EFFECT OF PERIOPERATIVE HYPOTHERMIA ON RECOVERY IN YOUNG ADULTS: A SYSTEMATIC REVIEW

A Major Paper Presented

by

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# Effect of Perioperative Hypothermia on Recovery in Young Adults: A Systematic Review

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## Abstract

Perioperative hypothermia is a common occurrence in the operating room setting and can lead to several adverse events. Some potential complications include discomfort, shivering, platelet dysfunction, coagulopathy, increased vasoconstriction, higher risk of wound infection, and an increased risk of postoperative cardiac events. Anesthesia providers play a pivotal role in the management of patient temperature in the perioperative period and there are several interventions that have been implemented to combat this problem. Not all patients respond to hypothermia in the same manner and based on a patient's personal health history, illnesses, and co-morbidities, hypothermia may be tolerated better by some and not as well by others. To evaluate operative risk, the American Society of Anesthesiologist has formulated an ASA class scoring system. This scoring system assesses risk by combining overall health status and comorbidities. It is unlikely that patients will have the same physiologic response to hypothermia across the various ASA classes. This systematic review was conducted to evaluate the effect of perioperative hypothermia on anesthetic recovery times as it relates to healthy ASA class I and II patients. Identifying the impact of hypothermia on young adults will help determine how much of an impact hypothermia has on their anesthesia recovery, and thus can help guide perioperative care for this population.

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# Effect of Perioperative Hypothermia on Recovery in Young Adults: A Systematic Review

## Background/Statement of the Problem

All patients undergoing surgery are at risk of developing hypothermia, and up to 70% develop hypothermia perioperatively (Burger & Fitzpatrick, 2013). 'Perioperative' is defined as combined preoperative, operative, and postoperative periods. According to McSwain et al. (2015), perioperative hypothermia is associated with many clinical consequences, including discomfort, shivering, platelet dysfunction, coagulopathy, increased vasoconstriction, and higher risk of wound infection. It is also thought to be linked to the increased occurrence of postoperative cardiac events. 'Postoperative' is defined as the period of time in which the patient is in the Post Anesthesia Care Unit (PACU) recovering from anesthesia. Hypothermia may affect pharmacokinetics and prolong both postoperative recovery times and length of hospital stay (McSwain et al., 2015). According to Lenhardt et al. (1997), perioperative hypothermia is most common in the elderly population, patients with a low body mass index, patients with preexisting conditions, and those who undergo complicated and prolonged surgery.

Surgery is very common within the United States and only seems to be increasing annually. According to the National Quality Forum (2017), the rate of procedures performed in freestanding ambulatory surgery centers increased by 300% from 1996 to 2006. In addition, according to the Agency for Healthcare Research and Quality, 17.2 million patients who were either ambulatory or inpatient underwent some form of invasive or therapeutic surgery in 2014. More than half (57.8%) of all surgical procedures occur in a hospital-owned ambulatory surgery setting while the rest (42.2 %) happen in an inpatient setting (Steiner et al., 2020). In 2010, it is estimated approximately 20% percent of all surgical procedures were performed on those between the ages of 18 -45, while approximately 6.5% were carried out on those under 15 years of age. Patients less than 45 years of age generally fall within the ASA class of I-II and still make up a good portion of the surgeries performed annually (Hall et al., 2017).

A search of the literature reveals there are no studies that exclusively focus on the young adult population age 18-45 with an American Society of Anesthesiologists (ASA) score of I-II. While members of this age group are represented in studies regarding hypothermia in the perioperative period, they tend to be bundled in with a larger age range of patient participants. Studies today regarding perioperative hypothermia and anesthesia recovery tend to focus on either the very young or the very old. For example, Pearce et al. (2010) in their observational cohort study investigated the prevalence, risk factors, and outcomes of perioperative hypothermia in pediatric patients. In a prospective randomized controlled study, Ma et al. (2017) focused on the elderly patient population and examined benefits of prewarmed infusion during bilateral hip replacement.

Young healthy adults with low ASA scores generally do not require as many surgical procedures as their elderly counterparts with many co-morbidities and higher ASA scores, and thus are not as readily available for study. Investigating this topic will lead to a better understanding of how hypothermia affects healthy young adults in low ASA categories with no significant pre-existing conditions in the postoperative period.

Prior to entering the operating room, all patients undergoing surgery are scored using the ASA Physical Status Classification System (Figure 1). This scoring system evaluates operative risk based on comorbidities. The scoring system ranges from ASA I to ASA VI. According to the American Society of Anesthesiologists, ASA I is classified as a normal healthy patient. ASA II is classified as a patient with mild systemic disease. ASA III is classified as a patient with severe systemic disease. ASA IV is classified as a patient with severe systemic disease resulting in a persistent threat to life. ASA V is considered a moribund patient who is not expected to survive without a life-saving operation. Lastly, ASA VI is a patient who is declared to be brain dead and is being prepared for organ harvesting (American Society of Anesthesiologists, 2020). Patients of different ASA classes are, by definition, physiologically dissimilar and as such, are unlikely to all develop hypothermia, progress to a similarly significant degree of hypothermia or be as affected by internal temperature changes across the ASA class spectrum. This review aims to better define the development and effect of hypothermia in the ASA Class I patient.

Therefore, the purpose of this research is to investigate the effect of perioperative hypothermia on anesthetic recovery in young healthy adults aged 18-45 without significant co-morbidities (ASA I-II). The variables in the study are patient temperature perioperatively and anesthetic recovery as evidenced by the length of PACU stay. The research question guiding this study is: in young adults without serious medical conditions (ASA I-II), does perioperative hypothermia prolong anesthetic recovery compared to young adults without perioperative hypothermia?

**Figure 1**

*ASA Physical Status Classification System*

(American Society of Anesthesiologists, 2020)

| ASA PS Classification | Definition of Patient Status |
|---|---|
| ASA I | Normal health |
| ASA II | Mild systemic disease |
| ASA III | Severe systemic disease |
| ASA IV | Severe systemic disease that is constant threat to life |
| ASA V | Moribund, not expected to survive without operation |
| ASA VI | Declared brain-dead |

ASA indicates American Society of Anesthesiology.

# Literature Review

## Thermoregulation

Thermoregulation is a mechanism by which some mammals maintain body temperature via tightly controlled self-regulation, regardless of surrounding temperature. Temperature regulation is maintained by homeostasis, a self-regulating process that biological systems use to preserve a stable internal state for survival. Human beings have a normal core temperature of approximately 37 degrees Celsius. When the body's ability to thermoregulate becomes altered, blood flow is reduced, and in the extreme case hypoxia, ischemia and multi-organ failure can occur, resulting in death (Osilla & Sharma, 2019).

Hypothermia is defined as an internal body temperature of less than 35 degrees Celsius. When a patient becomes hypothermic, vasoconstriction occurs in the visceral muscles as a protective mechanism to maintain perfusion to essential organs and to prevent brain hypoxia. Hypothermia decelerates all physiologic mechanisms including metabolic rate, mental awareness, nerve conduction, neuromuscular reaction times, and both the cardiovascular and respiratory systems. Vasoconstriction due to hypothermia causes renal dysfunction and eventually cold diuresis due to the decreased levels of anti-diuretic hormone resulting in hypovolemia, shock, and vascular collapse. There are two different types of hypothermia: primary and secondary. During primary hypothermia, the cold environment is the external pathologic stimulus. Secondary hypothermia is caused by internal pathology (Osilla & Sharma, 2019).

**Types of Heat Loss**

Loss of heat is caused by five main mechanisms, including radiation, convection, conduction, evaporation, and respiration. Radiation is a form of heat loss through infrared rays. This involves the transfer of heat from one object to another, with no physical contact involved. An example of this is heat radiation from the sun. Convection is the process of losing heat through the movement of air or water molecules across the skin. An example of convection would be the use of a fan to cool the body. The fan creates a current that transfers heat away from the object or person as cool air moves across the external surface. Conduction of heat occurs between two objects that are in direct contact and where a temperature gradient exists between them. An example of this is when a patient is placed on a cold operating room (OR) table. The heat from the patient's body transfers to the cold metal of the table. Evaporation refers to latent heat losses. When a liquid converts to a gas, it needs to gain energy in order to do so. This energy is taken from the body in the form of heat. An example of this would be the evaporation of perspiration. The act of respiration also results in a form of evaporative heat loss (Sullivan & Edmondson, 2008).

**Heat Loss During Anesthesia**

Both general and regional anesthesia have been shown to reduce core body temperature with losses of 0.5–1°C within the first hour due to redistribution of heat from the core to the periphery, and a further loss of 0.3°C thereafter. It should be noted that a 1000 ml bag of fluid at room temperature could reduce body temperature by 0.5°C. Volatile anesthetic agents lower the thermoregulatory threshold so that protective mechanisms are triggered at lower than normal temperatures. Metabolic production of heat is greatly depressed during anesthesia.

There are three phases which occur during hypothermia. Hypothermic patients have a reduced cardiac output and are prone to ventricular arrhythmias below 30°C. At the same time, blood viscosity increases, and hematocrit rises. The hematocrit level is identified through laboratory values and describes the ratio of the volume of red blood cells to the total volume of blood (Merriam-Webster, 2020). This, combined with a left shift in the hemoglobin-oxygen dissociation curve, which indicates that hemoglobin has an increased affinity for oxygen, can cause ischemic changes in myocardium due to reduced oxygen delivery at the tissue level (Sullivan & Edmondson, 2008).

**Heat Loss in the Operating Room**

In the human body heat is primarily concentrated in the core rather than in the extremities. Thus, a person's core body temperature may be higher than their mean body temperature. All types of anesthesia, including general, regional and nerve blocks, re-distribute heat throughout the body mitigating the difference between the core and mean body temperatures. The reallocation of body heat from the core to the periphery is the most common cause of hypothermia in the first hour after anesthesia induction, and usually ranges from

1-1.5 °Celsius. After redistribution, heat is lost to the environment through the mechanisms previously mentioned: radiation, convection, evaporation, and conduction (Open Anesthesia, 2020).

The main mechanism of heat loss in the operating room is radiation. Convection heat loss also contributes to the problem of hypothermia in the operating room environment. As the surrounding layer of cold air in the OR moves over a patient, it is constantly removing body heat and contributing to hypothermia. Conduction heat loss however, does not play a significant role in this environment because patient skin is in contact with cushioned material that insulates well. The air temperature in the OR is kept particularly cold to deter bacterial growth and prevent infection. Patients under anesthesia typically do not sweat, thus heat loss from evaporation does not play a major role in the OR. Of the two mechanisms of undesired heat loss in the OR, impaired thermoregulation secondary to anesthesia is more important than the low ambient temperature of the operating theatre (Open Anesthesia, 2020).

**Hypothermia Risk Factors**

The study participants underwent a variety of surgical procedures, including general, orthopedic, urologic, neurosurgery, plastic and reconstructive surgery. The aim of the study was to determine the incidence of inadvertent hypothermia in operative patients and the risk factors that are involved in the development of hypothermia. Study participant ASA scores ranged from ASA I-III. The findings of this study concluded there are several factors that increase the risk of inadvertent intraoperative hypothermia. ASA score, preoperative body temperature, and operating room temperature were found to affect the development of inadvertent hypothermia during the operating period. In addition, the administration of premedication, preoperative and postoperative body temperature, and the operating room temperature were found to affect the development of inadvertent hypothermia in the postoperative period. In this study, both a multivariate and univariate analysis was performed. It should be noted that ASA score was only found to be a risk factor in the univariate analysis and was found to have no effect in the multivariate analysis. Limitations of the study include small sample size and restriction of the study group to ASA Class I-III patients; factors which reduce the generalizability of the results. One strength of the study was that the researchers captured 12 data points which could potentially confound the temperature results, contributing to the value and methodological robustness of the study.

**Post Anesthesia Care**

The post anesthesia period provides close monitoring during transition from the intraoperative period to optimal recovery. This period can be separated into three levels of care: Phase I, Phase II, and Extended Care. During Phase I, the focus is on the patient's recovery from anesthesia and recognizing, minimizing, and managing any issues or complications until there is a return to baseline vital signs. This includes applying PACU scoring criteria, including muscle activity, respiratory efficiency, cardiovascular homeostasis, and level of consciousness. Respiratory and hemodynamic changes are managed in this phase, and analgesia may be provided as needed. It is in this phase of anesthesia recovery that hypothermia would be addressed. This is generally accomplished by the application of warmed blankets, a passive conduction method. Phase II focuses on preparing the patient, family, and/or significant other for care in the home, or an extended care environment. Extended Care begins when the patient is discharged to the oversight of a responsible adult and leaves the hospital. Generally, the patient is advised to anticipate a post-operative telephone call within 72 hours of the procedure after discharge (American Association of Nurse Anesthetists, 2020).

**Hypothermia and Recovery Time**

Lenhardt et al. (1997) conducted a prospective, randomized quantitative study which reviewed the relationship between core temperature and fitness for discharge from a post-anesthesia care unit. Investigators looked at fitness for discharge using specific criteria and were blinded to both group assignments and core body temperature postoperatively. Found to be linked to an enhanced potency of anesthetics, reduced drug metabolism, escalated cardiovascular instability, and curtailed cognition, it was concluded by the researchers that mild hypothermia does increase recovery time. The study sample included patients aged 18 to 80 years old who were undergoing elective abdominal surgery. Patients were assigned to two temperature management groups. The first group received extra warming (the normothermic group) and the second group received routine thermal management (the hypothermic group). Core temperatures were measured at the tympanic membrane and values were recorded pre-operatively, at 10-minute intervals intra-operatively, and at 20-minute intervals postoperatively. The results of the study showed that hypothermic patients required approximately 40 minutes longer than normothermic patients to reach criterion for discharge. The criterion for discharge from the PACU was based on a scoring system that assessed patient activity/movement, respiratory pattern and rate, oxygen saturation levels, level of consciousness, blood pressure, heart rate, gastrointestinal motility, and renal function/urine formation (Lenhardt et al.,1997).

The findings suggest that hypothermia significantly delays fitness for discharge from the post-anesthesia care unit. In critiquing this research study, limitations include the multiple factors that play a part in each participant's fitness for discharge. These multiple unrelated factors include bed availability, transportation, nursing habits, and protocols. In addition, approximately 100 of the research subjects also participated in a simultaneous thermoregulatory protocol where treatment was implemented for symptomatic patients. Early intervention could have affected one's fitness for discharge and thus the clinical outcomes of the study (Lenhardt et al.,1997). Furthermore, this study included patients aged 18 to 80 and made no distinction between age groups or ASA classes. Not all hypothermic patients required additional time to discharge. At each time interval denoted there were some hypothermic patients who met discharge criterion.

**Post Anesthesia Care Unit Recovery**

Research has shown that patients recovering in the post anesthesia care unit are prone to reduce body temperature. A pilot study conducted by Mendonca et al. (2019) evaluated risk factors for postoperative hypothermia in 78 patients from 18 to 85 years old. The incidence of temperatures <36 ºC at postoperative care unit admission was 69.2%. Patients who received spinal anesthesia, morphine and sufentanil were found to have significantly lower temperatures over time. Combined anesthesia resulted in higher rates of hypothermia, followed by regional and general anesthesia. Although the study had a small sample (n=78) and may be non-representative of the general population, and the participants were in the age group of 18-85, the findings have clinical significance and implications for nursing practice, since more than half of the patients who participated in the study had postoperative hypothermia. It is notable, however, that no distinction was made between age or ASA class referable to hypothermic outcome. Further research is necessary to determine whether the same findings would result from a larger sample size and a narrower age range that targets hypothermic outcomes with a view to ASA Class. For example, given that over 30% of patients did not evidence hypothermia at PACU admission, it would add much to the findings of this study if detailed information on which groups (age/ASA Class) were prone to hypothermia under the circumstances defined by the study.

In a study by Ma et al. (2017), the authors conducted a prospective randomized controlled study to determine the benefits of prewarmed infusion in elderly patients who underwent bilateral hip replacement. A total of 64 patients were included in the study with 32 patients in the control group and 32 patients in the warming infusion group. Patients receiving a prewarmed infusion had a significantly shorter time to spontaneous breathing, eye opening, consciousness recovery, and extubation than the control group. In addition, significant differences were found in the Steward Post-Anesthetic Recovery and Visual Analog Scale (VAS) scores between the 2 groups. The Steward score evaluates patient consciousness, airway stability, and mobility while the Visual Analog Score assesses patient pain level using a range of facial expressions. Moreover, the warming infusion group also showed an obviously decreased incidence of shivering and postoperative cognitive dysfunction. The study had a small sample size (n=64) and focused mainly on elderly patients. Nonetheless, the findings warrant further research to determine if a similar response in postoperative temperature is demonstrated in the younger ASA Class I and Class II patient population, the focused clinical population for this author's research study. All of the focused end-points of this study are appropriate for evaluation in this systematic review of ASA Class I / II patients.

**Hypothermia, Transfusion Requirements, and Hospital Duration**

A study by Sun et al. (2015) evaluated esophageal core temperatures in 58,814 adults undergoing surgery lasting >60 minutes who were warmed with forced air. The study aimed to evaluate the relationship between hypothermic exposure, transfusion requirement and duration of hospitalization. In every subgroup, core temperature dropped during the first hour. The mean lowest core temperature during the first hour was 35.7 ± 0.6°C. Sixty-four percent of the patients reached a core temperature of <36°C 45 minutes after induction; 29% reached a core temperature of <35.5°C. Almost 50% of patients had sustained core temperatures <36°C for over an hour and 20% were <35.5°C for more than an hour. Almost 5% of patients were transfused, and it was concluded that there was a notable association between temperatures below 37°C and transfusion requirement, such that transfusion requirements progressively increased from 1 to 8 °C below 37°C. Findings included prolonged mean duration of hospitalization for hypothermic patients, but this attained a low-level significance (Sun et al., 2015).

This study is clinically relevant because it clearly indicates that hypothermia poses a real threat to post-anesthesia outcomes and recovery, however, the study end-points did not take into consideration the preponderance of patients most likely to experience these effects according to ASA Class. The sample size of this study was quite large making it a good representative sample. Out of 143,157 patients considered for the study, 58,814 met criteria for inclusion in their descriptive analysis. Factors that weaken this study's validity include the fact that researchers were unable to access accurate preoperative temperatures. In addition, patients in this study were actively warmed, which can also skew study results.

**ASA Class, Hypothermia, Risk factors, and Outcomes**

A retrospective study conducted by Emmert et al. (2018) investigated 339 patients undergoing surgical intervention of the lung, including pneumonectomy, lobectomy, and various types of lobe resection. The study concluded that body surface area, induction time, and impaired lung function were significant factors influencing the incidence of hypothermia. Furthermore, no correlation was found to exist between perioperative hypothermia and frequency/ length of postoperative mechanical ventilation or increased ICU length of stay. To the contrary, patients in the hypothermic group were noted to have been discharged from the hospital significantly earlier than those in the normothermic group. They noted, however, that according to the rank sum test, the normothermic group evidenced a significantly higher ASA score, leading to the hypothesis that co-morbidities rather than internal temperature had impacted the length of hospital stays in their study. Similarly, the authors were unable to document the influence of hypothermia on the transfusion rate. They postulated this may have been caused by the low frequency of transfusion (4.7%).

The limitations of the study are similar to the accepted limitations of retrospective studies as a group; that is, the analysis of data collected for a purpose other than the specific theoretical hypothesis being evaluated is already methodologically restricted, such that misleading associations can arise. For example, controls are often recruited by convenience sampling, and are thus not representative of the general population but are instead prone to selection and/or misclassification bias and potentially subject to confounding when other unmeasured risk factors may be present (Kyoungmi, 2017).

As one of the few studies in the literature concerning hypothermia, which considers ASA status, the suggestion that patient co-morbidities might be more important than hypothermic criterion as pertains to length of stay outcomes is interesting but requires further evaluation by prospective means.

**Mechanisms of Warming**

There are many ways in which providers can combat hypothermia in the perioperative period. Several devices have been constructed that help patients remain warm while undergoing operations under general anesthesia. Intravenous fluid warming combined with other heat conserving methods has been found to significantly reduce the rate of perioperative hypothermia and has also been shown to be effective in various surgeries such as abdominal (Camus et al., 1996), gynecological (Smith et al., 1998), and orthopedic surgery (Hasankhani et al., 2007). Intravenous warmed fluid has also been shown to improve Apgar scores after cesarean section when administered during obstetric surgery. Forced-air warming is a process that involves heating and distributing air that is generated from a powered device. The device connects to a blanket and will transfer heat over the patient's body during surgery. This type of warming utilizes the process of air convection to transfer heat to the patient and has been shown to significantly improve core body temperature postoperatively. Resistive heating is a type of warming method that uses a low-voltage electrical energy to generate heat. This process warms the patient via conduction. The negative pressure warming system is a heating process that involves using sub atmospheric pressure with a thermal load to improve tissue perfusion and shunt patency, this in turn promotes the transfer of heat from the periphery to the body core (John et al., 2014).

**Summary of the Literature**

In conclusion, hypothermia is clearly a concern in the operating room setting. While under anesthesia, the body is unable to adequately thermoregulate. This problem is further exacerbated by the cold environment of the operating room. In addition to being unable to conserve heat, patients also lose heat primarily in the form of radiation heat loss (Sullivan & Edmondson, 2008). Clinical consequences of hypothermia have been documented and include increased need for blood products in the operative period (Sun et al., 2015), increased risk of cardiac events (Yi et al., 2017), and increased risk of postoperative infection (Lenhardt et., 1997). All of these clinical outcomes can ultimately lead to an increase in the risk of postoperative mortality. Investigating this problem further in the young adult population that has not been as widely researched will help fill this gap in knowledge. In addition, researching the effect of hypothermia based on varying ASA scores will help define how populations with different co-morbidity risk will cope with hypothermia in the post-anesthesia recovery period and aid in the understanding of expected clinical consequences of hypothermia within each ASA class.

## Theoretical Framework

The theoretical framework used for this research will be the Neuman Systems Model (NSM) (Figure 2). The NSM is an operating framework designed to guide health professionals in managing patient stressors that deter health and combat wellness. This model focuses on the relationship between, patient, environment, and the current state of patient health. Health can be considered a spectrum that ranges from wellness to illness. Optimal wellness exists when physiologic needs are met; when physiologic needs are not fulfilled, illness exists. When vital requirements to support life are not available, death occurs. According to this model, humans are viewed as open systems that interact with both internal and external environmental forces or stressors. The human body is dynamic and in a constant battle between maintaining physiologic stability and combatting varying degrees of illness (Gonzalo, 2019).

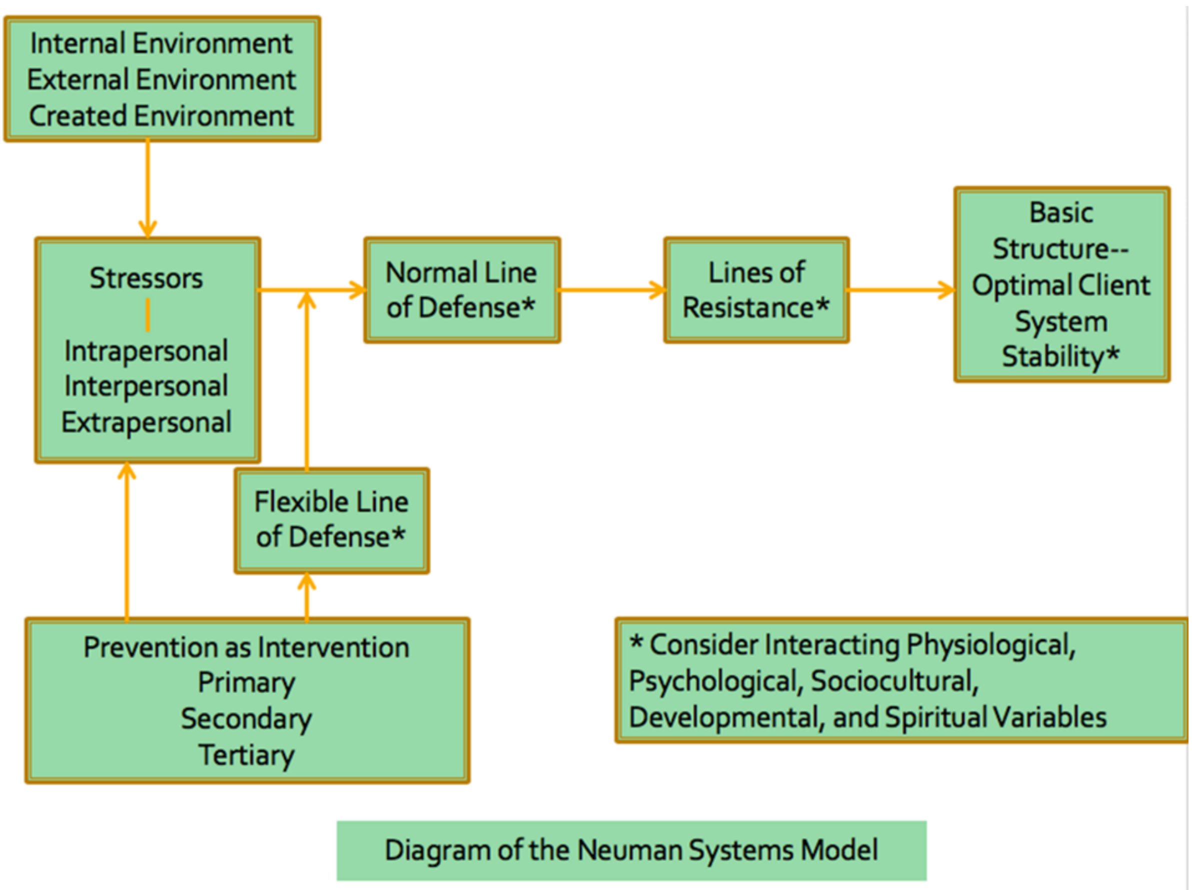
The environment plays an important role in determining the physiologic state of different body systems and their functions. According to the NSM, there are three relevant environment types. These include the internal, external, and created environments. The internal environment consists of the conditions within the body. The external environment involves the conditions outside the body. Lastly, the created environment is an unconsciously developed mechanism aimed at protecting system functions. This mechanism can be spontaneously generated, up-regulated, or down-regulated, as warranted by certain conditions, or needs (Gonzalo, 2019).

As it relates to perioperative hypothermia, patient recovery, and outcomes, Bitner et al. (2007) compared postoperative temperature of patients who underwent total joint arthroplasty with no preoperative warming to those who underwent the same procedure but received preoperative warming with a forced-air warming blanket. The study focused on staff institution of a new activity to prevent hypothermia by way of the "plan-do-check-act" (PDCA) Model of continuous improvement. Under the "plan" stage, the authors defined the reason for improvement, collected baseline data, and analyzed the data to evaluate the current state of the problem. The "do" phase involved implementing countermeasures to combat the problem. The "check" phase involved re-evaluating those results. Lastly the "act" phase involved formulating standards and developing plans for future practice. Patient temperature data was collected upon arrival to PACU and then every 15 minutes. The results of the study demonstrated an improvement in patient hypothermic events with use of a preoperative forced-air warming blanket and revealed that staff were more likely to implement a new activity if they were provided with data which evidenced a measurable effect on patient care improvement. The authors concluded that the use of the PDCA model demonstrated that attempts to alter clinical practice is a dynamic process requiring data, feedback, and revision.

PDCA is considered a model for "continuous improvement" because the more you repeat the cycle, the closer you will be to finding a solution or reaching the end goal. It is one of the few methods that can be used in any situation. The first step is planning, and it is here that the problem or goal to be achieved is defined and a strategy designed in order to implement it. The second step involves implementing the actions which are necessary to comply with the plan. Next, the results are obtained and evaluated in order to discover which actions either worked (or did not work) to solve the problem or reach the intended goal. Finally, the actions that worked are adopted, or a new plan is designed to fix what did not work. The cycle can be repeated as often as necessary.

Bitner, et. al (2007) explains that nursing goals seek to minimize the effects of certain variables that cause stress. In doing so, “patient defense mechanisms” (processes that protect the individual) are enhanced, and wellness is promoted. Nurses can minimize stressors by proactively maintaining normothermia and avoiding hypothermia. This study utilized preoperative forced air warming blankets to achieve an improvement in hypothermic events.  However, a variety of ways to achieve this goal exist, and have been outlined in the section above entitled, Mechanisms of Warming.  The PDCA method can be utilized to evaluate the efficacy of each of these warming tools and it coordinates well with the NSM Model, which focuses on the response of the patient to actual or potential environmental stressors and the use of primary, secondary, and tertiary interventions for the attainment and maintenance of patient wellness.

**Figure 2**
*Neuman Systems Model*
(Fawcett, 2018)



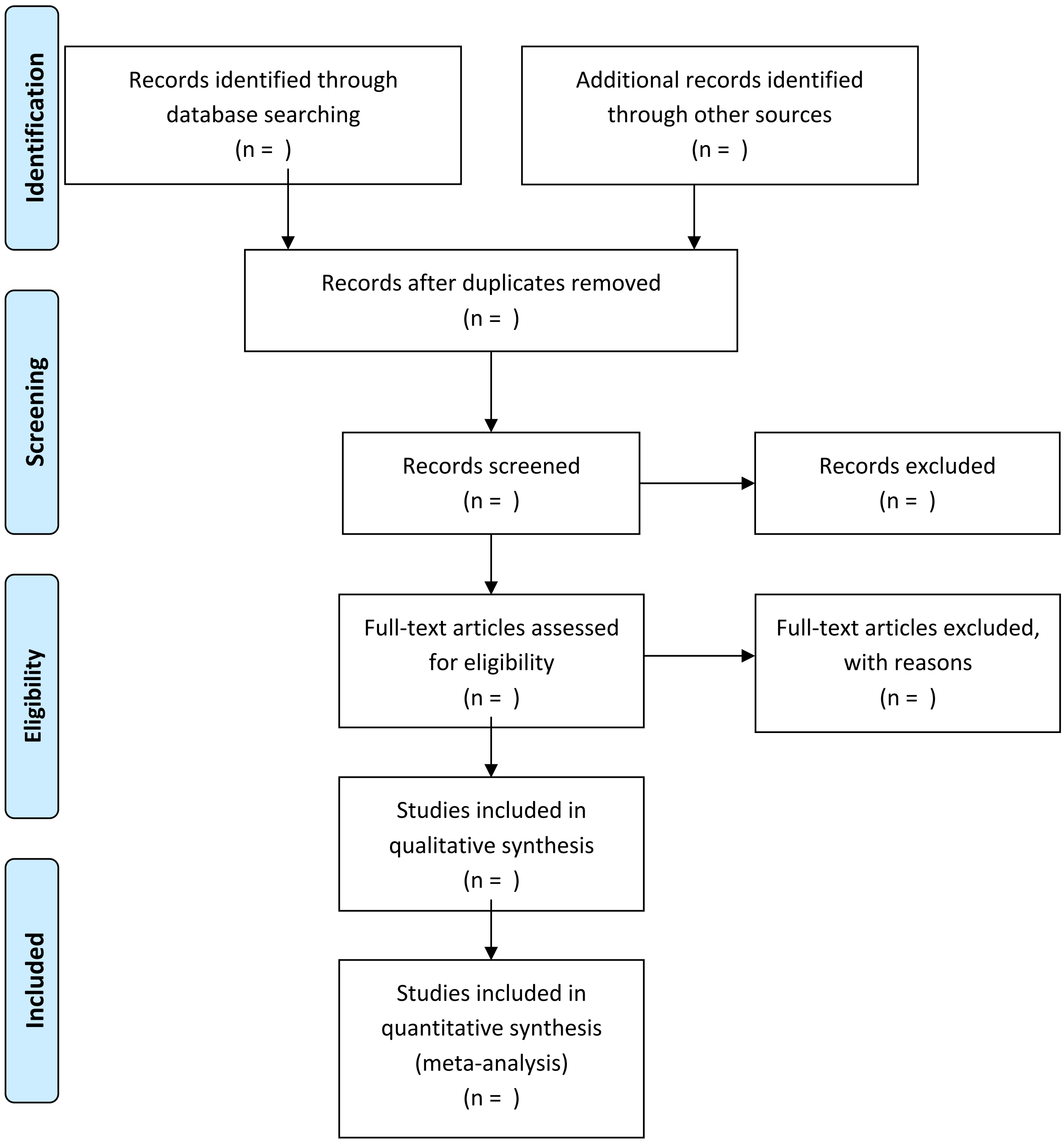
**The Use of PRISMA in this Research**

According to Polit and Beck (2017), the P*referred Reporting Item for Systematic Reviews and Meta-Analyses* (PRISMA) is a reporting guideline for meta-analyses of randomized controlled trials. Liberati et al. (2009) explain that systematic reviews and meta-analyses are necessary for accurate and reliable summarization of evidence relating to health care interventions. Moher et al. (2010) state that systematic reviews and meta-analyses have become increasingly important in the field of health care. When systematic reviews are not properly carried out, their value to health care providers who look to these reviews for guidance in best practices is diminished (Liberati et al., 2009).

The PRISMA Statement consists of a 27-item checklist and a four-phase flow diagram. The checklist includes items that are fundamental to transparent reporting of a systematic review and breaks these down into sections that include title, abstract, introduction, methods, results, and discussion. Underneath these sections are subcategories which guide the assessment of identified studies. The four phases of the PRISMA flow diagram (Figure 3A) include identification, screening, eligibility, and inclusion of studies (Liberati et al., 2009). According to McInnes et al. (2018), PRISMA can enable transparent reporting of reviews, assist in the evaluation of validity and relevance, and make the results from systematic reviews more useful.

The use of PRISMA in this research will guide the systematic review of articles pertaining to perioperative hypothermia and post anesthesia recovery. It will enable this author to clearly display research methods and processes utilized, evaluate research studies and their findings, assess for validity, and relay research information in a systematic way. See Appendix A for PRISMA Checklist.

**Figure 3A**
*PRISMA Four Phase Flow Diagram*
(Altman et al., 2009)



# Method

## Purpose

The purpose of this systematic review is to determine the effect of perioperative hypothermia vs perioperative normothermia on anesthetic recovery in young adults. The research question guiding this study is: in young healthy adult patients, does perioperative hypothermia prolong anesthetic recovery compared to young adults without perioperative hypothermia? The outcomes to be examined are patient temperature perioperatively and anesthetic recovery as evidenced by the length of PACU stay.

## Inclusion/Exclusion Criteria

Randomized studies that evaluate core body temperature in patients from ages 18-45 during the intraoperative and postoperative phase and that primarily focus on ASA class I and II will be reviewed for inclusion. Only studies written in English will be included. Exclusion criteria will include non-human studies, studies not written in English, and patients who suffer from primary or secondary causes of autonomic dysfunction due to the fact that these patients may exhibit an a priori temperature regulation disorder.

## Search Strategy

Research studies within the last 10 years will be sought through data bases that include PubMed, CINHAL, and Embase. Search terms will include hypothermia, anesthetic recovery, young adult, perioperative, postoperative, and PACU. Additional literature will be sought using Google Scholar.

**Data Collection**

For each study, the PRISMA guidelines will be followed to accurately appraise the research. The PRISMA flow diagram (Figure 3A) will be used to screen for eligible studies. The study information to be collected includes aim, design, sample, method, and outcomes. Outcome specific data sought will include post anesthesia recovery time. The solicited variable will be quantitative data on core body temperature differences and postoperative recovery time analysis.

The systematic review will begin January 2021. Data Collection will be completed by April 2021. Critical appraisal analysis and final written study will be completed by July 2021. Articles will be reviewed methodically. Each study will be transferred into data collection tables created by this researcher. Two tables have been formulated and tailored to meet the focus of this systematic review. Data to be collected and displayed in Table 1 include: author, aim, design, sample, method, outcomes. Data to be collected and displayed in Table 2 include: author, ASA, patient temperature, and anesthesia recovery time.

**Table 1**
*Data Collection Tool 1*

| Author | Aim | Design | Sample | Method | Outcomes |
|---|---|---|---|---|---|
| | | | | | |

**Table 2**
*Data Collection Tool 2*

| Author | ASA Class | Patient Temperature (Intraoperative and Postoperative) | Anesthesia Recovery Time |
|---|---|---|---|
| | | | |

**Critical Appraisal Analysis**

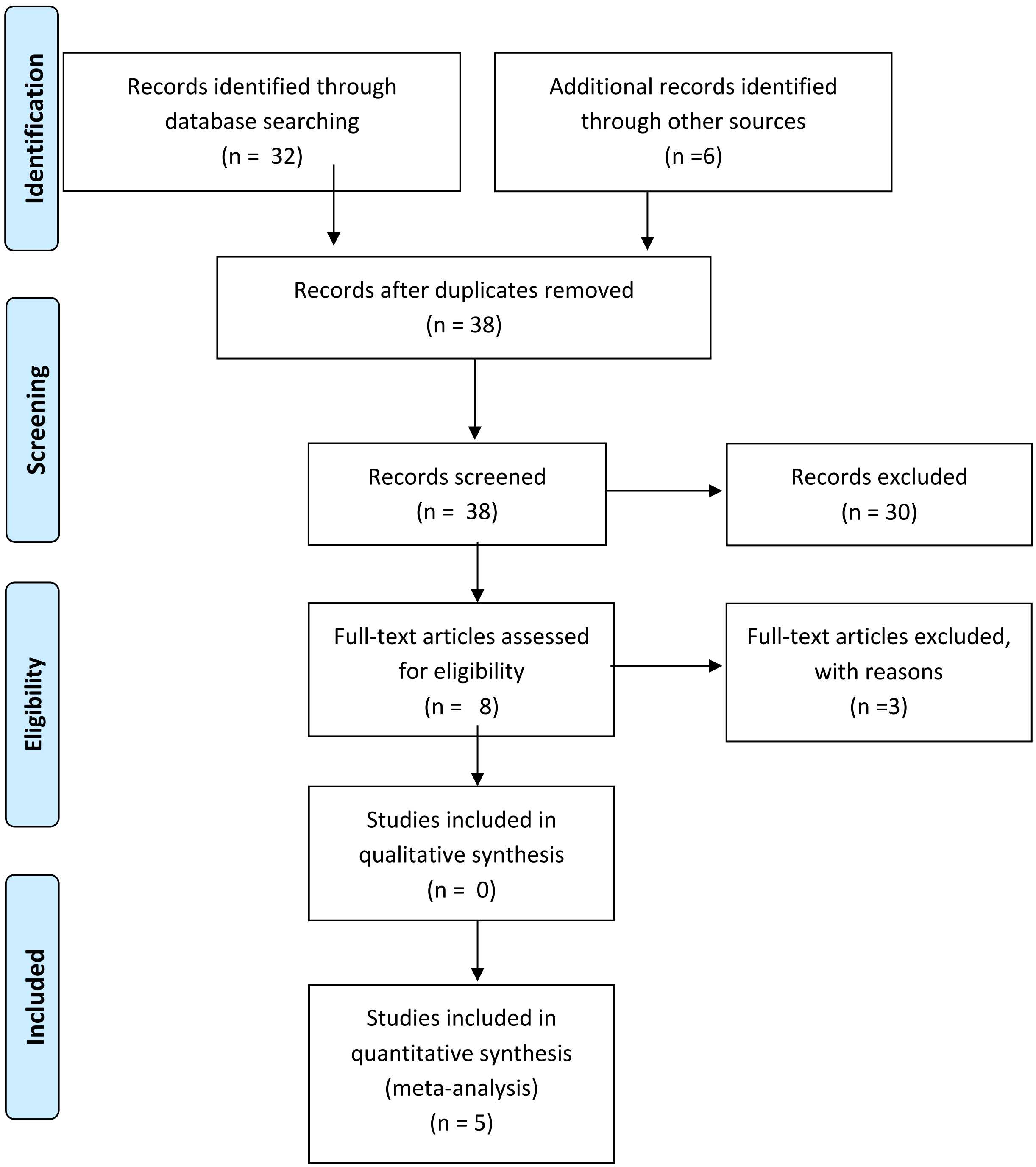
For this author's research, the Critical Appraisal Skills Programme (CASP) will be used. CASP consists of eight appraisal tools designed to be used when reading research, including Systematic Reviews. The CASP checklist consisting of eleven questions will be utilized to systematically appraise chosen articles for quality and validity (Appendix B). This checklist is divided into three sections. The first section is used to assess study validity, the second section to detail study results, and the third section to apply the study to the designated target population (CASP, 2018). Data will be organized using a cross-study analysis table. Relevant data will be collected from each study and entered into a table in order to analyze the similarities and differences among the studies and formulate a conclusion. The cross-study analysis will evaluate the similarities and differences regarding patient recovery time and patient temperature perioperatively.

Through the use of the established NSM theoretical framework, the PRISMA reporting guidelines, and the CASP appraisal tool, this author intends to conduct a systematic review to investigate the effect of perioperative hypothermia on anesthetic recovery in young healthy adults ages 18-45 with ASA classes I and II scores compared to young healthy adults who were not hypothermic perioperatively. There is a paucity of literature on the effects of perioperative hypothermia in this group, perhaps due to a conventional wisdom which suggests that young healthy adults may be little affected by conditions which are generally associated with less than desirable outcomes in older adults, such that precautions taken for elderly or infirm patients may be overlooked in the ASA Class I / II group during the perioperative period. However, this assumption may be erroneous. Young adults may be at risk from hypothermia in a surprising variety of ways, which will only be manifested by scientific research that provides further insight and can help guide future perioperative safeguards, aiding and highlighting optimal anesthesia recovery for this group.

Dissemination refers to a planned procedure involving thoughtful deliberation of both the target audience and the setting in which research findings are to be received. Other considerations include diving into wider policies which may facilitate the use of the research in both current and future decision-making processes and clinical practice policies (Wilson et al., 2010). Disseminating research findings requires determining who the intended audience is and how to reach them. The audience should include those who are likely to have an interest in or benefit from the topic. This author accepts it as a scholarly duty to disseminate the findings of this proposed research to colleagues and institutional policymakers in order to affect clinical protocols regarding the prevention of perioperative hypothermia. To generate such change, it would be most effective to present the review findings during in-house institutional conferences and via publications such as institutional or professional organization newsletters and journals. Providing information on best practices to combat the common problem of unintentional hypothermia will lead to better patient outcomes, earlier post-anesthesia care unit recovery times, and shorter hospital stays. This author will be presenting a digital poster at the MSN Poster Presentations. The SR will be available on Digital Commons, an electronic repository of academic papers.

## Results

**Figure 3B**
*PRISMA Four Phase Flow Diagram*
(Altman et al., 2009)



Five studies were included in this systematic review. The Prisma Flow Diagram was utilized to display search results (Figure 3B). Studies were analyzed and data was collected and placed into tables which can be seen in the "Data Tables" Section.

Bayter-Marin et al. (2018) conducted a randomized controlled clinical trial which focused on the effect of hypothermia in patients undergoing body contouring. The study included women between 18 and 55 years of age undergoing procedures lasting more than 3.5 hours (either lipoabdominoplasty alone or in combination with breast augmentation). Only ASA Class I patients were included. The 122 patients included in the study were divided into 3 groups.

In Group 1, no protective measures were taken to prevent hypothermia. In Group 2, intraoperative interventions which protected against hypothermia were implemented for the duration of the surgical procedure. Lastly, in Group 3 both preoperative and intraoperative interventions against the development of hypothermia were implemented. Group 1 consisted of 43 participants, there were 39 patients in Group 2 and 40 patients in Group 3.

A bivariate analysis was performed, considering hypothermia as the dependent variable. Independent variables were chosen from general data corresponding to the postoperative period. Nine statistically significant variables with $P < 0.05$ were identified, namely:  no protection, intraoperative protection, preoperative and intraoperative protection, required morphine, start temperature < 36 degrees Celsius, cold time < 10 minutes, shivering time < 5 minutes, postoperative pain < 4 and morphine dose < 4 mg.

Protective factors were identified as intraoperative thermal protection [RR of 0.77 ($P = 0.0007$)] and preoperative and intraoperative thermal protection [RR of 0.55 ($P \geq$

0.0001)]. A lack of protective actions was an associated risk factor [RR of 1.27 (P = 0.016)]. Patients who had a preoperative temperature < 36°C (96.8°F) were 1.21 times more likely to develop more significant hypothermia (P = 0.041).

Feeling cold for > 10 minutes and shivering for > 5 minutes were found to be risk factors for hypothermia [RRs of 1.52 (P = 0.0090) and 1.96 (P ≥ 0.0001)], respectively. Postoperative pain of 4 on a scale from 1 to 10 (RR of 1.62, P ≥ 0.0001), a requirement of analgesic morphine (RR 1.72, P ≥ 0.0001) and the need for doses higher than 4 mg of morphine (RR 1.11, P = 0.0119) were classified as associated risk factors. One hundred and four patients (85.25%) developed hypothermia: 76 (73.08%) reported feeling cold postoperatively, 60 (57.69%) experienced tremors, and 88 (84.62%) required morphine analgesia.

Patients in both Groups 1(no thermal protective measures) and 2 (only intraoperative thermal protective measure) required morphine, while only 15% in Group 3 (both preoperative and intraoperative thermal protective measures) required IV analgesia with morphine. Important differences were also observed with respect to pain, shivering, duration of cold sensation, and nausea. Of the patients in Groups 1 and 2, all developed hypothermia, in comparison with 22 (55%) of the patients in Group 3. All patients in Group 1 experienced a significant degree of hypothermia, longer anesthesia recovery time, longer overall recovery, heightened pain, increased complaints of feeling cold, as well as more nausea. They also required a higher opioid dose compared with those in Groups 2 and 3.

The study was critically appraised using the CASP tool (Appendix B1). A total of 122 patients were randomized into three groups to evaluate hypothermia in patients undergoing plastic surgery and the effect of certain interventions to prevent hypothermia during surgery. Groups were similar at the start of the study. The study had a clear focus of evaluating the effect of hypothermia on patients undergoing body contouring procedures. Groups were noted to have received equal treatment, including the same anesthetic technique, according to the protocol. Treatment consisted of total intravenous anesthesia (TIVA) with remifentanil and propofol with bispectral monitoring of the depth of anesthesia (bispectral index [BIS]). After intubation, an esophageal temperature monitor was used to assess core body temperature. At the end of surgery, the patients were transported to the post anesthesia recovery area, where they were provided with heating blankets and forced hot air at 38°C (100.4°F).

Statistical analysis was performed and groups were compared using the Mann-Whitney U test or Fisher's exact test. The association between each of the independent variables and the observed outcomes was evaluated by calculating relative risk (95%), confidence intervals (95%) and P values. The average time spent in the recovery room until the patient was transferred to the hospital floor unit was 108 minutes for patients in Group 1(no thermal protection) (89 to 122 minutes), 84 minutes for patients in Group 2(only intraoperative thermal protection) (60 to 102 minutes), and 63 minutes for patients in Group 3(both intraoperative and preoperative thermal protection) (50 to 70 minutes). Clinically important outcomes were taken into consideration by the researchers and the results are applicable to the context of this systematic review. The report of a postoperative pain level of 4 on a scale from 1 to 10 (RR of 1.62, $P \geq 0.0001$), the need for analgesic morphine (RR 1.72, $P \geq 0.0001$) and the requirement of doses higher than 4 mg (RR 1.11, $P = 0.0119$) were all identified as associated outcomes related to hypothermia. It can be inferred that patients who suffer from high levels of pain requiring increased analgesia will require longer PACU stays, as pain is included in PACU discharge criteria.

The second study by Lee et al. (2015), was a randomized, parallel-group, safety-assessor-blinded phase IV study. The study included sixty ASA Class I-II patients between the ages of 21–64 undergoing elective abdominal surgery. Sixty participants were randomly assigned to either the hypothermia group (n = 30) (core temperature between 34.5°C and 35°C) or the control group (n = 30) (core temperature between 36.5°C and 37°C).

Hypnotic depth was evaluated using a bispectral index (BIS) XP monitor. Core body temperature was continuously observed by a thermocouple placed in the distal esophagus. Core temperature was manipulated utilizing forced-air warming to maintain ranges of 36.5°C - 37°C in the control group and by surface cooling and an air conditioner fan to maintain ranges of 34.5°C - 35°C in the hypothermia group.

The ulnar nerve was stimulated supramaximally at wrist level with a TOF mode every 15 seconds. PTC stimulation was initially performed 10 min after obtaining complete NMB, and was repeated manually every 6 min thereafter. Thirty minutes after the initial dose, Rocuronium was continuously infused to adjust to PTC 1 – 2. Following application of the surgical dressing, PTC 1 – 2 was confirmed on the TOF-Watch SX® reading, after which sugammadex 4 mg/kg was administered.

The mean recovery time to TOF ratio of 0.9 after sugammadex administration was 171.1 seconds in the hypothermia group, in comparison to 124.9 seconds in the normothermia group (p = 0.005); a difference of approximately 46 seconds. A significant majority of patients (83%) in the normothermia group evidenced a recovery time to TOF ratio of 0.9 in < 180 seconds. By contrast, only 60% of patients in the hypothermia group recovered within 180 seconds.

The study was critically appraised using the CASP tool (Appendix B2). The study focus was made clear by the researchers. Treatment was randomized among participants. All sixty patients involved in the study were accounted for in the statistical analysis. The safety assessor was blinded to the study groups. The study groups were similar across the following variables: BIS monitoring, core temperature, demographic profile, end tidal concentration of sevoflurane, rocuronium dose, surgery type and time under anesthesia. Groups were treated equally during the study. The effect of hypothermia on mean recovery to train of four ratio of 0.9 was shown to be significantly prolonged (p=0.005) compared to the normothermic group. Categorical data was compared between groups by virtue of chi-squared analysis. Between-group comparisons were evaluated using unpaired t-tests. A repeated measures ANOVA was implemented for the changes of blood pressure and heart rate. A p-value less than 0.05 was considered statistically significant. These results are applicable to the focus of this systematic review, as they demonstrate the prolongation of anesthesia recovery in the ASA class of interest. The benefit of this study is that it provides a better understanding of the consequences of hypothermia on neuromuscular blockade recovery.

The third study, conducted by Hostler et al. (2010) was a prospective, randomized, single-center, four-way crossover laboratory study. The study evaluated the effect of lowered temperature on CYP3A4/5 activity in healthy human subjects by ascertaining changes in the metabolism of midazolam. It included six healthy ASA Class

I male subjects between 19 and 39 years of age. Each participant was tested on four separate occasions, one week apart. Monitoring included a standard three-lead electrocardiogram, blood pressure, pulse oximetry, and end-tidal carbon dioxide. Blood pressure and subjective thermal sensation were measured at 5-min intervals throughout the infusion and every 10 min thereafter. A universal Ramsay sedation scale was used to evaluate the sedation state caused by the administration of midazolam. Core body temperature was monitored on a continuous basis using an ingestible thermometer pill. Temperature values recorded by this mechanism are intermediate to esophageal and rectal temperatures.

Mild hypothermia was affected by the infusion of cold (4°C) saline over 30 min, with or without 4 g of magnesium sulfate. The normothermic controls were infused with warm (37°C) saline, with or without magnesium. Each of the 6 participants are represented in each of the following four treatment groups: 37°C saline infusion, 37°C saline with magnesium sulfate infusion, 4°C saline infusion, and 4°C saline with magnesium sulfate infusion. Six individual midazolam time-plasma concentration profiles were documented for each treatment group.

A total of 6 mg of intravenous midazolam was administered as three separate 2-mg doses at 0, 10, and 20 min from the start of the saline infusion. Blood samples were collected at baseline and at 5, 15, 25, 30, 50, 80, 140, and 200 minutes. Blood and urine samples were collected to evaluate both the plasma levels of midazolam and 1′-hydroxymidazolam formation clearance.

Infusion of 37°C (warm) saline resulted in a non-significant 0.4 ± 0.2°C decline from baseline temperature. Infusion of warm saline with magnesium also resulted in a non-significant temperature reduction of 0.9 ± 0.3°C. Exposure to a 4°C (cold) saline infusion produced a diminishment in core temperature of 1.4 ± 0.3°C with a further 1.8 ± 0.3°C decrease from baseline with a cold + magnesium infusion. A statistically significant effect on core temperature was noted with cold saline ($p = 0.015$) and cold saline with magnesium ($p = 0.035$).

Midazolam, a well-known CYP3A probe, was used as an index of CYP3A4/5 metabolism. Midazolam's primary metabolite (~70%) is 1′-hydroxymidazolam. Consistent with previous clinical studies, results demonstrated that even in hypothermia of short duration, the 1′-hydroxymidazolam formation clearance in the cold + magnesium group was significantly lower than in the normothermia group.

Systemic and intercompartmental clearance of midazolam were both affected by core temperature. The lowest core temperature in this study (34.8°C) resulted in a clearance 29.6% lower than that noted at the highest core temperature (37.8°C). An estimated 11.1% reduction in midazolam clearance for every 1°C reduction in core temperature was described.

The study was critically appraised using the CASP tool (Appendix B3). This study had a very narrow focus of addressing the effect of hypothermia on midazolam metabolism and clearance. It was a randomized laboratory study that consisted of six ASA class I volunteers. There were a total of four interventions as described above, and each of the 6 participants received a different type of intervention every week for 4 weeks. Researchers did not note whether or not participants were blinded to the intervention they received in any given week. The treatment effect revealed a significant decrease in clearance of midazolam between the cold saline with magnesium group and the warm group (P=0.0168). A p-value of less that 0.05 was considered significant. Based on the model, it was predicted that midazolam clearance would decrease 11.1 % for each degree core body temperature dropped below 36.5°C. All clinically important outcomes were considered by the researchers. The benefit of the study is that it provides a detailed overview of how mild hypothermia can significantly delay the metabolism of a frequently used anesthetic agent such as midazolam, and therefore, affect the length of time it takes this patient population (ASA class I) to recover from anesthesia.

The fourth study by Luís et al. (2012) conducted a prospective observational study of 340 patients which aimed to evaluate the incidence, predictors, and outcomes of inadvertent postoperative hypothermia (IPH). The incidence of IPH on admission to the PACU was 32%. In univariate analysis: admission visual analogue scale (VAS) for pain score > 3, age, amount of intravenous fluids infused, BMI, duration of anesthesia and high risk surgery, type of anesthesia, revised cardiac risk index (RCRI) and use of forced-air warming were found to be predictors of hypothermia. Independent predictors of IPH according to multiple logistic regression analysis included age ($p = 0.045$, for age > 65 years), RCRI ($p = 0.041$, for RCRI > 2), admission VAS for pain ($p = 0.007$) and duration of anesthesia ($p < 0.001$). Patients with IPH at PACU admission had longer PACU stays.

The study was critically appraised using the CASP tool (Appendix B4). The study had a clear focus to estimate the incidence, predictors and outcome of core hypothermia on admission to PACU. This prospective study collected data from willing postoperative participants admitted to the PACU. Temperature measurements were recorded using a tympanic membrane thermometer that was calibrated for accuracy. A univariate analysis was utilized to establish determinants for hypothermia. The Mann-Whitney U test was used to compare continuous variables and the Chi-square or Fisher's exact test was used to compare proportions between the two study groups. Finally, multiple logistic regression analysis with an odds ratio (OR) and 95% confidence interval (CI) was employed to assess independent predictors of hypothermia. Confounding factors were identified such as duration of anesthesia, surgical procedure, and the use of intravenous colloids. Patients were followed throughout their stay in the PACU. Results of this study can be applied to the local population and are consistent with other similar studies. A p-value of $\leq 0.05$ was considered statistically significant. Hypothermia was found to be a risk factor for longer length of post anesthesia care unit stay ($P = 0.009$). However, in this study hypothermia was not found to be a predictor for longer hospital stay. The benefit of the study is that it enhances our body of knowledge critical to the prevention of peri-operative hypothermia in an effort to optimize clinical care.

The fifth study conducted by Yi et al. (2017), is a multi-site cross-sectional study that aimed to ascertain the incidence of inadvertent intraoperative hypothermia and its related clinical outcomes among patients undergoing elective surgery. More than 87% of the participants fell into ASA Classes I or II. The following outcomes were assessed within 30 days: incidence of shivering (17.53% vs. 5.04%, $p<0.0001$), intensity of shivering (level 3 shivering: 5.63% vs. 1.55%, $p<0.0001$; level 4 shivering: 1.73% vs. 0.23%, $p<0.0001$), postoperative hospital stay ($16.97 \pm 8.93$ days vs. $14.99 \pm 8.25$ days, $p<0.0001$) and length of stay in PACU ($1.77 \pm 3.07$ h vs. $1.25 \pm 1.47$h, $p<0.0001$), surgical site infection, and postoperative mortality rate. Among the 3132 participants, 55.7% were normothermic while 44.3% experienced hypothermia. Hypothermic patients evidenced a greater prevalence and intensity of shivering, significantly longer PACU/postoperative in-hospital stay and were more likely to be admitted to the ICU (postoperative ICU admit rate: 10.03% vs. 4.64%, P<0.0001). There was no significant difference noted in surgical site infection or 30-day mortality.

The study by Yi et al. was critically appraised using the CASP tool (Appendix B5). The focus of the study was clear and aimed to determine the incidence of inadvertent intraoperative hypothermia and any of its outcomes that were associated with undesirable clinical consequences. IRB approval was granted, and randomized sampling was used at the 28 major teaching hospital sites where study subjects were obtained. To minimize bias, the thermometer was calibrated and validated according to the manufacturer's manual before use. Student t -test and chi-square were performed for continuous variables and categorical variables, respectively. Multivariate logistic regression was applied to evaluate the potential risk factors for inadvertent intraoperative hypothermia. Potential confounders were identified and included in the regression model, including age, gender, body mass index, ASA, baseline core temperature (prior to anesthesia), ambient temperature of the operating room, type of patient warming system used, amount of intravenous fluid replacement, duration of anesthesia, and magnitude of surgery. Patients were followed up for 30 days after surgery. Investigators who performed the follow-up were not blinded to intraoperative anesthesia care. Length of stay in PACU, incidence and intensity of postoperative shivering, postoperative length of stay, length in the hospital length of stay in ICU, PACU length of stay in hospital, infection rate of surgical sites, and mortality rate postoperatively within 30 days were recorded. The study outcomes, such as the increased length of PACU stay and overall hospital stay were consistent with other literature findings and supports the focus of this systematic review.

## Data Tables

**Table A1.**

*Data Collection Tool 1: Article #1*

| Author | Aim | Design | Sample | Method | Outcomes |
|---|---|---|---|---|---|
| Bayter-Marin, J. E., Cárdenas-Camarena, L., Durán, H., Valedon, A., Rubio, J., & Macias, A. A. (April, 2018). Effects of thermal protection in patients undergoing body contouring procedures: a controlled clinical trial. Aesthetic Surgery Journal, 38(4), 448-456. https://academic.oup.co | To evaluate the effect of hypothermia in patients undergoing plastic surgery and the effect of initiating easy measures to prevent perioperative hypothermia. | A randomized controlled clinical trial was performed evaluating 3 groups of patients who underwent body contouring surgery lasting > 3.5 hours. | 122 patients: 43 in group 1, 39 in group 2, and 40 in group 3. | Statistical analysis was performed with Stata software version 10.0. Groups were compared utilizing the Mann-Whitney U test or Fisher's exact test, and the association between each of the independent variables and the observed outcomes was calculated by evaluating relative risk (RR), 95% confidence intervals (95% CI) and P values.<br><br>Group 1: No Thermal Protection Measures<br>An esophageal temperature monitor was placed without perioperative temperature protection.<br>Group 2: Intraoperative Thermal Protection Measures | All patients in group 1 (no protective measures) experienced a greater degree of hypothermia, both longer anesthesia and overall recovery times, greater pain, increased perception of cold, and intensified nausea. They also required higher doses of opioids compared with the patients in groups 2 (only intraoperative |

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| m/asj/article/38/4/448/4566037 | | | | Only intraoperative protection measures were implemented: operating room air conditioning was deactivated before entering the room, before making intraoperative position changes, and half an hour prior to the end of surgery; intraoperative room temperature was maintained between 20°C and 22°C (68-71.6°F); subcutaneous fluids were kept at 37.5°C (99.5°F); aseptic and antiseptic fluids were preheated to 37°C (98.6°F); efforts were made to keep the exposed operative area dry.<br>Group 3 received the same measures Group 2, but in addition, received active pre-operative warming with hot air at 39°C (102.2°F) for 1 hour prior to surgery.<br>Core body temperature was measured until the end of the procedure to ascertain temperature decreases. All intraoperative variables were recorded by the | protective measures) and 3 (both preoperative and intraoperative protective measures). Many of these results were found to be statistically significant. |

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| | | | | anesthesiologist in a special format. Time between procedure end and patient awakening was recorded, as was time between procedure end and recovery room arrival. Evidence of shivering was documented. | |

**Table A2.**

*Data Collection Tool 1:* Article #2

| Author | Aim | Design | Sample | Method | Outcomes |
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| Lee, H. J., Kim, K. S., Jeong, J. S., Kim, K. N., and Lee, D. C. (January 21, 2015). The influence of mild hypothermia on reversal of rocuronium-induced deep neuromuscular block with sugammadex. BMC Anesthesiology, 15(7). https://www-ncbi-nlm-nih-gov.proxy.library.sto | To determine the reversibility of deep rocuronium-induced NMB for the PTC 1–2 steady block with sugammadex during mild hypothermia with core temperatures between 34.5°C and 35°C or normal thermal conditions. | Randomized, parallel-group, safety-assessor-blinded phase IV study | Sixty patients of both sexes, between 21–64 years, undergoing elective abdominal surgery under general anesthesia | Patients were randomly assigned to either the hypothermia group (n = 30) (mild hypothermia with core temperatures between 34.5°C and 35°C) or the control group (n = 30) (normal thermal condition with core temperatures between 36.5°C and 37°C) using a computer-generated program.<br><br>Sixty patients were randomly (1:1) allocated to the mild hypothermia and normothermia groups, defined as having core temperatures between 34.5 - 35°C and 36.5 - 37°C, respectively. | The mean recovery time to TOF ratio of 0.9 after sugammadex 4.0 mg/kg was 171.1 (62.1) seconds in the hypothermia group compared with 124.9 (59.2) seconds the normothermia group (p = 0.005)<br><br>The study confirmed that the recovery time to the TOF ratio of 0.9 after sugammadex administration in deep NMB was prolonged by 46 s during mild hypothermia (171.1 seconds) compared with the normal |

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| nybrook.edu/pmc/articles/PMC4430027/ | | | | Patients received 0.6 mg/kg of rocuronium, followed by 7 – 10 µg/kg/min to maintain a deep NMB [post-tetanic count (PTC) 1–2]. After surgery, the deep NMB was reversed with sugammadex 4.0 mg/kg. The primary end-point was the time until the train-of-four (TOF) ratio was 0.9. | thermal condition (124.9 seconds). |

**Table A3.**

*Data Collection Tool 1:* Article #3

| Author | Aim | Design | Sample | Method | Outcomes |
|---|---|---|---|---|---|
| Hostler, D., Zhou, J., Tortorici, M. A., Bies, R. R., Rittenberger, J. C., Empey, P. E., Kochanek, P. M., Callaway, C. W., & Poloyac, S. M. (May, 2010). Mild hypothermia alters | The primary goal of the study was to evaluate the effect of hypothermia on CYP3A4/5 activity by evaluating alterations in midazolam metabolism. | Prospective, randomized, single-center, four-way crossover study. | Six ASA I male participants between 19-39 years of age completed all study phases | A nonparametric bootstrap approach using sampling with replacement was used to assess validity of pharmacokinetic model estimates in 4 test groups.<br>Continuous core temperature was observed using an ingestible thermometer capsule. Core and skin surface temperatures were recorded every 2 minutes during either normothermic or hypothermic infusions of either saline or saline & magnesium, as well as every 10 minutes thereafter, in each of the 4 groups.<br>6 mg of midazolam, divided into three separate 2-mg doses, was administered intravenously. Doses were given at 0, 10, and 20 minutes from the start of the saline | A significant decrease in the 1′-hydroxymidazolam clearance was noted during cold saline + magnesium compared with the other 3 groups (P = 0.0168). |

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| midazolam pharmacokinetics in normal healthy volunteers. Drug Metabolism and Disposition, 38(5), 781–788. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2872942/ | | | | or saline & magnesium infusions. Blood samples were collected at baseline and at 5, 15, 25, 30, 50, 80, 140, and 200 min. An aliquot of urine was collected from the total volume accumulated at the end of rewarming to establish 1′-hydroxymidazolam formation clearance. | |

**Table A4.**
*Data Collection Tool 1:* Article #4

| Author | Aim | Design | Sample | Method | Outcomes |
|---|---|---|---|---|---|
| Luís, C., Moreno, C., Silva, A., Páscoa, R., and Abelha, F. (October 20, 2012). Inadvertent postoperative hypothermia at post-anesthesia care unit: incidence, predictors, and outcome. Open Journal of | The aim of this study was to assess inadvertent core hypothermia on admission to the post-anesthesia care unit. | This prospective study was carried out in the Post-Anesthesia Care Unit at a 1100-bed community teaching hospital. All adult patients admitted to the PACU who underwent non-cardiac and non-intracranial surgery during a defined 22-day period were eligible for the study. | Of a total of 357 patients, 340 were included in the study (Table 1), 17 were excluded: 7 were admitted directly to SICU, 3 were incapable of furnishing informed consent or evidenced MMSE < 25, 3 did not undergo surgery, 1 underwent a neurosurgical procedure, 1 was not included because he | The variables recorded on admission to the PACU were admission temperature / pain Visual Analogic Scales, age, ASA status, BMI, gender, preadmission comorbidities and vital signs. The Revised Cardiac Risk Index was calculated, allocating one point for each of the following risk factors: cerebrovascular disease, high-risk surgery, insulin therapy for diabetes, | Participants exhibiting hypothermia had a longer duration of anesthesia (median 150 vs 102 min, P < 0.001) and surgery (median 110 vs 70 min, P < 0.001) and increased visual analogue scale of pain scores (VAS > 3, median 2.4 vs 1.0, P = 0.031). Hypothermia was also noted to be a risk factor for lengthier PACU stays (65 - 125 vs 75 - 147 min., |

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| Anesthesiology, 2, 205-213. https://www.scirp.org/pdf/ojanes20120500003_17496994.pdf | | | was younger than 18 years old, 1 did not speak the native language and 1 declined to consent to participate. | ischemic heart disease, and renal failure. Data collection included duration of anesthesia and surgery, amount of intraoperative fluids administered, type of active warming utilized, and the type of anesthesia, including the specific anesthetic agents utilized. Length of PACU / hospital stays were documented.<br><br>Core temperature was measured using an infrared tympanic membrane thermometer. Study participants were | P = 0.009), but did not prognosticate extended hospital stays. |

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| | | | | characterized as either hypothermic (< 35˚C) or normothermic (≥ 35˚C). | |

**Table A5.**

*Data Collection Tool 1:* Article #5

| Author | Aim | Design | Sample | Method | Outcomes |
|---|---|---|---|---|---|
| Yi, J., Lei, Y., Xu, S., Si, Y., Li, S., Xia, Z., Shi, Y., Gu, X., Yu, J., Xu, G., Gu, E., Yu, Y., Chen, Y., Jia, H., Wang, Y., Wang, X., Chai, X., Jin, X., Chen, J., Xu, M., Xiong, J., Wang, G., Lu, K., Yu, W., Lei, W., Qin, Z., Xiang, J., Li, L., Xiang, Z., Pan, S., | The study intended to ascertain the incidence, risk factors and clinical outcomes associated with intraoperative hypothermia by virtue of a national survey performed in China. | This was a national cross-sectional study with 30 days postoperativ e follow-up from November 2014 through August 2015. | A total of 3132 patients who had been administered general anesthesia were randomly selected from 28 hospitals throughout China. More than 87% of participants fell into ASA Class I or II. | Randomized sampling was used to select study subjects. The following demographic data were collected: age, ASA status, BMI, gender, and medical history. The following risk factors potentially linked to hypothermia were also gathered: amount of intravenous fluid administered, baseline core temperature (prior to induction of anesthesia), duration of anesthesia, magnitude of surgery, operating room ambient temperature and type | Among 3132 patients, 1386 (44.3%) evidenced hypothermia and 1746 (55.7%) were normothermic. Compared to the normothermic group, hypothermic patients had a greater prevalence (P<0.0001) and more vigorous shivering (levels 3 & 4, P<0.0001). Both PACU and hospital stays were significantly longer (P<0.0001), and there were more admissions to ICU in the hypothermic group than in the normothermic group (P<0.0001). No significant difference was noted in either surgical site infection (2.41% vs. 2.59%) or 30-day |

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| Zhan, L., Qiu, K., Yao, M., & Huang, Y. (June 8, 2017). Intraoperative hypothermia and its clinical outcomes in patients undergoing general anesthesia: national study in china. PLoS One, 12(6). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5464536/ | | | | of warming system utilized. Types of warming were classified as passive (for example: cotton blanket, surgical draping, etc.) or active (heating blanket, space heater, etc.). | postoperative mortality (0.35% vs. 0.44%). |

**Table A6.**

*Data Collection Tool 2*: Article #1

| Author | ASA Class | Patient Temperature (Intraoperative and Postoperative) | Anesthesia Recovery Time |
|---|---|---|---|
| Bayter-Marin, J. E., Cárdenas-Camarena, L., Durán, H., Valedon, A., Rubio, J., & Macias, A. A. (April, 2018). Effects of thermal protection in patients undergoing body contouring procedures: a controlled clinical trial. Aesthetic Surgery Journal, 38(4), 448-456. https://academic.oup.com/asj/article/38/4/448/4566037 | Limited to ASA Class I patients. | All patients in Groups 1 and 2 developed intraoperative hypothermia, as compared to 55% of patients in Group 3. The average temperature upon arrival to the PACU was 33.9°C in Group 1, 35.1°C in Group 2, and 35.5°C in Group 3. These results suggest that when measures are taken to protect body temperature, patients are less prone to develop hypothermia, as assessed in the immediate postoperative period. | Average recovery times were as follows: Group 1, approximately 108 min, Group 2, 84 min and Group 3, 63 min.<br><br>There was a 33% curtailment in the time spent between the end of surgery and arrival to the PACU between Groups 1 and 2, and an additional 39% mitigation between Groups 2 and 3. In terms of overall recovery time prior to discharge to the hospital floor, Group 1 spent 33% more time in the PACU in relation to Group 2, and Group 2 spent 25% more time in the PACU in relation to Group 3. These findings were attributed to |

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| | | | decreased drug metabolism, increased pain and tremor (shivering), the requirement of higher doses of morphine with associated nausea in Group 1 as compared to Group 2, and Group 2 relative to Group 3. |

**Table A7.**
*Data Collection Tool 2*: Article #2

| Author | ASA Class | Patient Temperature (Intraoperative and Postoperative) | Anesthesia Recovery Time |
|---|---|---|---|
| Lee, H. J., Kim, K. S., Jeong, J. S., Kim, K. N., & Lee, D. C. (January 21, 2015). The influence of mild hypothermia on reversal of rocuronium-induced deep neuromuscular block with sugammadex. BMC Anesthesiology, 15(7). https://www-ncbi-nlm-nih-gov.proxy.library.stonybrook.edu/pmc/articles/PMC4430027/ | Sixty patients limited to ASA class I - II | Patients were randomly assigned to the hypothermia and normothermia groups, defined as experiencing core temperatures between 34.5 - 35°C and 36.5 - 37°C, respectively. | The mean recovery time to TOF ratio of 0.9 after sugammadex 4.0 mg/kg was 171.1 seconds in the hypothermic group vs 124.9 seconds in the normothermic group ($p = 0.005$) Recovery time to the TOF ratio of 0.9 after sugammadex administration was extended by 46 seconds during mild hypothermia. |

**Table A8.**
*Data Collection Tool 2*: Article #3

| Author | ASA Class | Patient Temperature (Intraoperative and Postoperative) | Anesthesia Recovery Time |
|---|---|---|---|
| Hostler, D., Zhou, J., Tortorici, M. A., Bies, R. R., Rittenberger, J. C., Empey, P. E., Kochanek, P. M., Callaway, C. W., & Poloyac, S. M. (May, 2010). Mild hypothermia alters midazolam pharmacokinetics in normal healthy volunteers. Drug Metabolism and Disposition, 38(5), 781–788. https://www.ncbi.nlm.nih.g | All participants were young males who met classification criterion for ASA Class I. | 37°C saline administration resulted in a 0.4 ± 0.2°C decline from baseline temperature. 37°C saline + magnesium administration resulted in a temperature decrease of 0.9 ± 0.3°C. Cold (4°C) saline infusion lowered core temperature 1.4 ± 0.3°C from baseline. Cold (4°C) saline + magnesium infusion lessened core temperature 1.8 ± 0.3°C from baseline. In cold and cold + magnesium groups, the duration of mild hypothermia was 47.0 ± 24.5 and 101.3 ± 26.6 min, respectively. Statistically, there was an effect of cold saline ($p = 0.015$) and cold saline + magnesium ($p = 0.035$) on core temperature. Mean skin temperature changed over time but did not differ significantly in relation either to the | This study illustrated a reduction in midazolam metabolism during short duration of mild hypothermia in young healthy volunteers and supplied the basis for calculating changes in midazolam clearance referable to mildly hypothermic states.<br>The cold saline + magnesium infusion with midazolam reduced the core temperature in the absence of anesthesia. In addition, the midazolam clearance was significantly impaired by decreasing body temperature. Utilizing this model, study results predict midazolam clearance will be reduced by |

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| ov/pmc/articles/PMC28729 42/ | | infusion temperature or the addition of magnesium. | 11.1% for each degree of core temperature under 36.5°C.<br><br>Warm saline infusion with midazolam evidenced a small 0.4 ± 0.2°C reduction from baseline. Addition of magnesium evidenced a temperature decrease of 0.9 ± 0.3°C. |

**Table A9.**
*Data Collection Tool 2*: Article #4

| Author | ASA Class | Patient Temperature (Intraoperative and Postoperative) | Anesthesia Recovery Time |
|---|---|---|---|
| Luís, C., Moreno, C., Silva, A., Páscoa, R., & Abelha, F. (October 20, 2012). Inadvertent postoperative hypothermia at post-anesthesia care unit: incidence, predictors, and outcome. Open Journal of Anesthesiology, 2, 205-213. https://www.scirp.org/pdf/ojanes20120500003_17496994.pdf | ASA physical status: I/II**:** 277 patients III/IV/V**:** 63 patients | Admission median core temperature was 35.3˚C. Incidence of PACU admission hypothermia on the admission was 32.4% (95% CI, 29.8%, 34.9). Eighty-six percent of patients evidenced a core temperature of < 36.0˚C. | Hypothermic participants evidenced a longer duration of anesthesia (median 150 vs 102 min, P < 0.001) and of surgery (median 110 vs 70 min, P < 0.001) and showed greater visual analogue scale of pain scores on PACU admission (VAS > 3, median 2.4 vs 1.0, P = 0.031). Hypothermia was shown to be a risk factor for longer length PACU stays (65 - 125 vs 75 - 147 min., P = 0.009), but did not predict for extended hospital stays. |

**Table A10.**
*Data Collection Tool 2*: Article #5

| Author | ASA Class | Patient Temperature (Intraoperative and Postoperative) | Anesthesia Recovery Time |
|---|---|---|---|
| Yi, J., Lei, Y., Xu, S., Si, Y., Li, S., Xia, Z., Shi, Y., Gu, X., Yu, J., Xu, G., Gu, E., Yu, Y., Chen, Y., Jia, H., Wang, Y., Wang, X., Chai, X., Jin, X., Chen, J., Xu, M., Xiong, J., Wang, G., Lu, K., Yu, W., Lei, W., Qin, Z., Xiang, J., Li, L., Xiang, Z., Pan, S., Zhan, L., Qiu, K., Yao, M., & Huang, Y. (June 8, 2017). Intraoperative hypothermia and its clinical outcomes in patients undergoing general anesthesia: national study in china. PLoS One, 12(6). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5464536/ | The majority of participants were either class ASA I (10.70%) or ASA II (77.62%). | Among 3132 subjects, 1386 (44.3%) experienced hypothermia and 1746 (55.7%) remained normothermic. | PACU length of stay was significantly prolonged in hypothermic subjects as compared to normothermic patients (1.77±3.07 h vs 1.25 ± 1.47h, P<0.0001). Hypothermic participants evidenced longer hospital stays postoperatively, as compared to normothermic patients (16.97 ± 8.93 days vs 14.99 ± 8.25 days, P<0.0001). Moreover, hypothermic subjects were more likely to be admitted to ICU than those who remained normothermic (10.03% vs 4.64%, P<0.0001). |

**Table A11.**
*Cross Study Analysis Table*

| Author | ASA Class Status | Temperature | Recovery and Outcomes | Recommendations |
|---|---|---|---|---|
| Article #1 (Bayter-Marin et al. 2018) | The study population was limited to ASA Class I patients | All patients in groups 1(n=43) and 2(n=39) were hypothermic at the end of surgery, as compared to 55% of patients in group 3(n=40).<br><br>The average temperature upon arrival to the recovery area was 33.9°C in group 1, 35.1°C in group 2, and 35.5°C in group 3. | All patients in group 1 (no thermal protection group) experienced more significant hypothermia, longer recovery time from anesthesia, longer overall recovery time, increased pain, increased feeling of cold, more nausea and a greater requirement for opioids compared with the patients in groups 2 (only intraoperative thermal protection group) and 3 (preoperative and intraoperative thermal protection group). | Study was only performed using one clinical location. Increasing data across multiple healthcare settings would generate a better randomized sample.<br><br>In addition, the study could have been improved by evaluating differences among the 3 groups in overall hospital length of stay. |
| Article #2 (Lee et al. 2015) | Sixty patients of both sexes, ASA status I - II | Patients were randomly allocated to the mild hypothermia and normothermia groups, defined as having core temperatures between 34.5 - 35°C and 36.5 - 37°C, respectively. | The mean recovery time to TOF ratio of 0.9 after sugammadex 4.0 mg/kg was 171.1 s in the hypothermia group compared with 124.9 s in the normothermia group ($p = 0.005$) | The study could have been improved by evaluating twitch height (T1), which should be considered to confirm suitable recovery during the first 6 minutes after reversal with sugammadex (Kim et al., 2016). |
| Article#3 (Hostler et al. 2010) | All participants were ASA Class I young males | Core body temperature was monitored using a pre-calibrated ingestible thermometer that continuously measured temperatures in the range of | This study demonstrated that midazolam metabolism is reduced by mild short duration of hypothermia in normal healthy volunteers. | A larger sample size could have bolstered the credibility of this study (n=6) |

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| | | 0 to 50°C. Values recorded by this device are intermediate to esophageal and rectal temperatures. The capsule was administered 60 min before the beginning of the protocol. The protocol was initiated after three consecutive measurements indicated a stable core temperature reading. | | |
| Article#4 (Luís et al., 2012) | ASA physical status:<br><br>I/II: 277 patients<br><br>III/IV/V: 63 patients | Median core temperature at admission was 35.3˚C; 32.6˚C was the lowest temperature recorded and 37.5˚C the highest. Incidence of hypothermia on PACU admission was<br><br>32.4% (95% CI, 29.8%, 34.9). Eighty-six percent of patients evidenced a temperature of less than 36.0˚C. | Hypothermia patients evidenced higher scores for visual analogue scale of pain at PACU admission and hypothermia was a noted risk factor for longer length PACU stay (65 - 125 versus 75 - 147 min., P = 0.009) | The authors did not adequately define and categorize the types of warming methods utilized. |
| Article #5 (Yi et al., 2017) | The majority of subjects were either ASA I (10.70%) or ASA II (77.62%) status. | Among 3132 participating patients, 1386 (44.3%) experienced hypothermia and 1746 (55.7%) were normothermic. | Length of PACU stay was significantly longer in hypothermic participants than in normothermic participants.<br><br>Hypothermic participants experienced longer hospital stays postoperatively than normothermic patients.<br><br>Hypothermic patients were admitted to ICU more often than normothermic patients. | The preponderance of literature defines hypothermia as less than or equal to 35 degrees Celsius. This study defines hypothermia as less than 36 degrees Celsius, rendering the study findings less meaningful when compared to the body of literature regarding hypothermia. |

## Summary and Conclusions

A systematic review was conducted to evaluate the effect of inadvertent perioperative hypothermia (IPH) on anesthesia recovery times as it relates to the young adult in the ASA class I-II category. Searches were completed using PubMed, CINHAL, and Embase and Google Scholar. A comprehensive literature review highlighted the impact that IPH can have on anesthesia recovery times as evidenced by the endpoint of length of PACU stay. The literature review revealed the magnitude of the problem of hypothermia in the perioperative period. There was a large amount of literature on hypothermia, but very few articles focused solely on the ASA class of interest in this systematic review. In addition, many studies discussed the incidence of intraoperative hypothermia, but failed to evaluate its effect on recovery from anesthesia.

After reviewing the existing research and formulating inclusion and exclusion criteria, a total of five studies were identified for inclusion. The PRISMA checklist and four phase flow diagram were used to assess study quality and validity, as well as to ensure the proper components fit the systematic review. In addition, the CASP checklist tool (See Appendix B) was implemented for each study in order to assess further for quality, validity, and relevance to the topic of research, as well as to approach the articles in a structured manner and thereby improve the quality of the screening process.

Inadequate management of hypothermia in the perioperative period can lead to undesirable outcomes for patients during their recovery phase. As previously discussed, hypothermia can lead to the prolonged metabolism of frequently utilized anesthetic drugs. This is made evident by Hostler et al. (2010), in which researchers concluded that Midazolam metabolism is reduced by mild short duration of hypothermia in normal healthy volunteers. Hypothermia can also prolong the recovery from neuromuscular blocking agents as concluded in Lee et al. (2015) and can lead to increased visual analogue pain scores in post anesthesia recovery patients, as demonstrated by Luís et al. (2012). Bayter-Marin et al. (2018) concluded that hypothermia can cause an increased feeling of cold, more nausea postoperatively, and a greater requirement for opioids in the anesthesia recovery period. Yi et al. (2017) concluded that perioperative hypothermia increased the incidence and intensity of shivering, prolonged length of PACU stay, led to longer postoperative hospital stays, and was found to be associated with admission to the ICU.

Of the five studies that were included in this systematic review, three of them found that hypothermia leads to prolonged anesthesia recovery times, while the other two studies demonstrated that hypothermia prolongs the metabolism of and recovery from specific anesthetic drugs (midazolam and sugammadex), potentially leading to increased length of PACU stay.

As with all studies, there were some limitations to this systematic review. Only five studies met the inclusion criteria for this study; clearly, further research is indicated. In addition, one of the 5 studies that was included had only six participants, which makes it difficult to extrapolate findings to the general ASA class I-II population.

In summary, each of these five studies were examined extensively and appraised using the previously mentioned tools, revealing that perioperative hypothermia has a measurable effect on various physiologic mechanisms during the perioperative period and thus can significantly impact anesthesia recovery times as demonstrated by an increased length of PACU stay in the ASA I and II populations.

## Recommendations and Implications for Advanced Nursing Practice

Hypothermia is an ongoing problem that is encountered by CRNAs, anesthesiologists, and post-anesthesia care unit nurses on a regular basis. Patients undergoing anesthesia lose the ability to properly thermoregulate, leading to varying degrees and duration of hypothermia. This is of concern because of the frequency the phenomenon of inadvertent perioperative hypothermia is encountered, as well as the effects which occur in relation to it, such as prolonged metabolism of anesthetics, increased pain scores, increased analgesia usage and shivering which affect the patient's well-being as evidenced by prolonged PACU stays.

The preoperative holding area is an important area in the surgical suite, where peri-operative nursing staff help patients prepare for their surgical procedures. It is here that the CRNA can be instrumental in providing education on the importance of the thermoregulatory perioperative challenges that patients will face, as well as pre-operative interventions which can help minimize the potential for the development of inadvertent hypothermia. Ultimately, this collaboration would lead to an implementation of a pre-operative warming policy. Thus, providing teaching presentations on the subject, becoming a member of committees or attending meetings for the purpose of discussing potential policy needs should be considered a CRNA targeted intervention, where evidence-based measures can be utilized to implement a system-wide change which helps optimize patient outcomes. In addition, intra-operative protocols should be considered that encourage more frequent use of intravenous fluid warmers and combined upper and lower forced air warming when possible.

The primary goal of the anesthesia practice is to provide a safe an effective anesthetic while combatting any potential adverse events related to the surgical procedure and the administered anesthetic itself.

Diligent temperature monitoring throughout the intraoperative period and proper postoperative evaluation of thermodynamic status is critical in treating perioperative hypothermia and avoiding its potential complications. Anesthesia providers have several interventions to deal with this issue in the operating room setting. Some of these tools include, forced air warming systems, warmed intravenous fluid administration, pre-warming patients prior to surgery, and diligent core temperature monitoring. Effective preventive measures should be evidence based and include targeted approaches that are based on the patient's ASA risk scores.

Focusing attention on this ASA class of patient and this age group provides insight for anesthesia practice. In recent years, ambulatory surgery centers have become more common place and young healthy patients with lower ASA class scores are frequently seen in this setting. Surgeries such as Orthopedic rotator cuff repairs, torn meniscal repairs, sports medicine surgery, reproductive, and cosmetic surgery are frequently encountered procedures in this age group and ASA category. It is important to remember as anesthesia providers that despite the lower level of risk in the ASA class I and II patient, no surgery is benign and there will always be some level of risk that must not be ignored.

Recommendations for additional research include optimum preoperative temperature for preventing intraoperative hypothermia in ASA Class I / II patients, as well as the effects of combined methods of perioperative warming as compared with a single method. In addition, future studies should evaluate the optimal use of hypothermia treatment bundles for each ASA Class based on current findings in the literature.

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# Appendix A

## PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | |



*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

## Appendix B: CASP Checklist

**Table B1:** Article #1

Bayter-Marin, J. E., Cárdenas-Camarena, L., Durán, H., Valedon, A., Rubio, J., & Macias, A. A. (April, 2018). Effects of thermal protection in patients undergoing body contouring procedures: a controlled clinical trial. Aesthetic Surgery Journal, 38(4), 448-456.

| Questions | Yes | Can't Tell | No |
|---|---|---|---|
| **1.Did the Trial address a clearly focused issue?**<br><br>The purpose of the study was to evaluate the effect of both hypothermia and specific interventions to prevent hypothermia in patients undergoing plastic surgery. | ✓ | | |
| **2. Was the assignment of patients to treatments randomized?** | ✓ | | |
| **3. Were all of the patients who entered the trial properly accounted for at its conclusion?** | ✓ | | |
| **4. Were patients, health workers and study personnel 'blind' to treatment?** | | | ✓ |
| **5. Were the groups similar at the start of the trial?** | ✓ | | |
| **6. Aside from the experimental intervention, were the groups treated equally?**<br><br>All patients received the same anesthetic technique according to the clinic's protocol. Treatment consisted of total intravenous anesthesia (TIVA) with remifentanil and propofol, and endotracheal intubation with bispectral | ✓ | | |

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| monitoring of the depth of anesthesia (bispectral index [BIS]). After intubation, an esophageal temperature monitor was used to assess core body temperature. At the end of surgery, the patients went to post anesthesia recovery and were provided with heating blankets and forced hot air at 38°C (100.4°F). | | | |
| **7. How large was the treatment effect?**<br><br>Nine statistically significant variables with $P < 0.05$ were identified, namely: no protection, intraoperative protection, preoperative and intraoperative protection, required morphine, start temperature < 36 degrees Celsius, cold time < 10 minutes, shivering time < 5 minutes, postoperative pain < 4 and morphine dose < 4 mg. | ✓ | | |
| **8. How precise was the estimate of the treatment effect?**<br><br>RALLOC statistical software (version 6.0) was employed, and patients were randomized into three groups utilizing the Randomizer Pro App version 1.0.<br><br>Statistical analysis was accomplished with Stata software version 10.0. Groups were compared by applying the Mann-Whitney U test or Fisher's exact test, and the connection between each of the independent variables and the observed outcomes was evaluated by calculating relative risk (RR), 95% confidence intervals (95% CI) and P values. | ✓ | | |
| **9. Can the results be applied to the local population, or in your context?** | ✓ | | |
| **10. Were all clinically important outcomes considered?** | ✓ | | |
| **11. Are the benefits worth the harms and costs?** | ✓ | | |

**Table B2:** Article #2

Lee, H. J., Kim, K. S., Jeong, J. S., Kim, K. N., & Lee, D. C. (January 21, 2015). The influence of mild hypothermia on reversal of rocuronium-induced deep neuromuscular block with sugammadex. BMC Anesthesiology, 15(7).

| Questions | Yes | Can't Tell | No |
|---|---|---|---|
| **1.Did the Trial address a clearly focused issue?** | ✓ | | |
| **2. Was the assignment of patients to treatments randomized?** | ✓ | | |
| **3. Were all of the patients who entered the trial properly accounted for at its conclusion?** | ✓ | | |
| **4. Were patients, health workers and study personnel 'blind' to treatment?**<br><br>This was a phase IV randomized, parallel-group, safety-assessor-blinded study. | | ✓ | |
| **5. Were the groups similar at the start of the trial?**<br>Both randomized groups consisted of ASA Class I and II patients with similar demographic profiles. | ✓ | | |
| **6. Aside from the experimental intervention, were the groups treated equally?** | ✓ | | |

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| **7. How large was the treatment effect?**<br><br>The mean recovery time to TOF ratio of 0.9 after sugammadex administration was 171.1 seconds in the hypothermia group, in comparison to 124.9 seconds in the normothermia group (p = 0.005); a difference of approximately 46 s.<br><br>A significant majority of (83%) in the normothermic patients evidenced a recovery time to TOF ratio of 0.9 was < 180 s. By contrast, only 60% of patients in the hypothermia group recovered within 180 s. | ✓ | | |
| **8. How precise was the estimate of the treatment effect?**<br><br>The study revealed that 4 mg/kg sugammadex reversed patients in the normothermia control group from a rocuronium-induced NMB within 124.9 s; approximately 46 s faster than was noted in the hypothermia group. | ✓ | | |
| **9. Can the results be applied to the local population, or in your context?** | ✓ | | |
| **10. Were all clinically important outcomes considered?** | ✓ | | |
| **11. Are the benefits worth the harms and costs?** | ✓ | | |

**Table B3:** Article #3

Hostler, D., Zhou, J., Tortorici, M. A., Bies, R. R., Rittenberger, J. C., Empey, P. E., Kochanek, P. M., Callaway, C. W., & Poloyac, S.M. (May, 2010). Mild hypothermia alters midazolam pharmacokinetics in normal healthy volunteers. Drug Metabolism and Disposition, 38(5), 781–788.

| Questions | Yes | Can't Tell | No |
|---|---|---|---|
| **1.Did the Trial address a clearly focused issue?** | ✓ | | |
| **2. Was the assignment of patients to treatments randomized?** | ✓ | | |
| **3. Were all of the patients who entered the trial properly accounted for at its conclusion?** | ✓ | | |
| **4. Were patients, health workers and study personnel 'blind' to treatment?** | | | ✓ |
| **5. Were the groups similar at the start of the trial?** | ✓ | | |
| **6. Aside from the experimental intervention, were the groups treated equally?** | ✓ | | |
| **7. How large was the treatment effect?**<br><br>A significant decrease in the 1′-hydroxymidazolam formation clearance was observed during cold + magnesium compared with the warm group (2.43 ± 0.782 versus 3.41 ± 0.735 ml/min/kg, p | ✓ | | |

| | | | |
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| = 0.0168). Systemic clearance during cold + magnesium compared with the warm saline group demonstrated a trend toward a significant reduction during hypothermia versus normothermia (3.76 ± 0.386 versus 4.49 ± 0.560 ml/min/kg, p = 0.0568). | | | |
| **8. How precise was the estimate of the treatment effect?**<br><br>This model predicted that midazolam clearance would decrease 11.1% for each degree lower in core temperature from 36.5°C. In our normothermia group, warm saline infusion with midazolam resulted in a small 0.4 ± 0.2°C decrease from baseline. Addition of magnesium resulted in a temperature reduction of 0.9 ± 0.3°C. | ✓ | | |
| **9. Can the results be applied to the local population, or in your context?**<br><br>Due to the small sample size and the fact that the study consisted of only young males, it may not be generalizable to the local population | | | ✓ |
| **10. Were all clinically important outcomes considered?** | ✓ | | |
| **11. Are the benefits worth the harms and costs?** | ✓ | | |

**Table B4: Article #4**

Luís, C., Moreno, C., Silva, A., Páscoa, R., & Abelha, F. (October 20, 2012). Inadvertent postoperative hypothermia at post-anesthesia care unit: incidence, predictors, and outcome. Open Journal of Anesthesiology, 2, 205-213.

| Questions | Yes | Can't Tell | No |
|---|---|---|---|
| **1.Did the Trial address a clearly focused issue?** | ✓ | | |
| **2. Was the cohort recruited in an acceptable way?** | ✓ | | |
| **3. Was the exposure accurately measured to minimize bias?** | ✓ | | |
| **4. Was the outcome accurately measured to minimize bias?** | ✓ | | |
| **5a. Have the authors identified all important confounding factors?** | ✓ | | |
| **5b. Have they taken account of the confounding factors in the design and/or analysis?** | ✓ | | |
| **6a. Was the follow up of subjects complete enough?** | ✓ | | |
| **6b. Was the follow up of subjects long enough?** | ✓ | | |

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| **7. What are the results of this study?**<br><br>Hypothermia was a risk factor for longer length postanesthesia care unit stay (65 - 125 versus 75 - 147 min., P = 0.009), but was not a predictor for longer hospital stay. | ✓ | | |
| **8. How precise are the results?**<br><br>Descriptive analysis of variables was used to summarize data and the Mann-Whitney U test, Fisher's exact test or Chi-square test was used. Univariate and multivariate analyses were done with logistic binary regression with calculation of an Odds Ratio (OR) and its 95% Confidence Interval. | ✓ | | |
| **9. Do you believe the results?** | ✓ | | |
| **10. Can the results be applied to the local population?** | ✓ | | |
| **11. Do the results of this study fit with other available evidence?** | ✓ | | |
| **12. What are the implications of this study for practice?**<br><br>Knowledge regarding the predictors of perioperative hypothermia may be critical to its prevention and to optimize clinical care. | ✓ | | |

**Table B5:** Article #5

Yi, J., Lei, Y., Xu, S., Si, Y., Li, S., Xia, Z., Shi, Y., Gu, X., Yu, J., Xu, G., Gu, E., Yu, Y., Chen, Y., Jia, H., Wang, Y., Wang, X., Chai, X., Jin, X., Chen, J., Xu, M., Xiong, J., Wang, G., Lu, K., Yu, W., Lei, W., Qin, Z., Xiang, J., Li, L., Xiang, Z., Pan, S., Zhan, L., Qiu, K., Yao, M., & Huang, Y. (June 8, 2017). Intraoperative hypothermia and its clinical outcomes in patients undergoing general anesthesia: national study in china. PLoS One, 12(6).

| Questions | Yes | Can't Tell | No |
|---|---|---|---|
| **1.Did the Trial address a clearly focused issue?** | ✓ | | |
| **2. Was the cohort recruited in an acceptable way?** | ✓ | | |
| **3. Was the exposure accurately measured to minimize bias?** | ✓ | | |
| **4. Was the outcome accurately measured to minimize bias?** | ✓ | | |
| **5a. Have the authors identified all important confounding factors?** | ✓ | | |
| **5b. Have they taken account of the confounding factors in the design and/or analysis?** | ✓ | | |
| **6a. Was the follow up of subjects complete enough?** | ✓ | | |

| | | | |
|---|---|---|---|
| **Incidence and intensity of postoperative shivering, PACU / ICU / hospital length of stay and postoperative mortality rate within 30 days were recorded on the standard Case Report Form.** | | | |
| **6b. Was the follow up of subjects long enough?**<br><br>Patients were followed up for 30 days after surgery. | ✓ | | |
| **7. What are the results of this study?**<br><br>Among 3132 participating patients, 44.3% developed hypothermia and 55.7% were normothermic. Hypothermic patients had a greater prevalence (17.53% vs. 5.04%, P<0.0001) and more intense (level 3 shivering: 5.63% vs. 1.55%, P<0.0001; level 4 shivering: 1.73% vs. 0.23%, P<0.0001) shivering. The PACU LOS was significantly longer in hypothermic patients (1.77±3.07 h vs. 1.25 ± 1.47h, P<0.0001). Hypothermic patients had longer hospital stays (16.97 ± 8.93 days vs. 14.99 ± 8.25 days, P<0.0001), and were shown to be more likely to be admitted to ICU (ICU admission rate: 10.03% vs. 4.64%, P<0.0001). | ✓ | | |
| **8. How precise are the results?**<br><br>Descriptive analysis, including frequencies, percentages, mean, and standard deviation were presented. Student t test and chi-square were calculated for both continuous and categorical variables. Results were shown as odds ratios together with a 95% confidence interval (95% CI). | ✓ | | |
| **9. Do you believe the results?** | ✓ | | |
| **10. Can the results be applied to the local population?** | ✓ | | |

| | | | |
|---|---|---|---|
| **11. Do the results of this study fit with other available evidence?** | ✓ | | |
| **12. What are the implications of this study for practice?**<br><br>In the United States, perioperative hypothermia is considered a preventable adverse event, and its avoidance has been recommended. Practice guidelines recommend surgical patients be actively warmed. However, in developing countries like China, awareness of the adverse consequences related to hypothermia and lack of reimbursement policy on perioperative warming lead to a low utilization of available warming systems. This finding suggests that education and adequate reimbursement are two important variables which can affect the practice of peri-operative patient warming. | ✓ | | |