelha 2005) in 185 patients investigated the effect of the duration of anaesthesia on the incidence of IPH (temperature less than 35.0°C) in ICU in 185 patients. The study reported that the duration of anaesthesia, as subdivided into above and below 3 hours, was analysed in a multivariate analysis, but no results were given. It is assumed not to be significant. The range of anaesthesia time was 44 minutes to 11 hours.

Two studies recorded the effect of duration of surgery as a risk factor for the incidence of IPH in PACU or ICU. Kongsayreepong (2003) (temperature less than 36.0°C) and Vorrakitpokatorn (2006) (temperature less than 35.0°C) both investigated the duration of surgery, as subdivided into above and below 2 hours. The studies differed as follows:

- In their definitions of hypothermia (less than 36.0°C and less than 35.0°C respectively)
- In their recovery areas, which were respectively ICU and PACU
- In the range of durations of surgery: Kongsayreepong (2003) had a range of 0.25 to 10.25 h; Vorrakitpokatorn (2006) had a mean duration of 2 h (SD 49 minutes)
- Kongsayreepong (2003) also had 49% patients receiving warming mechanisms, which factor was not used in the multivariate analysis.

There was a statistically significant effect for Kongsayreepong (2003) favouring shorter times, but no significant difference for Vorrakitpokatorn (2006). In the meta-analysis of the two studies, there was significant heterogeneity (I^2=85%, p=0.01), and the confidence intervals are wide.

Figure 14: Duration of surgery above and below 2 hours – incidence of hypothermia



Overall the GDG concluded that the Kongsayreepong (2003) study was more reliable because of the greater range of operation durations and the definition of hypothermia, however there may have been confounding because of patient warming.

c) Change in core temperature intraoperatively

One study (Frank 1992) in 97 patients investigated the effect of time in the theatre, as a continuous variable, for mean durations of 4.4 to 6.6 h. The authors reported that there was no significant effect, but no data were given.

d) Core temperature in PACU

One study (Frank 2000) in 44 patients investigated the effect of duration of surgery as a continuous variable, for a range of surgery of 65 to 155 minutes. The authors reported that there was no significant effect (p=0.22), but no data were given.

e) Time to rewarm to 36°C

One cohort study (Frank 1992) in 97 patients reported the time to rewarm the patients to 36°C. The authors reported that there was no significant effect of duration of surgery as a continuous variable, for mean durations of 4.4 to 6.6 hours, but no data were given.

Conclusions

The view of the GDG was that the likely cut-off point for duration of anaesthesia would be one hour, but few studies had short term operations. The exceptions were Flores Maldonado (1999) and Kongsayreepong (2003). Therefore, most of the studies were considered unsuited to investigating duration of anaesthesia/surgery as a risk factor.

The Flores Maldonado (1999) study, in 130 patients, showed no significant effect of duration of anaesthesia, as a continuous variable on the incidence of IPH (temperature less than 36.0°C) intraoperatively (mean 83 minutes, SD 59).

The Kongsayreepong (2003) study, in 184 patients showed a significant effect of duration of surgery above and below 2 hours, on the incidence of IPH (temperature less than 36.0°C) in ICU (range 0.25 to 10.25 h).

3. Height of spinal block

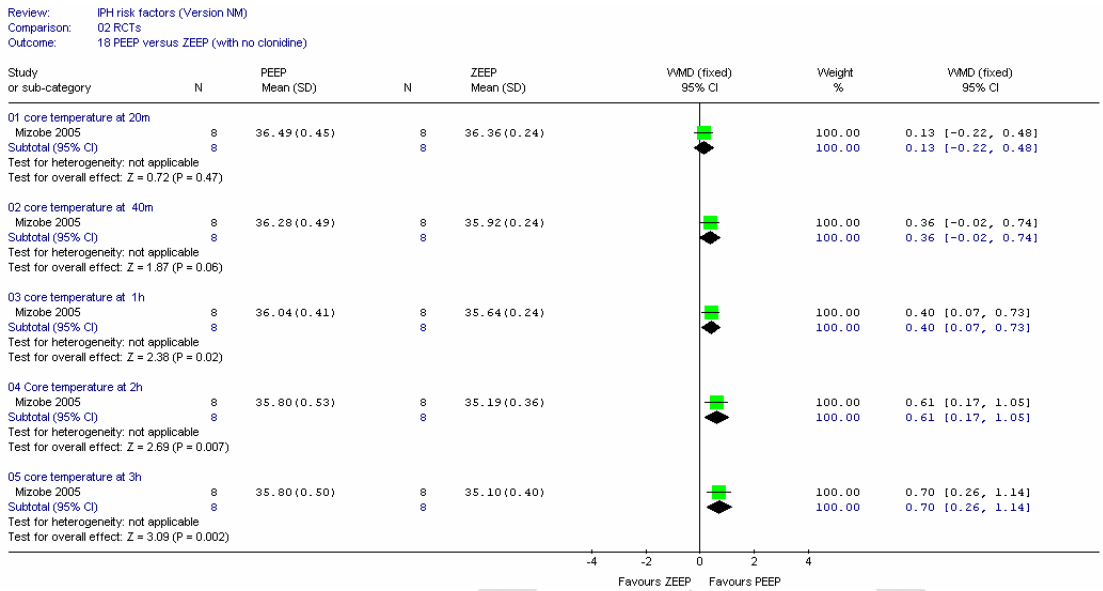
One small cohort study (Frank 2000, n=44) reported a statistically significant difference in the effect of the height of the spinal block, but no data were given for the multivariate regression analysis; the p values was reported to be p=0.002. The outcome measured was core temperature in PACU for height of block as a categorical variable in the range T3 to T8, with a high level of blockade giving low core temperatures. We note that the Frank (2000) study had too many variables in total for the number of patients (44/6 = 7), so this is treated as weak evidence.

4. Positive end expiratory pressure (PEEP)

One study (Mizobe 2005) compared a positive end expiratory pressure (PEEP) at 10cm H_2O versus zero end expiratory pressure (ZEEP) in 16 patients undergoing lower abdominal surgery.

There was no significant difference between 10 cm H_2O PEEP and ZEEP at 20 and 40 minutes, but significantly higher core temperatures at 1 to 3 hours for patients given PEEP. This study is small, however, and the evidence is insufficient to make recommendations.

Figure 15: Positive end expiratory pressure versus zero pressure – core temperature



NB: Scale -4 to +4°C

C. SURGERY RISK FACTORS

1. Magnitude of surgery

Three cohort studies (Abelha 2005 (n=185); Flores Maldonado 1997 (n=130); Kongsayreepong 2003 (n=184)) investigated the effect of magnitude of surgery on the incidence of IPH. One of the studies (Flores Maldonado 1997) divided operations into major and minor (but only defined 'major'). In the other two studies a third category, intermediate, was defined. Operations were divided by the authors into:

- Major: body cavities and/or major vessels exposed (e.g. major abdominal, thoracic, major vascular, hip arthroplasty)
- Intermediate: body cavities exposed less than major (e.g. appendectomy)
- Minor: superficial surgery.

1.1 Major versus minor

The three studies had different definitions of hypothermia, and recorded the incidence at different stages.

a) Incidence of hypothermia intraoperatively

One study (Flores Maldonado 1997) recorded the incidence of IPH (temperature less than 36.0°C) intraoperatively in 130 patients. There was a statistically significant effect of magnitude of surgery, with major surgery giving rise to a higher incidence of IPH.

b) Incidence of hypothermia in ICU

Two studies recorded the incidence of IPH in ICU (Abelha 2005, temperature less than 35.0°C; Kongsayreepong 2003, temperature less than 36.0°C). Meta-analysis of the two studies in 369 patients, showed a statistically significant effect, with major surgery giving rise to a higher incidence of IPH. There was significant heterogeneity, however (I^2=74%, p=0.05). Each study was significant individually.

The GDG decided that the odds ratio in Kongsayreepong (2003) was unexpectedly high and so decided to carry out a meta-analysis of the other two studies, despite the differences between them in time of measurement, definition of hypothermia and possible differences in the definition of minor surgery. This meta-analysis gave an odds ratio of 3.20 (95%CI 1.68, 6.07), with no heterogeneity (I^2=0%, p=0.62). This probably erred on the side of caution.

Figure 16a: Magnitude of surgery, major versus minor – incidence of hypothermia

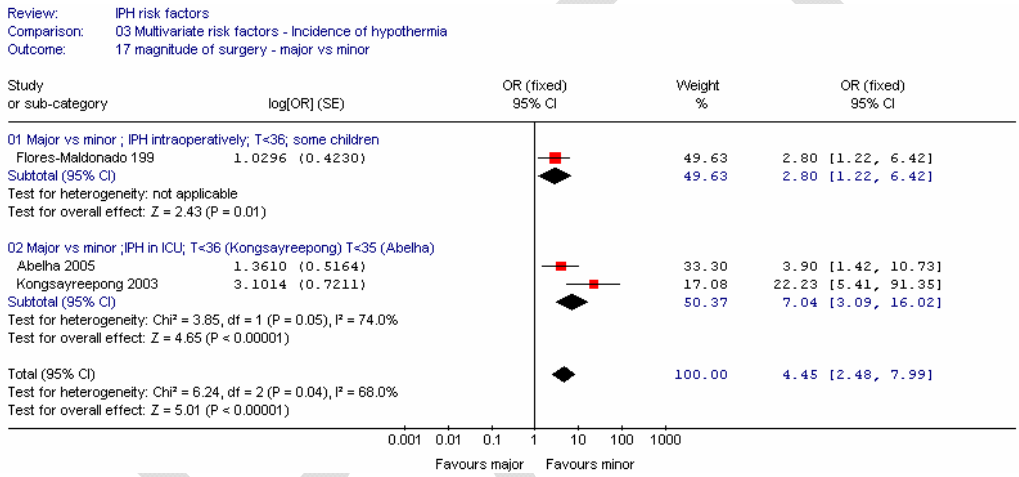
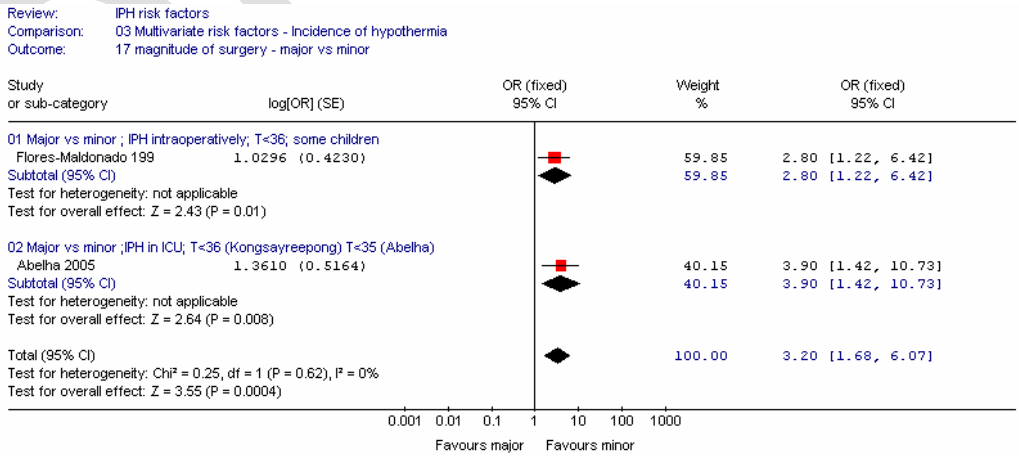


Figure 16b: Sensitivity analysis for magnitude of surgery, Kongsayreepong excluded



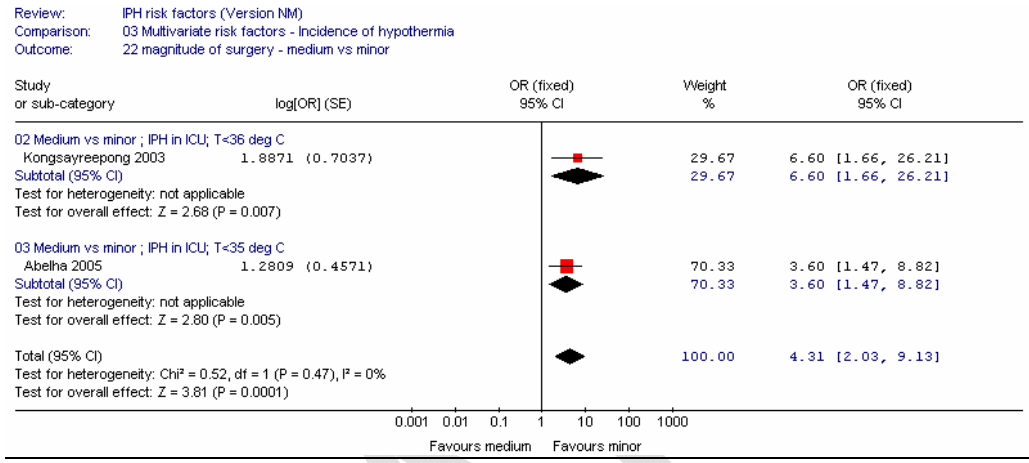
1.2 Intermediate versus minor

Two studies compared intermediate and minor surgery (Abelha 2005; Kongsayreepong 2003). The studies had different definitions of hypothermia.

a) Incidence of hypothermia in ICU

Two studies recorded the incidence of IPH in ICU (Abelha 2005, temperature less than 35.0°C; Kongsayreepong 2003, temperature less than 36.0°C). Meta-analysis of the two studies in 369 patients showed a statistically significant effect, with intermediate surgery giving rise to a higher incidence of IPH; OR 4.31 (95%CI 2.03, 9.13). There was no heterogeneity (I^2=0%, p=0.47).

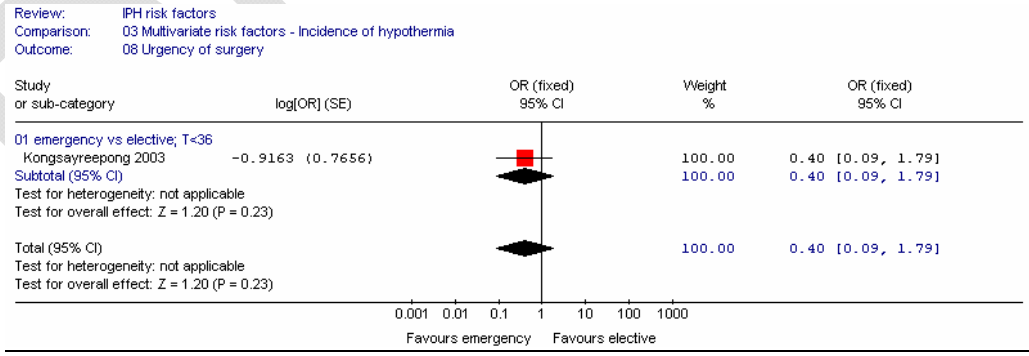
Figure 17: Magnitude of surgery, intermediate versus minor



2. Urgency of surgery – elective or emergency

One cohort study (Kongsayreepong 2003 (n=184)) investigated the effect of urgency of surgery on the incidence of IPH (temperature less than 36.0°C) in ICU. There was no significant difference between elective and emergency surgery.

Figure 18: Urgency of surgery, emergency versus elective – incidence of hypothermia



3. Type of surgery

Two RCTs (Nguyen 2001 (n=101); Danelli 2002 (n=44)) compared laparoscopic and open procedures, for gastric bypass and colorectal surgery respectively. Both studies reported significantly longer durations of surgery for the laparoscopic procedure (64 minutes median difference for Danelli and 30 minutes mean difference for Nguyen). Danelli (2002) gave all

patients warmed fluids; Nguyen (2001) reported that all patients had forced air warming, but fluids were not warmed.

Danelli (2002) reported median and range core temperatures, but stated that there was no significant difference between the two interventions at any time intraoperatively or postoperatively. There was no signfiicnt difference in core temperature intraoperatively for Nguyen (2001), but there were significantly higher temperatures in PACU for the open procedure (Figure 19). For the incidence of hypothermia, the confidence intervals were too wide to determine if there is a difference (Figure 20).

Figure 19: Type of surgery, laparoscopy versus open procedure – core temperature

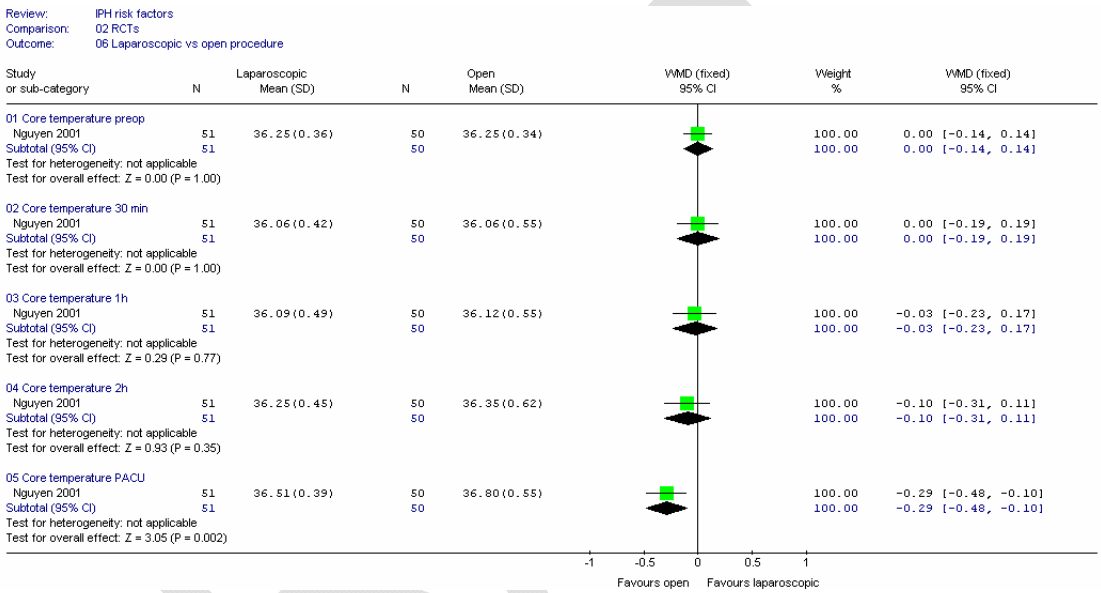
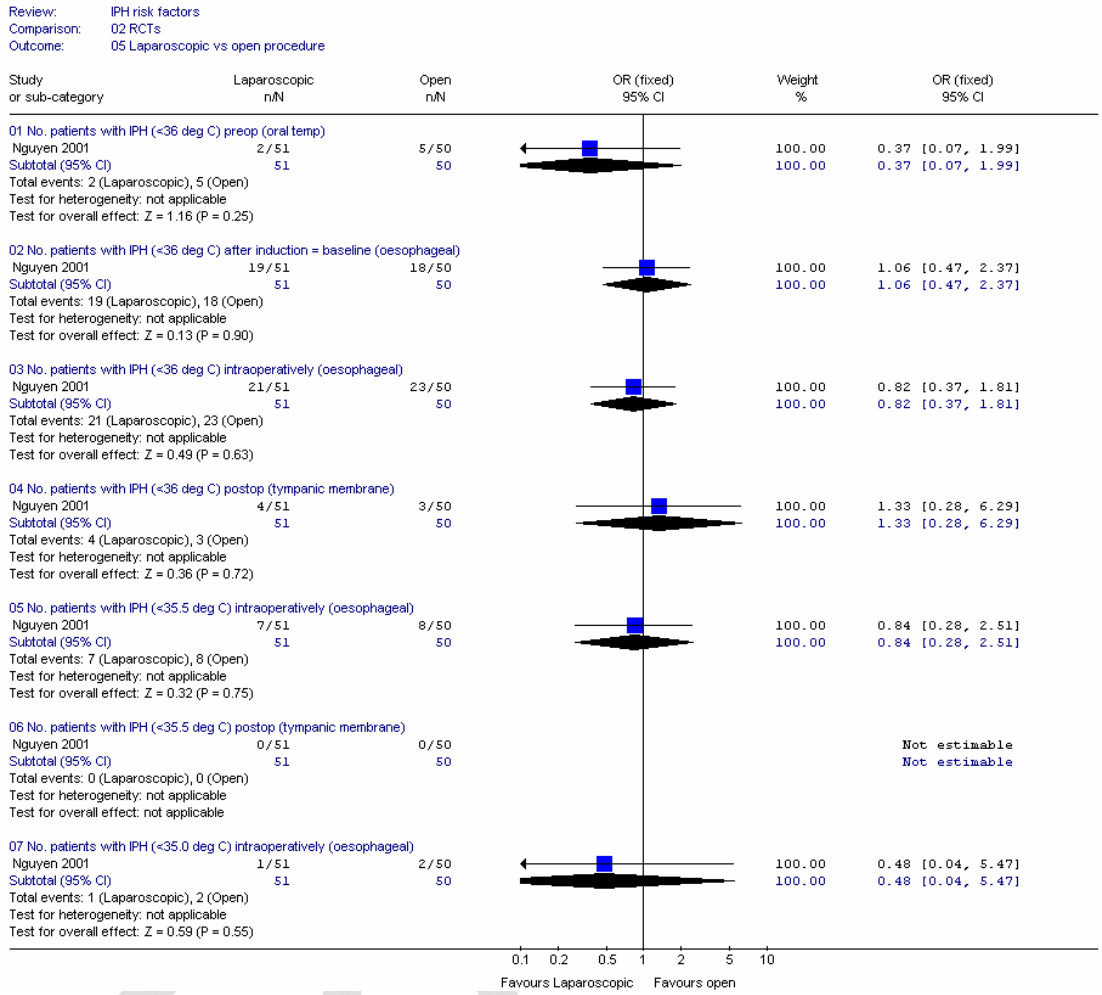


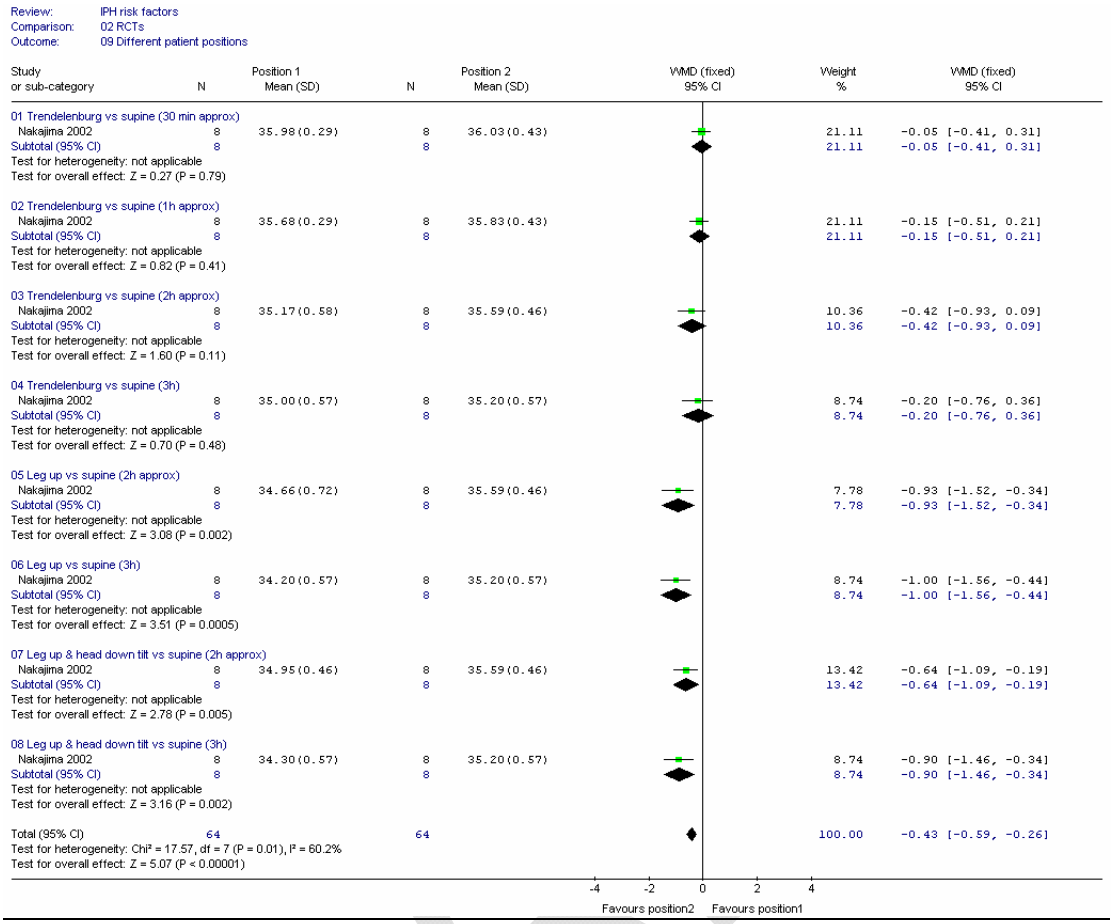
Figure 20: Type of surgery, laparoscopy versus open procedure – incidence of IPH



4. Patient position

One small RCT (Nakajima 2002) investigated the effect of patient position during surgery. The patients were randomly assigned to one of four positions: supine (n = 8); 15° to 20° head-down tilt (Trendelenburg position, n = 8); leg-up (lithotomy position, n = 8); leg-up combined with head-down tilt (n = 8). The designated positions were initiated 10 min after the induction of general anaesthesia and were maintained for 3 hours. There was no significant difference in core temperature between the Trendelenburg and supine positions at any time, although the confidence interval was fairly wide. There were significantly higher core temperatures at 2 and 3 hours for leg-up and leg-up with head-down tilt, in comparison with the supine position, however, the confidence intervals were fairly wide. The GDG considered that the small numbers in each comparison precluded drawing conclusions.

Figure 21: Position of patient in surgery – core temperature



NB: Scale -4 to +4°C

D. OTHER RISK FACTORS

1. Intravenous fluid infusion

Three cohort studies investigated the effect of intravenous fluids. Two investigated the incidence of hypothermia in ICU: Kongsayreepong (2003), temperature less than 36.0°C, n=184; Abelha (2005), crystalloid, temperature less than 35.0°C, n=185. Neither study stated if the fluids were warmed, with Abelha (2005) reporting that the number receiving warmed fluids was unknown. For Kongsayreepong (2003) the volume of fluids given was 0.1 to 11.2 litres and the volume was dichotomised into above and below 4 litres. The confidence interval was fairly wide. This study shows that fluid volume above and below 4 litres did not have a significant effect on the incidence of hypothermia.

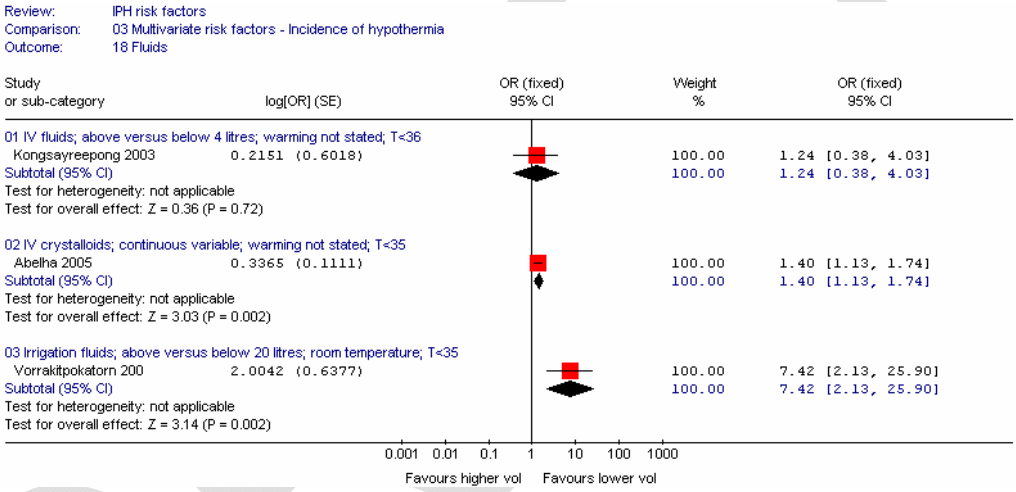
Abelha (2005) reported a range of crystalloid fluid volumes from 0.2 to 10.5 litres, with a mean of 2.9 litres, and crystalloid volume was analysed as a continuous variable. This was found to have a statistically significant effect, with lower volumes giving less hypothermia in ICU: OR 1.4 (95%CI 1.1, 1.7). The study also included volume of colloid and this was found to be non-significant in univariate analyses.

A third study (Hind 1994a, n=30) investigated the effect of room temperature IV fluids, as a continuous variable, on the change in intraoperative temperature. The patients received 0.14 to 1.25 litres over one to two hours, and reported no significant effect. We note that this study had some methodological limitations and also reported an interaction of IV fluid volume and age.

2. Irrigation fluids

One study (Vorrakitpokatorn 2006) in 128 patients reported a large significant effect of room temperature irrigation fluid, above and below 20 litres, on the incidence of hypothermia in PACU (temperature less than 35.0°C). This was a large effect, in which lower volumes of irrigation fluids resulted in less hypothermia: OR 7.42 (95%CI 2.13, 25.94). The confidence interval was fairly wide.

Figure 22: Fluid volume – incidence of hypothermia in PACU

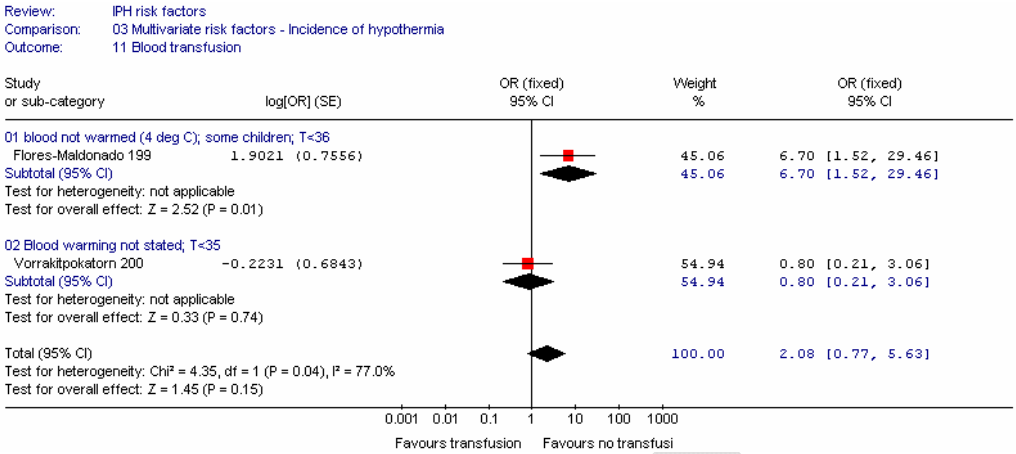


3. Blood transfusion

Two cohort studies investigated the effect of blood transfusion versus no transfusion on the incidence of hypothermia; Flores Maldonado (1997) gave 13 of 130 patients blood at 4°C and Vorrakitpokatorn (2006) gave 16% of the 128 patients blood (8% had two units), but warming was not stated. Flores Maldonado (1997) found a statistically significant difference in the incidence of core temperatures below 36.0°C, but Vorrakitpokatorn (2006) found no significant difference in the incidence of temperatures below 35.0°C. The GDG thought it likely that the blood was warmed in the Vorrakitpokatorn (2006) study.

One RCT analysed by multiple regression (Frank 1992), in 97 patients, gave 0.7 to 1.2 units of warmed blood and found no significant difference in the change in intraoperative temperature or in the time to rewarm to 36.0°C, for blood transfusion treated as a continuous variable. We note that this study used sublingual temperature measurements.

Figure 23: Blood transfusion – incidence of hypothermia in PACU



Conclusions – fluids and blood

For intravenous fluids in the Kongsayreepong (2003) study, we considered the 4 litre threshold to be too high to be representative of the effect of fluids, and we noted that there were methodological limitations in the Hind (1994) study. The remaining study (Abelha 2005) gave weak evidence that volume of IV fluids may a risk factor for hypothermia, but the effect was fairly small. The lack of information on whether the fluids were warmed was a limitation.

There was acceptable evidence to show that a volume of more than 20 litres of unwarmed irrigation fluids was a significant risk factor for IPH.

There was acceptable evidence to show that transfusion of unwarmed blood (4°C) significantly increases the risk of IPH intraoperatively. Other studies investigating this risk factor did not state if the blood was warmed, so it was unclear whether their conclusions of no significant effect were reliable.

E. ENVIRONMENTAL RISK FACTORS

1. Theatre temperature

Six studies investigated the effect of theatre temperature on the incidence of IPH or on the core temperature (Flores Maldonado 1997; Frank 2000; Hind 1994a; Kongsayreepong 2003; Frank 1992; Morris 1971). Hind (1994) was treated with caution because only two of four risk factors were included in the multivariate analysis and the study also had too many variables in total for the number of patients (30/6 = 5).

a) Incidence of IPH intraoperatively

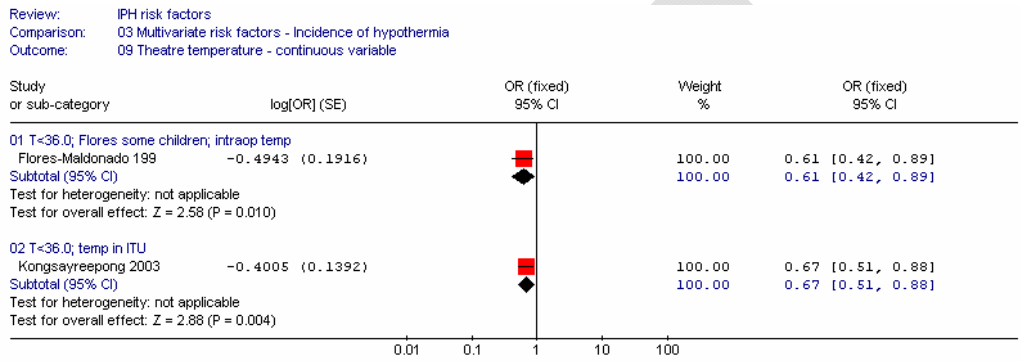
One study (Flores Maldonado 1997) in 130 patients reported the effect of theatre temperature, as a continuous variable, on the incidence of IPH intraoperatively (temperature less than 36.0°C). This showed a large statistically significant effect of theatre temperature

for a mean of 22.9°C (SD 1.2) in patients undergoing either general or regional anaesthesia; OR 0.61 (95%CI 0.42, 0.89).

b) Incidence of IPH in ICU

One study (Kongsayreepong 2003) in 184 patients undergoing combined, general or regional anaesthesia, for a theatre temperature of mean 19.5 to 20.6°C (SD 1.8), reported the incidence of IPH in ICU (temperature less than 36.0°C), and showed an almost identical odds ratio to that obtained intraoperatively (Figure 24), statistically significantly in favour of warmer theatres.

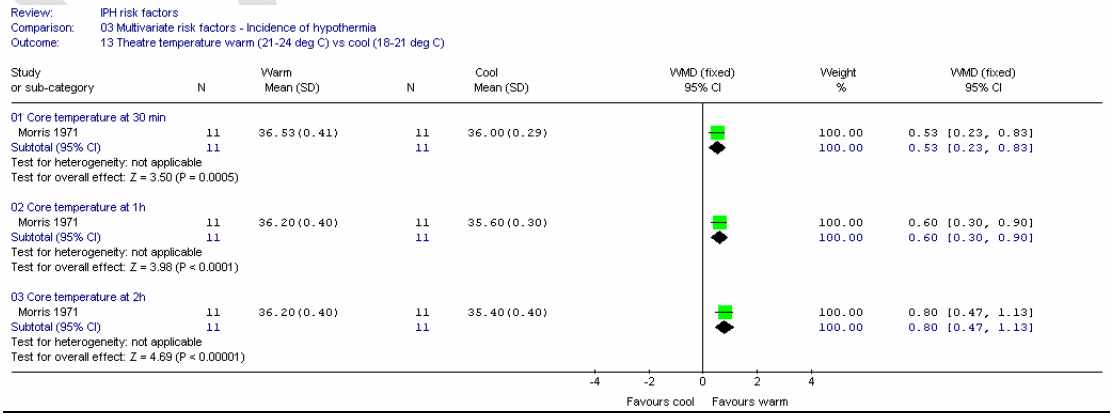
Figure 24: Effect of theatre temperature – incidence of IPH intraoperatively and in ICU



c) Core temperature intraoperatively

One small cohort study (Morris 1971), in 22 patients undergoing general anaesthesia, compared the effect of theatre temperature in two groups: cool theatre (18 to 21°C) and warm theatre (21 to 24°C). There was a statistically significant effect at all times (Figure 25). The control group was hypothermic at one hour in the cooler theatre.

Figure 25: Effect of theatre temperature – core temperature intraoperatively and in ICU



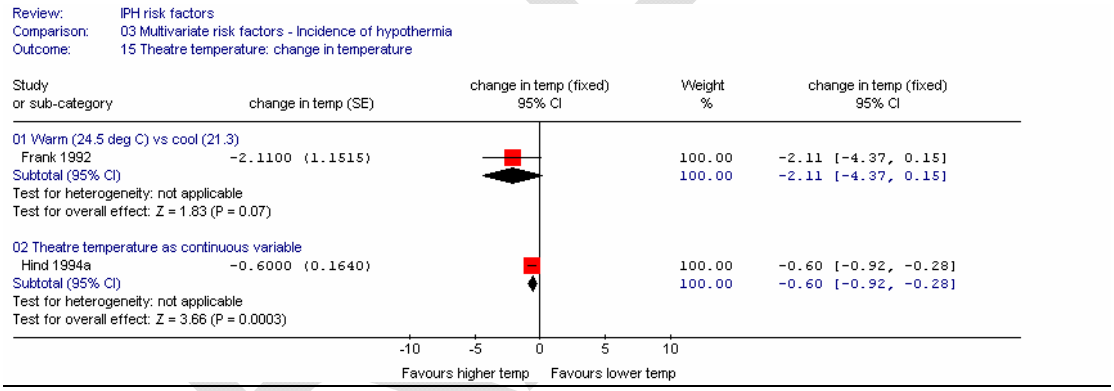
d) Change in temperature intraoperatively

Two studies reported the effect of theatre temperature on the change in temperature intraoperatively.

Frank (1992) (n=97) compared warm (24.5°C) and cool theatres (21.3°C) in patients undergoing either general or epidural anaesthesia and reported no statistically significant effect of theatre temperature on the difference between the 'first postoperative temperature' and the preoperative temperature (p=0.07). The forest plot demonstrates the confidence interval is wide, but warmer theatre temperatures are favoured (Figure 26).

Hind (1994a), in 30 patients undergoing general anaesthesia, reported a statistically significant effect (p<0.001) of theatre temperature for a mean of 21.3°C (SD 1.2); range 19.6 to 23.3. We note that this study reported correlations between age and theatre temperature, which the authors attributed to older patients being in the theatre at the start of the list when the theatre was at its coldest. Hind (1994a) was also of poorer quality.

Figure 26: Effect of theatre temperature – change in core temperature intraoperatively



e) Core temperature in PACU

Another cohort study (Frank 2000) in 44 patients, reported that, in a multiple regression analysis, there was no statistically significant effect (p=0.70) of theatre temperature for a mean of 20.9°C (SD 0.13), with a range of 18.7 to 22.9°C. No other numerical data were given. This study only included patients receiving spinal anaesthesia.

f) Time to rewarm to 36.0°C

One study (Frank 1992) in 97 patients reported no significant effect of theatre temperature on rewarming patients in warm (24.5°C) versus cool theatres (21.3°C) in patients undergoing either general or epidural anaesthesia).

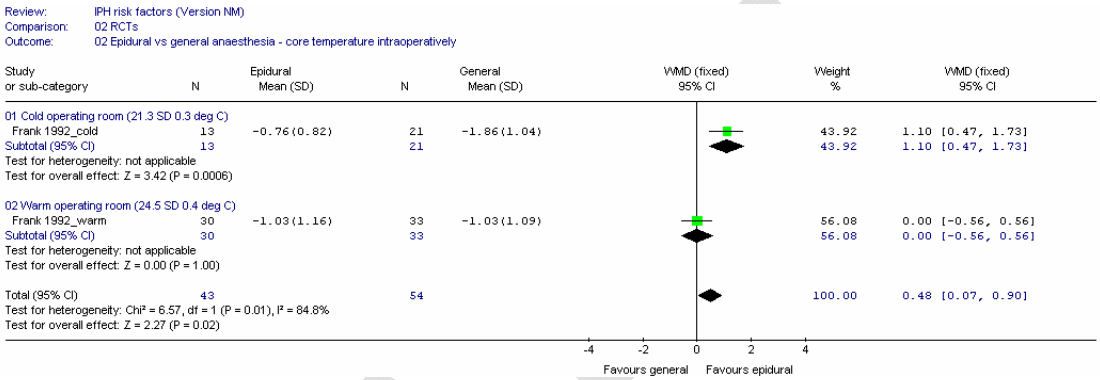
2. Interaction between theatre temperature and type of anaesthesia

a) Change in core temperature

One study (Frank 1992) in 97 patients included interaction terms in the multivariate analysis, and reported a statistically significant effect of a combination of theatre temperature and

type of anaesthesia on the change in temperature intraoperatively between the 'first postoperative temperature' and the preoperative temperature. There was a greater decrease in temperature for general anaesthesia versus epidural in a colder theatre (21.3°C), than in a warmer theatre (24.5°C). This is illustrated in Figure 27. We note that these are not randomised groups. There is a statistically significant difference in the colder theatre, favouring epidural anaesthesia, but there is no significant difference at warmer temperatures. The confidence intervals are wide.

Figure 27: Epidural versus general anaesthesia for theatre temperature subgroups



These subgroup results support the observation found for the Frank (2000) study in spinal anaesthesia, in which there was no effect of theatre temperature (for a range of 18.7 to 22.9°C).

3. Interaction between theatre temperature and age

a) Change in core temperature

One study (Frank 1992) in 97 patients reported no significant effect of a combination of theatre temperature and age on the change in temperature intraoperatively between the 'first postoperative temperature' and the preoperative temperature.

Conclusions

The evidence suggests that:

- In patients undergoing general (mainly) or combined or regional anaesthesia, an increase in theatre temperature is protective of patients becoming hypothermic, both intraoperatively and in ICU.
- In patients undergoing general anaesthesia, one small study (n=22) reported that increased core temperatures are obtained intraoperatively in a warmer theatre (24°C versus 21°C).
- In patients undergoing spinal anaesthesia, one study reported no significant effect of theatre temperature in the range 18.7 to 22.9°C.

- One moderately sized study (n=97) reported there is an interaction between type of anaesthesia and theatre temperature, such that there is a smaller effect of theatre temperature for epidural compared with general anaesthesia
- There does not appear to be a threshold above which further increases in theatre temperature have no effect.

3. Humidity

One study (Hind 1994a), in 30 patients, investigated the effect of theatre humidity in the range 50 to 65%, and found that this was not significantly correlated with the core temperature, so this risk factor was excluded from the multivariate analysis. We note that Hind (1994a) is poorer quality.

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