THE EFFECTIVENESS AND SAFETY OF PERIOPERATIVE ENTERAL FEEDING IN PATIENTS WITH BURN INJURIES: A SYSTEMATIC REVIEW

A thesis submitted for the degree of Master of Clinical Science

JBI

Faculty of Health and Medical Sciences

The University of Adelaide

Michelle Cork

BSc (Nutr&FoodSc), Grad Dip Dietetics

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Supervisory Team

Ms Alexa McArthur, RN RM MPHC MClinSc

Senior Research Fellow Transfer Sciences

JBI, Faculty of Health and Medical Sciences, The University of Adelaide, South Australia

Winthrop Professor Fiona M Wood FRACS AM

Director of the Burns Service of WA

Director of the Burn Injury Research Unit UWA

Dr Helen Douglas MBChB MSc MD FRCS(Plast)

Consultant Plastic and Burns surgeon, Burns Service WA

Senior Clinical Lecturer, University of Western Australia

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Executive Summary

This systematic review was undertaken as a result of a clinical question. The question being, "what is the optimum perioperative fasting/feeding regime for patients with burn injuries?" Fasting for theatre has been identified in research to have deleterious effects on surgical patients' nutrient intake, wellbeing and insulin resistance. Perioperative fasting is however intended to protect patients from regurgitation and pulmonary aspiration during surgery and immediately thereafter. Within the burns specialty, it was noted that some published research existed which investigated either short fasting or intraoperative feeding on clinical outcomes in patients with burn injuries. This systematic review aimed to synthesise all of the available research evidence and provide evidenced-based recommendations as to whether perioperative nutrition was safe for patients with burn injuries and whether it influenced patient outcomes. A quantitative review of effectiveness, in keeping with JBI methodology, was identified as the most appropriate approach to address the aims and objectives of this research.

The population of interest in this systematic review was people admitted for primary management of an acute burn injury which required surgical management. The intervention of either intraoperative enteral feeding or short fasting (less than 2 hours before surgery) was compared to perioperative fasting. Outcome measures were mortality, wound infection, length of stay, pulmonary aspiration events, pneumonia, Calorie delivery, ventilator days, wellbeing as well as any other relevant outcomes (e.g. bacteremia, clinical sepsis, antibiotic days, intensive care length of stay, supplemental albumin and length of stay per percentage of full-thickness burn).

Key databases searched were PubMed, CINAHL, Embase, Web of Science and Cochrane Central Register of Controlled Trials. Only studies published in English were considered. There were no date limits. Full texts of selected studies were retrieved and assessed against inclusion criteria. Studies that did not meet the inclusion criteria were excluded and reasons provided. Where possible, data synthesis was pooled in a statistical meta-analysis. When statistical pooling was not possible, the findings are presented in narrative form.

The systematic search identified 327 studies for potential inclusion (after duplicates were removed) however 320 studies were excluded. Seven studies were identified to have met the inclusion criteria. Two of the included studies were randomised controlled trials, three were retrospective cohort studies, one was a case series and one was a case report.

The results of the systematic review indicate intraoperative post pyloric feeding was safe in the patient groups investigated, since there were nil aspiration events in a combined intervention population of 509 patients. The safety of short fasting (feeds up to 1 hour before surgery) on aspiration events in non-ventilated patients with nasogastric enteral nutrition was less clear. There were nil aspiration events recorded but there was only one included study with 7 patients who received short fasting for nasogastric nutrition.

The effectiveness of perioperative nutrition was demonstrated by the consistent result of increased Caloric provision in patients who received intraoperative post pyloric feeding. Other outcome measures relating to the effectiveness of perioperative nutrition had varied results. Patient wellbeing was improved with shorter perioperative fasting in the singular case report and this result is consistent with literature for other surgical patients, but the certainty of the results from the included case report was very low. The outcomes of mortality, wound infection, length of stay, and ventilator days were inconsistent, with some studies showing improvements with perioperative feeding and others indicating worsening of these outcome measures. Two studies reported on pneumonia and both reported a slightly higher occurrence of pneumonia in the patient groups who received intraoperative post pyloric enteral feeding. Small sample sizes, high heterogeneity and major confounding factors between control and intervention groups contributed to very low certainty of findings.

Although this systematic review indicated perioperative enteral nutrition is safe and improves Caloric intake in patients with burn injuries, further research is needed to determine whether perioperative feeding has an impact on other patient outcomes. A recommendation for future research could be a large-scale multi-centre research project where patients are randomly allocated to receive either standard treatment or post pyloric perioperative feeding. Outcome measures could include patient wellbeing, insulin resistance, as well as wound infection, length of stay, mortality, pneumonia, ventilator days and Caloric intake.

Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint award of this degree.

I give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

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I do not have any conflicts of interest with this research topic.

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Chapter 1: Introduction

1.1 Background

The incentive for this systematic review came from a workplace clinical question. I was asked to investigate the optimum feeding/fasting regime for patients with burn injuries. The clinical question emerged because members of my burns team had increasing awareness of ERAS (enhanced recovery after surgery) protocols being introduced in other surgical specialties, for example colorectal surgery, orthopaedics and major head and neck cancer surgery.[1] An aspect of ERAS is perioperative nutritional care with some guidelines recommending preoperative carbohydrate oral liquids up to two hours before surgery and overall minimal perioperative fasting.[2,3] Evidenced-based ERAS protocols have been identified as best practice standards in perioperative care.[4] A review of literature indicated there were not any ERAS evidenced-based guidelines for the burns surgical specialty and also no identified published research on the provision of preoperative carbohydrate-rich oral fluids to patients with burn injuries. There were however, research papers reporting on the safety and effectiveness of perioperative enteral feeding in burns patients. The existence of several studies and the lack of evidence-based conclusions relating to whether patients with burn injuries could benefit from perioperative nutrition provided the foundation for this systematic review.

1.2 Context of the review

Burn injuries cause the most extreme physiological and metabolic stress of all critical illness.[5] Adequate nutritional support is a key element of caring for patients with major burns, in order to effectively manage the associated increased metabolic demand, protein catabolism and weight loss.[5,6] Nutritional care has been identified to have many benefits for patients with burn injuries including preservation of lean body mass, promotion of wound healing, reduction of gut mucosal permeability, enhancement of immunologic defences reduction in Curling's ulcers, increased insulin levels, reduced catecholamine levels and reduced mortality.[7,8,9] In a similar manner whereby adequate nutritional care is beneficial to patients with burn injuries, literature also suggests that nutritional inadequacy and subsequent malnutrition negatively impacts patient outcomes. Nutritional inadequacy of patients with burns is reported to increase patient mortality, increase length of stay, elevate the risk of infection, worsen lean muscle mass loss, delay wound healing and prolong ventilator time.[5,10] If adequate nutrition support is not initiated in a person with a major burn, their subsequent malnutrition can reach a lethal level in just 3-4 weeks.[6] In order to meet the metabolic and nutritional demands of patients with burn injuries, guidelines recommend specialised

assessment of patient needs, implementation of evidence-based nutritional support strategies and regular re-evaluation of regimes based on clinical circumstances.[7]

Where possible, patients with burn injuries should aim to meet their nutritional requirements through nourishing and adequate oral intake.[6] The severity, size and location of burns however can make it extremely difficult for patients to consistently consume their required energy and nutrients.[6] If patients with burns are either unable or unlikely to meet their nutrition requirements by consuming oral diet and fluids, then enteral tube feeding is recommended. Enteral feeding is a broad term which is defined as the provision of nutrients through the gastrointestinal tract and may include either feeding into the stomach or the small intestine.[11] Enteric feeding into the stomach is normally referred to as intragastric feeding and may be delivered through either a nasogastric feeding tube, orogastric feeding tube or a gastrostomy tube. Enteral feeding into the small intestine is often referred to as post pyloric feeding and may be delivered via either a nasoduodenal, nasojejunal or jejunostomy feeding tube. For the purposes of this research, enteral feeding will be used to define the provision of nutrients via an enteric feeding tube which terminates either in the patient's stomach (intragastric) or into the patient's small intestine (post pyloric).

There are clinical practice guidelines which recommend commencement of enteral feeding in patients who have a burn injury above a certain percentage total body surface area (TBSA). These guidelines are overall similar but there are some differences between associations. For example, the Australian and New Zealand Burn Association (ANZBA) recommends that children with greater than 15% TBSA burn injuries and adults with greater than 20% TBSA burn injuries should be assessed for enteral nutrition support.[7] Similarly, the European Society for Clinical Nutrition and Metabolism (ESPEN) endorsed guidelines recommends patients with major burns (greater than 20% TBSA) receive early nutritional therapy, preferentially by the enteral route.[8] The most recent evidence-based, physician-authored clinical guidelines from UpToDate® recommend enteral nutrition support for patients with moderate-to-severe burn injuries (greater than 20% TBSA) and some patients with less than 20% TBSA burns in at-risk groups (e.g. children, older adults and those with metabolic syndrome).[12] The International Society for Burn Injuries (ISBI) recommends patients with greater than 20% TSBA burns receive adequate calories and protein to meet their nutritional needs and requirements however these recommendations acknowledge that in resource-limited countries, access to enteric feeding tubes and formulae may be limited. As a result, the ISBI clinical practice guidelines do not provide specific recommendations on the percentage TBSA burn for patients to commence enteric tube feeding but recommend optimising nutrition using the best available resources.[6] In summary, clinical practice guidelines for patients with burn

injuries have some variation throughout the world, however they commonly recommend enteral nutrition support in patients with major burns (frequently cited as greater than 20% TBSA) and also patients within vulnerable patient subgroups.

Oral and enteral fasting for theatre has been identified as the most common reason patients with burn injuries miss-out on nutrition, however numerous factors have been identified which cause sub-optimal nutrition in this patient group.[13,14] Other barriers to nutrition support may include elevated gastric residual volumes, dressing changes, prolonged therapy times, diagnostic tests performed away from the unit, dislodged feeding tubes, clogged feeding tubes, fasting for extubation, emesis, and ileus.[15] Although some causes of stopping enteral feeding may be unavoidable, long periods of imposed perioperative fasting may be unnecessary and may contribute to negative patient outcomes.

There are three distinct areas discussed in literature where perioperative fasting has been directly linked to negatively influencing the clinical course of either patients with burn injuries or other patients undergoing surgical interventions. The three domains relate to causing overall energy deficits, detrimental effects on patient wellbeing and also negative metabolic effects.

The extent of perioperative fasting on energy deficits in patients with burn injuries

The scope of energy deficits associated with perioperative fasting in patients with burn injuries has been investigated in several audits. For example, Winkworth et al.[16] identified that adult and pediatric burns patients in their study (mean 20% TBSA injury) experienced an average overall energy deficit of 12% per week due to perioperative fasting.[16] Similarly, Lyons and Clemens[13] retrospectively reviewed the nasogastric enteral nutrition of their intubated and ventilated adult burn patients (>20% TBSA and mean 40% TBSA injury). They found that the patients experienced a deficit of 18% of estimated energy requirements due to feeds being stopped perioperatively.[13] The nutritional deficits associated with perioperative fasting has been identified to potentially impact patient recovery and outcomes such as mortality and wound infection however the authors also noted further investigations are required.[16]

The impact of perioperative fasting on patient wellbeing

Fasting for surgery may not only cause energy deficits in patients with burn injuries but could also have deleterious impacts on patient well-being.[17] Burns-specific studies investigating a relationship between perioperative fasting and patient wellbeing could not been identified by this author, however a systematic review by Bilku et al.[18] reported on the impact of

preoperative carbohydrate loading on elective surgery patients' wellbeing compared to the traditional fast from midnight. This study concluded that pre-operative carbohydrate drinks, up until the morning of surgery, significantly improved patient wellbeing after surgery, including reduced hunger, thirst, malaise, anxiety and nausea compared to patients who had either extended fasting or placebo.[18] Another study by Tosun et al. evaluated the effects of preoperative fasting and fluid limitation in 99 patients undergoing laparoscopic cholecystectomy.[19] They found that pre- and post-operative hunger, thirst, nausea and pain scores of patients fasting for longer than 12 hours were higher than those of patients fasting for less than 12 hours.[19] Although there is a lack of burns-specific research on the impact of fasting on patient wellbeing, at least one research paper found their patients with burn injuries (mean 32% TBSA, n=48) experienced a mean perioperative fasting time of 14.1 hours.[20] It is therefore highly conceivable that patients with burn injuries could experience similar negative impact on wellbeing with extended perioperative fasting as has been reported in research involving other elective surgery patients.

The negative metabolic effects of perioperative fasting

Perioperative fasting may have a negative metabolic effect by increasing postoperative insulin resistance. This topic has been widely discussed and researched in the general surgery patient population but an extensive literature search could not find burns-specific research on the relationship between perioperative fasting and insulin resistance. Insulin resistance develops as a response to virtually all types of surgical stress and is proportionate to the magnitude of surgery.[21,22] Evidence suggests that insulin resistance is not beneficial on patient outcomes.[21] Insulin resistance and hyperglycemia contribute to poor wound healing as well as muscle catabolism in burns patients.[23] Avoiding preoperative fasting has been shown to be related to a substantial reduction in postoperative stress and insulin resistance in elective surgery patients.[24] Two systematic reviews on elective surgery patients, concluded carbohydrate consumption before surgery, rather than the traditional fasting may attenuate postoperative insulin resistance.[18,25] Reduced fasting in burns patients may therefore have positive metabolic effects however research in a burns-specific population is still needed in order to draw definitive conclusions for this patient population.

The rationale for perioperative fasting

Although there is research which indicates perioperative fasting may negatively influence patient outcomes, fasting for theatre is intended to protect patients from adverse events. It aims to minimise the risk of regurgitation and pulmonary aspiration during non-emergency

surgery involving anesthesia.[26] Acute intraoperative aspiration is rare but is associated with substantial increased morbidity and hospital costs, therefore is an important consideration in burn patient care and safety.[27,28] The Australian and New Zealand College of Anaesthetists' guidelines for children over 6 months and adults are limited solid food (or breast milk/formula in infants) up to 6 hours prior to anaesthesia and consumption of clear fluids at a maximum of 200ml per hour up until 2 hours before surgery.[17] The American Society of Anaesthesiologists have similar practice guidelines and recommend a light meal up until 6 hours prior to procedures requiring anaesthesia and non-alcoholic clear fluids up to 2 hours before surgery.[29] Effective perioperative nutritional care of burns patients requires a balanced approach. The risk of aspiration needs to be minimised as do nutritional deficits and the potential deleterious wellbeing and metabolic effects associated with fasting in the perioperative period.

Parenteral nutrition (defined as the administration of nutrients by a route other than the alimentary canal) could bypass the need for perioperative enteral fasting, however literature suggests the risk of parenteral nutrition may outweigh any potential benefits.[11] Parenteral nutrition may increase the secretion of pro-inflammatory mediators and has been associated with liver dysfunction. It also has an increased risk of infectious complication rates of catheters. Increased mortality has also been demonstrated when parenteral nutrition supplementation was given to burn patients compared to enteral nutrition.[30] There is currently insufficient evidence supporting parenteral nutrition during surgery for burns patients with a functioning gastrointestinal tract.[31] Nutrition delivered into the gastrointestinal tract remains the preferred method of nutrition support for patients with burn injuries and this recommendation is consistent across multiple burns nutritional care practice guidelines.[6-8,12,32]

Burns-specific research on a relationship between reduced perioperative fasting and patient outcomes

There have been strategies reported in literature which aim to safely reduce perioperative fasting in patients with burns. One strategy has been to introduce clinical protocols which provide evidenced-based guidelines on minimising enteral feeding stop times within individual burns care units.[20,33] These protocols have demonstrated improved Caloric intakes following protocol implementation but tend to lack data on other patient outcomes such as mortality, wound infection, length of stay and patient wellbeing.[20,33]

Another strategy aimed at safely reducing perioperative fasting times, as reported in burns research literature, is to implement either short perioperative fasting, continuous intraoperative post pyloric enteral feeding in non-mechanically ventilated patients or continuous intragastric enteral feeding in intubated patients receiving mechanical

ventilation.[34-38] Although there is some heterogeneity in these perioperative feeding methods, the research papers report on a range of patient outcomes including mortality, length of stay, aspiration rates, wound infection as well as Caloric delivery. It was identified that a systematic review could potentially provide an insight into whether perioperative enteral feeding could influence a range of patient outcome measures.

1.3 Overview of the science of evidence synthesis

This research aimed to inform clinical practice by synthesising the best available evidence relating to whether perioperative feeding for patients with burn injuries influences outcomes including mortality, length of stay, aspiration rates, wound infection, ventilator time and Caloric delivery. Simply put, the research aimed to identify the effectiveness of perioperative feeding in patients with burn injuries. It also aimed to investigate if perioperative feeding is safe and does not worsen patient outcomes such as increasing rates of perioperative aspiration and pneumonia.

A high-quality systematic review, with or without a meta-analysis, is considered the most reliable information source to inform evidenced-based clinical practice.[39] The process of conducting a systematic review is different to a literature review because it requires adherence to rigorous and reproducible methodology and a more objective and comprehensive synthesis of research findings.[40] Systematic reviews aim to answer a specific research question and inform evidence-based clinical care.[41] Research shows that utilisation of evidenced-based practice in healthcare leads to higher quality care, improved patient outcomes, reduced costs and greater staff satisfaction compared to traditional healthcare approaches.[42]

Evidence synthesis is a key element of the systematic review process.[43] It involves careful methodical and reproducible collection of data, critical evaluation of the certainty of evidence and conveyance of the overall conclusions drawn from the analysis of evidence.[43] The information gathered from comprehensive evidence synthesis can inform recommendations on the cost-effectiveness, clinical effectiveness and appropriateness of clinical practice.

There are tools available to assist streamline the process of evidence synthesis. For example, the JBI Manual of Evidence Synthesis provides critical appraisal checklists which assists in identifying the methodological quality of a study and assessing the risk of bias within the study.[40] JBI critical appraisal checklists for randomised controlled trials, retrospective cohort studies, case series studies and case report studies were used within this systematic review.

Another tool to facilitate the rating of the quality of evidence is the GRADEpro software program (McMaster University, ON, Canada). GRADEpro assists the researcher use the GRADE approach (Grading of Recommendations Assessment, Development and Evaluation)

to assess the quality of evidence presented in studies and the strength of recommendations made.[44] The approach of GRADE classifies findings based not only on study design but also considers other factors such as risk of bias, publication bias, inconsistency, indirectness, imprecision of evidence, effect sizes, dose-response relationships, and confounders of findings.[45] This GRADE approach has been endorsed by many reputable healthcare organisations including Cochrane, WHO, NICE and BMJ Clinical Evidence.[45] GRADEpro software and the GRADE approach were utilised as part of the evidence synthesis process in this systematic review.

1.4 The methodological basis of the chosen approach to synthesis

A quantitative review of effectiveness was identified as the most appropriate methodology to synthesise evidence in order to answer the research question. The initial planning and pre-research reading for this systematic review guided the decision as to the most appropriate type of systematic review to be undertaken. A quantitative review of effectiveness was chosen because these typically examine the extent to which an intervention achieves the intended effect.[46] It aligned with the purpose of the research which was to identify whether perioperative enteral feeding is effective and safe for patients with burn injuries. Quantitative reviews of effectiveness also typically include experimental studies, quasi-experimental studies and observational studies.[46] It was identified that the papers relating to perioperative nutrition in patients with burn injuries were primarily of this style. A quantitative systematic review approach was therefore identified as being ideally aligned with the goal of answering this particular research question.

There are a number of international organisations which provide methodology to facilitate the development of quantitative systematic reviews of effectiveness. Arguably two of the most well-known guidance methodologies are from JBI (Joanna Briggs Institute) and also the Cochrane Collaboration.[40,47] The systematic review conducted within this research thesis followed the JBI formal methodological guidance. The JBI systematic review methodology was deemed the most appropriate because it doesn't focus purely on randomised controlled trials, but also includes quasi-experimental and observational studies. Within the burns specialty, research is often broader than randomised controlled trials therefore a wider inclusive research scope was identified as being more relevant to the topic of perioperative enteral feeding in burns, compared to the methodology of only including randomised controlled trials.

1.5 Current literature relating to perioperative enteral feeding in burns.

An extensive initial search of the Cochrane Library, The JBI Evidence Synthesis journal, and PubMed located no systematic reviews published or currently underway on this topic, and no registered protocols with PROSPERO. The protocol for this systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (registration number CRD42018119034) on 21/12/2018. Publication of the protocol in the JBI Database of Systematic Reviews and Implementation Reports occurred on 20/03/2019.[48]

In March 2020, a systematic review was published on a similar topic, relating to the safety and efficacy of intraoperative enteral nutrition in critically ill burns patients. This systematic review by Pham et al. had not been registered with PROSPERO or had a protocol published.[49] Although there are similarities in the topic of interest, there are also substantial differences between the recently published systematic review, and the systematic review detailed within this thesis. Of particular note are that the systematic review by Pham et al.[49] did not include critical appraisal, and there were differences in the way synthesis was conducted. These differences are discussed further in chapter 4 and facilitate independent assessments of the outcomes and clinical recommendations.

A search was also conducted for other systematic reviews on enteral nutrition in burns patients. Two systematic reviews were identified however neither had comparable research topics. The first identified was by Wasiak et al.[50] They conducted a Cochrane systematic review on early versus delayed enteral nutrition support for burns injuries. Wasiak et al. identified three randomised control trials for inclusion in the review and concluded that the benefit of early enteral nutrition support in burns on outcomes such as length of stay and mortality remains inconclusive.[50] Another systematic review relating to enteral feeding in burns patients was conducted by Masters et al.[51] This Cochrane review investigated whether high-carbohydrate, high-protein, low-fat enteral feeding improved outcomes in burns patients compared to low-carbohydrate, high-protein, high-fat enteral feeds. Masters et al. identified two studies for inclusion and concluded that the use of higher carbohydrate, low fat enteral feeding might reduce the incidence of pneumonia compared with lower carbohydrate, high fat feeding however there was inconclusive evidence on the effect on mortality.[51] Although these two systematic reviews did have some topic similarities, neither investigated perioperative enteral feeding in burns patients.

1.6 The relationship between existing literature and the proposed systematic review

There is research specifically investigating the impact of perioperative nutrition on burn patient outcomes, with two similar methods reported.[34-38,52] The first is the continuation of enteral nutrition during theatre, via either post pyloric feeding or intragastric feeding in patients who have a previously protected airway (ventilated patients). The second method is enteral feeding up until 2 hours prior to surgery and immediately post-operatively (short fasting) in non-ventilated patients with nasogastric feeding tubes. Reported outcome measures appear to range greatly and include nutrient delivery, length of stay, wound infection, mortality, pneumonia as well as other outcomes. An initial scope of the literature indicated most of these studies are however small and are not able provide conclusive practice recommendations. A comprehensive systematic review is therefore timely to compare results of the published studies and assess whether evidence-based recommendations can be made as to whether perioperative enteral feeding is safe and effective for patients with burn injuries.

1.7 Definitions of terms

- Burn: Any injury to tissues of the body caused by hot objects or flames, electricity, chemicals, radiation or gases in which the extent of the injury is determined by the nature of the agent, length of time exposed, body part involved and depth of burn.[53]
- TBSA: total body surface area. The total area exposed to the outside environment.[53]
- Perioperative: pertaining to the time before, during and after surgery.[53]
- Intraoperative: pertaining to the time during a surgical procedure.[53]
- Enteral feeding: the delivery of a nutritional product, which contains nutrients that is delivered through an enteral feeding tube, regardless of the method of delivery (e.g. nasogastric, nasojejunal, naso-enteric, oro-gastric, percutaneous endoscopic gastrostomy or jejunal feeding tubes). [53]

Chapter 2: Methodology

2.1 Review question

The question of this review is: what is the effectiveness and safety of perioperative enteral nutrition in patients with burn injuries?

2.2 Aims

More specifically, this systematic review aimed to determine whether either short fasting (nasogastric feeding up to 2 hours prior to theatre and immediately thereafter) or nil fasting (nasogastric feeding in ventilated patients or post pyloric feeding in non-ventilated patients) improves burn patient outcomes such as length of stay, wound infection, mortality, ventilator days as well as Caloric provision. In addition, the research aims to analyse whether perioperative nutrition can be safely administered in patients with burn injuries, without increasing the adverse event of perioperative aspiration pneumonia.

2.3 Objectives

The primary objective of this research is to inform clinical practice and provide evidenced-based recommendations as to whether patient outcomes would be improved if patients with burn injuries received either short-fasting or intraoperative enteral nutrition. The secondary objective is to inform clinicians as to the evidence of whether perioperative enteral feeding is safe for patients with burn injuries and does not place them at increased risk of complications relating to reduced fasting times.

2.4 Criteria for considering studies for this review

A quantitative systematic review of effectiveness, in keeping with JBI[54] and Cochrane[47] methodologies, was identified as the most appropriate approach to address the aims and objectives of this research.

2.4.1 Types of studies

This systematic review includes both experimental and non-experimental studies. The preferential study design of interest was randomised controlled trials. In the absence of adequate randomised controlled trials, other types of studies were considered including non-randomised controlled trials and observational studies (e.g. prospective and retrospective cohort studies, case-control studies and analytical cross-sectional studies). Descriptive studies

(such as case reports) were also included in the review if they aligned with the inclusion criteria.

2.4.2 Types of participants

The included participants in this systematic review are either children (less than 18years) or adults (greater than or equal to 18 years) who have sustained an acute burn injury and undergone surgical management of their burn. The decision to use the inclusion criteria as "an acute burn injury and undergone surgical management of their burn," rather than a particular %TBSA burn was made because the severity of a burn can be influenced by the depth of the injury. In addition, the studies relating to perioperative nutrition, which were identified early during the scoping process, either did not always identify %TBSA, or varied as to the %TBSA they considered a "severe burn." As a result, in order to include the widest range of potential studies, the decision was made to have a very broad participant type.

Studies that include patients with significant multi-trauma in addition to an acute burn injury have been excluded.

2.4.3 Types of interventions

This review considers studies that evaluate patients who received perioperative enteral feeding. Perioperative enteral feeding was considered as either:

(a) enteral feeding up until 2 hours prior to surgery and resumed within 2 hours post-surgery in patients receiving intragastric feeding; or

(b) continuous enteral feeding during surgery in patients with a previously secured airway (i.e. ventilated patients) and/or a post pyloric feeding tube.

In this instance, enteral feeding is defined as the delivery of a nutritional product that is delivered through an enteral feeding tube, regardless of the method of delivery (e.g. nasogastric, nasojejunal, naso-enteric, oro-gastric, percutaneous endoscopic gastrostomy or jejunal feeding tubes). Those who received parenteral nutrition in addition to enteral nutrition during the perioperative period were excluded.

2.4.4 Comparators

This review considered studies that compare the interventions to patients who had enteral nutrition withheld for more than two hours prior to theatre and experienced prolonged post-operative fasting (i.e. enteral feeding recommenced after return to the ward).

2.4.5 Types of outcome measures

The following outcome measures were included:

Primary outcomes

1. All-cause incidence of mortality;
2. Length of acute care hospital stay (in days);
3. Frequency of wound infection (since diagnostic criteria can vary, all reported occurrences of wound infections were included with comparisons of diagnostic criteria between studies);
4. Rate of wound healing (all reported cases of time to either first donor site healing or time to wound closure with comparison of diagnostic criteria);
5. Incidence of aspiration pneumonia (all reported cases with comparison between diagnostic criteria).

Secondary outcomes

1. Energy intake (kilocalories) and protein intake (grams per day);
2. Patient-reported well-being and satisfaction including hunger, thirst, nausea and vomiting;
3. Nitrogen balance. Defined as the difference between nitrogen intake and output. It is formally represented by the following equation: Nitrogen balance = Nitrogen intake – (urinary nitrogen excretion + faecal nitrogen + sum of all other routes by which nitrogen is lost from the body). Urine is the major route for excretion of nitrogen therefore in a clinical setting, nitrogen balance is frequently assessed by the following method: 24-hour nitrogen intake – (24-hour urinary nitrogen + 0.5 g nitrogen/day to account for unmeasured nitrogen losses).[55]

Other reported outcomes were also considered for inclusion. These were:

- length of ventilator support time,
- supplemental albumin,
- antibiotic days,
- length of stay per %third degree burn,
- clinical sepsis,
- bacteraemia,
- ratio of intensive care unit (ICU) days per %TBSA burn,
- total number of ICU days,
- admit/discharge weight,
- or any other relevant outcomes.

Amendments to predetermined outcome measures may be required if, during the process of conducting the systematic review, it becomes apparent that modifications to outcome measures provide a better representation of results.

2.5 Review methods

The systematic review was conducted by following the JBI methodology for systematic reviews of effectiveness and in accordance with a peer reviewed and published a-priori protocol.[46]

2.5.1 Search strategy

The search strategy aimed to find both published and unpublished studies to fully investigate the effectiveness and safety of perioperative feeding in patients with burn injuries. This search strategy was conducted in three stages, in keeping with JBI methodology.

An initial limited search of PubMed and CINAHL was undertaken, followed by an analysis of the text words contained in the title and abstract, and of the index terms used to describe an article. This informed the development of a more extensive search strategy. A second comprehensive search using all identified key words and index terms was then undertaken across predefined databases. Thirdly, the reference list of all identified reports and articles was searched for additional studies. Only studies published in English were considered for inclusion in this review. There were no date limits for the search.

2.5.2 Information sources

The information sources included electronic databases as well as contact with study authors. The databases searched included PubMed, CINAHL (EBSCOhost platform), Embase (Ovid platform), Web of Science, Cochrane Central Register of Controlled Trials and Scopus. A search of grey literature was also included as a component of the search strategy, to minimise publication bias and selection bias through the identification of unpublished studies.[47] Sources of unpublished studies and grey literature searched included ClinicalTrials.gov, Australian New Zealand Clinical Trials Register, European Clinical Trials Register, MedNar, SumSearch 2, ProQuest Dissertations and Theses, Google Scholar, OpenGrey, OpenDOAR, Openthesis.org, WHO International Clinical Trials Registry Platform, Latin American and Caribbean Health Sciences Literature (LILACS database) and AllTrials. The details of the full search strategy for PubMed, CINAHL, Embase and Web of Science are provided in Appendices 1, 2, 3 and 4.

2.5.3 Study selection

Following the search, all identified citations were collated and uploaded into EndNote X9.2 (Clarivate Analytics, PA, USA) and duplicates were removed. Titles and abstracts were then screened by two independent reviewers for assessment against the inclusion criteria. Studies which potentially met the inclusion criteria were then retrieved in full and their details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; Joanna Briggs Institute, Adelaide, Australia). The full text of selected studies was then retrieved and assessed in detail against the inclusion criteria. Full-text studies which did not meet the inclusion criteria were excluded, and reasons for exclusion are provided in Appendix 6. Included studies underwent a process of critical appraisal. The results of the search is reported in full, in chapter three and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram.[56] Any disagreements which arose between the reviewers were resolved through discussion. A third reviewer was not required.

2.5.4 Assessment of methodological quality/ critical appraisal

Selected studies were critically appraised by two independent reviewers for methodological quality using the standardised critical appraisal instruments from JBI.[46] Any disagreements which arose were resolved through discussion. If the two reviewers were unable to reach consensus, then a third reviewer could have been involved but in this case, it was not needed. Following critical appraisal, there were no studies excluded due to not meeting the quality threshold. This quality threshold was based on a predetermined list of decision rules to limit risk of bias.

2.5.5 Data extraction

Data was extracted from papers included in the review using the standardised data extraction tool available in JBI SUMARI.[46] Data extraction was carried out by one reviewer with verification by another reviewer to minimise bias and potential errors. The data extracted included specific details about the populations, interventions, study methods and outcomes of significance to the review question and specific objectives. In addition, attempts were made to obtain missing data from the study reports by contacting the authors of the included papers. Any disagreements which arose between the reviewers were resolved through discussion. A third reviewer was not required.

2.5.6 Data synthesis

Papers, where possible, were pooled in a statistical meta-analysis using JBI SUMARI. Effect size is expressed as either odds ratios, relative risk (for dichotomous data) or weighted (or standardised) mean differences (for continuous data) and their 95% confidence intervals were calculated for analysis. Heterogeneity was assessed statistically using the standard chi-squared and I^2 tests. The choice of model (fixed effects) and method for meta-analysis are based on the guidance by Tufanaru et al.[57]

Subgroup analyses, for example, effects for children less than 18 years compared to adults greater than or equal to 18 years, and severity of injury was not conducted because there was insufficient data to investigate. Sensitivity analyses was conducted to test decisions made regarding conducting meta-analysis with and without the inclusion of poor-quality studies. Where statistical pooling was not possible, the findings are presented in narrative form including tables and figures to aid in data presentation. A funnel plot was not generated to assess publication bias because there were not ten or more studies included in any meta-analysis.

2.5.7 Assessing certainty in the findings

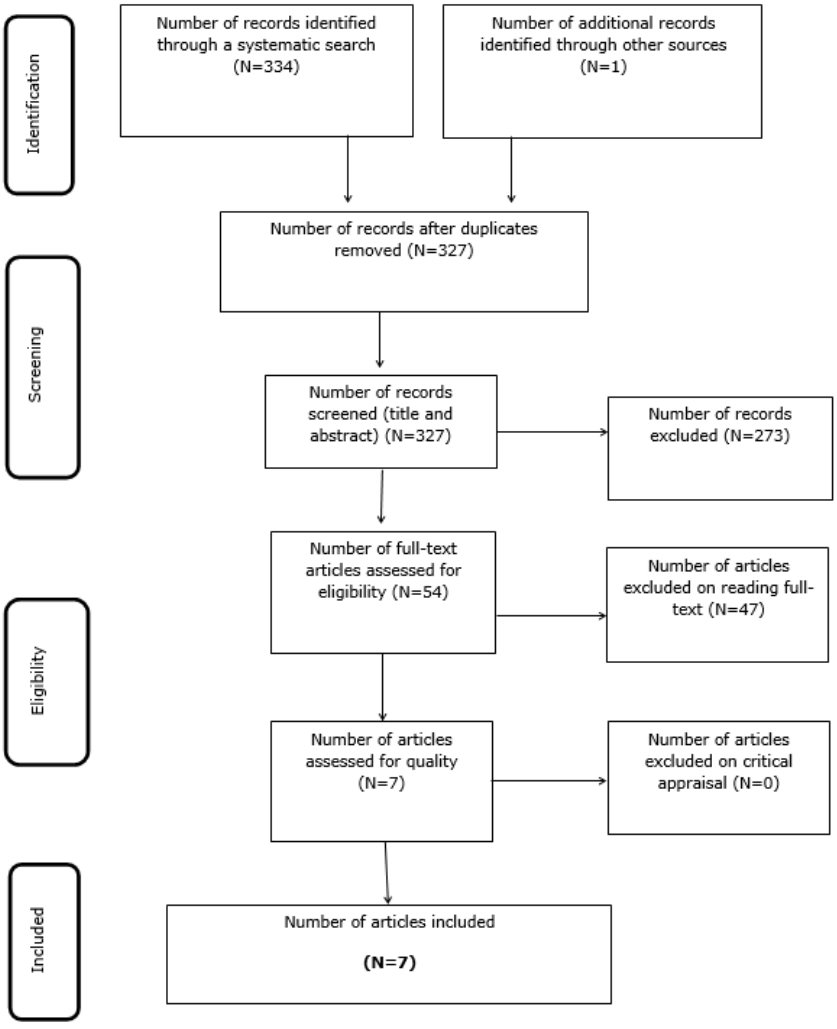
A Summary of Findings Table was created using GRADEPro software (McMaster University, ON, Canada). The GRADE approach for grading the quality of evidence was followed. The Summary of Findings table in chapter three presents the following information: absolute risks for treatment and control, estimates of relative risk, and a ranking of the quality of the evidence based on study limitations (risk of bias), indirectness, inconsistency, imprecision and publication bias. This is provided in the Handbook published by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group.[45]

Chapter 3: Results

3.1 Selection of Studies

Database searching identified 334 articles as a result of the search strategy. One article was identified shortly after the search was completed, via a database automated notification service. Eight articles were removed due to being duplicates. The remaining 327 articles were assessed by screening of abstracts. Fifty-four articles were identified as potentially meeting inclusion criteria. After obtaining the full text articles, 47 out of the potentially eligible 54 articles were excluded. Appendix 6 provides the complete list of excluded studies and details the reasons for exclusion. The screening process overall identified seven articles which met inclusion criteria. No studies were excluded during critical appraisal. Figure 1 is a PRISMA

Figure 1: PRISMA flow diagram depicting the searching and study selection process



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

flow diagram, which depicts the full process of searching and study selection.[56]

3.2 Description of included studies

Seven studies were identified for inclusion in this systematic review. Table 1 provides a list of included studies, their years of publication, countries of origin, descriptions of study types, methods used to gather information and also participant inclusion criteria.

The seven included studies were published between 1992 and 2019.[34-38,52,58] Six of these studies originated from the United States of America[34-38,52] and one originated from Indonesia.[58] Two of the studies were randomised controlled trials,[35,38] three were retrospective cohort studies,[34,37,52] one was a retrospective case series[36] and one was a case report.[58] One of the studies[38] which was included as a randomised control trial (RCT) actually had two phases of research, the first phase being a retrospective cohort and the second phase being a RCT. Only phase 2 (the RCT) adequately meet inclusion criteria and as a result, only phase 2 was included in data synthesis.

All studies used data generated as a result of an inpatient hospital admission for an acute burn however inclusion criteria differed between studies, as outlined in Table 1. One study included patients with >10% total body surface area (%TBSA) burns,[35] one study included patients with ≥ 15% TBSA burns,[37] two studies included patients with ≥20% TBSA burns[34,52] and one study included patients with ≥30% TBSA burns.[36] One paper did not use a specific percentage TBSA as their inclusion criteria, instead reporting that their included patients had severe burns, were receiving enteral tube feeding and underwent burn debridements.[38] The case report did not have particular inclusion criteria since this paper specifically reported on a single patient with a 67% TBSA burn.[58]

Table 1: Description of Included Studies

Study	Year of publication	Country	Study type	Method to gather information	Participant inclusion criteria
Jenkins et al.[35]	1994	USA	randomised controlled trial	prospective	greater than 10% TBSA acute burn, admitted within 7 days of injury, between Feb 1986 and May 1990 and required supplemental enteral nutrition support.
Pearson et al.[38]	1992	USA	randomised controlled trial (phase 2 only)	prospective	patients with severe burns who underwent burn debridements while they were receiving enteral feeding.
Imeokparia et al.[37]	2018	USA	retrospective cohort study	American Burn Association verified burn centre database	patients ≤ 18 years of age, with ≥ 15% TBSA burn, from Feb 2012 to Feb 2016. Patients who underwent surgery with general anaesthesia along with supplemental nutrition.
Varon et al.[34]	2017	USA	retrospective cohort study	chart review	patients admitted to American Burn Association-verified burn centre from Jan 2008 to Dec 2013. Acute burns ≥20% TBSA receiving enteral nutrition support
Carmichael et al.[52]	2019	USA	retrospective cohort study	chart review	patients admitted to an urban, American Burn Association verified burn unit between 2012 – 2017, with >20% TBSA burns >18 years and intubated at some point during their hospital admission.
Sunderman et al. [36]	2019	USA	case series	chart review	patients ≤ 18 years with ≥ 30% TBSA burns admitted to their particular medical facility between Jan 1995 and Dec 2014
Sutanto et al.[58]	2009	Indonesia	case report	not clearly stated	admitted to intensive care unit with a 67% TBSA thermal burn

3.2.1 Participant Characteristics

Details of the participant characteristics are presented in Table 2, including %TBSA burn range, %TBSA mean (± either standard deviation or standard error of mean), age range, age mean (± either standard deviation or standard error of mean), number of male participants, number of female participants, total number of surgeries, mean number of surgeries (± either standard deviation or standard error of mean) and number of participants. Each paper's participant characteristics are shown as a combined group and then stratified into control and intervention groups.

There was variability as to how each study reported patient demographics and characteristics, as can be noted by numerous sections in the table being not reported (NR). The range in percentage total body surface area burns of all participants in the seven included papers was 10% to 98% TBSA. There was also a wide range of ages of study participants with an age range of 0.3 years to 84 years. Four studies only had adult participants (≥ 18 years),[34,38,52,58] two studies only included children (≤ 18 years)[36,37] and one study had both children and adults

(range 0.3years to 26years).[35] Of the four studies which reported on the sex of participants, all had more males than females.[34-36,52]

The number of included participants in each study was small. Excluding the individual case report,[58] four out of the remaining six included papers had less than 50 participants[34,37,38,52] (range n=18-45) one paper had 80 participants[35] and one had 434 participants.[36] Overall, studies in this review included a combined total of 642 participants.

Table 2: Participant demographics and characteristics

Key: NR = Not reported, N/A = Not applicable, yrs = years, SD = standard deviation, SEM = standard error of mean, No. = number.

Study		**% TBSA burn range**	**%TBSA mean ±SD *(^±SEM)***	**Age range (yrs)**	**Age mean ±SD (^±SEM)**	**Male**	**Female**	**Total no. of surgeries**	**Mean no. of surgeries ±SD (^SEM)**	**No. of participants**
Jenkins et al.[35]	Combined	10-82	NR	0.3-26	NR	46	34	290	NR	80
	Control	NR	36.2±2.5^	NR	7.4±1.0^	22	18	129	3.2±0.3^	40
	Intervention	NR	27.0±2.4^	NR	7.5±1.0^	24	16	161	4.0±0.3^	40
Pearson et al.[38]	Combined	NR	NR	NR	NR	NR	NR	NR	NR	18
	Control	NR	47±5^	NR	46±3^	NR	NR	NR	NR	11
	Intervention	NR	41±6^	NR	39±3^	NR	NR	NR	NR	7
Imeokparia et al.[37]	Combined	16-86	28.0±14.4	1-18	7.5±5.5	NR	NR	81	3.5±3.2	31
	Control	16-37	21.8±6.5	1-18	9.3±6.5	NR	NR	30	2.3±1.5	13
	Intervention	16-86	32.4±17.0	1-14	6.3±4.3	NR	NR	51	4.4±3.8	18
Varon et al.[34]	Combined	20-78	NR	18-84	NR	25	8	NR	NR	33
	Control	20-78	45.7±18.9	25-78	49.8±16.7	13	3	NR	7.3±5.7	16
	Intervention	25-75	42.6±17.1	18-84	41.6±19.7	12	5	NR	7.7±4.0	17
Carmichael et al.[52]	Combined	20-84	44 (SD not stated)	18-65	NR	33	12	NR	4 (SD not stated)	45
	Control	NR	46±18	NR	41±14	23	7	NR	NR	30
	Intervention	NR	41±13	NR	37±17	10	5	NR	NR	15
Sunderman et al.[36]	Intervention only	30-98	51.3±17.4	0.6-18	6.4±5.1	293	239	3663	8.4±6.5	434
Sutanto et al.[58]	1 case only	67%	N/A	26	N/A	1	0	NR	N/A.	1

^ = Standard error of mean was presented, rather than standard deviation.

3.2.2 Interventions and Comparators

There was some variability between studies in how the interventions and comparators (controls) were implemented and measured. Details of interventions and controls for each study are presented in Table 3.

One of the RCT's prospectively compared patients who received post pyloric enteral feeding during theatre (intervention) to those who had enteral feeding withheld (control).[35] The second randomised controlled trial prospectively compared intragastric enteral feeding withheld for 1 hour prior to surgery (intervention) with intragastric feeding withheld for 4 hours prior to surgery for burn debridement (control).[38]

Two of the retrospective cohort studies investigated the outcomes of patients who received post pyloric enteral feeding delivered during surgery (interventions) with those who had post pyloric enteral feeding withheld during the perioperative period (control).[34,37] Of particular note, is that one of these retrospective cohort studies had a different timeframe for their control and intervention groups.[34] The control group was from prior to 2010 (before the introduction of a new protocol) and the intervention group was after 2010 (following the introduction of a new perioperative feeding protocol). The second retrospective cohort did not mention if the timeframe between the intervention and control were different.[37]

There was also a third retrospective cohort study which was different to the other two retrospective studies.[52] This investigation compared outcomes of ventilated patients when feeding was continued for ≥ 50% of operations (intervention) to those who had feeding withheld for >50% of operations (control). This study did not differentiate between patients who had intragastric enteral feeding and post pyloric enteral feeding. Eighty-six % of participants in this study received only nasogastric enteral feeding, seven percent of participants had only post pyloric enteral feeding and seven percent transitioned from nasogastric to post pyloric feeding.

The case series retrospectively reported on burns patients who only received continuous post pyloric enteral feeding throughout all surgeries (intervention).[36] There was no control in this research paper. [36]

The singular case study used the patient as his own control and then reported on wellbeing after experiencing different pre- and post-operative fasting times (total fasting times ranged from 4 hours 45 minutes to 26 hours 40 minutes).[58] There was no mention in this case report, of the type of enteral feeding (i.e. nasogastric or post pyloric) provided to the patient.

Table 3: Controls (comparators) and interventions for each of the included studies

Study	Control	Intervention
Jenkins et al.[35]	post pyloric feeding withheld during surgical procedures	post pyloric feeding during surgical procedures
Pearson et al.[38]	intragastric enteral feeding up until 4 hours prior to surgery	intragastric enteral feeding up until 1 hour prior to surgery
Imeokparia et al.[37]	post pyloric feeding withheld during surgical procedures	post pyloric feeding during surgical procedures
Varon et al.[34]	post pyloric feeding withheld during surgical procedures, prior to protocol introduced in 2010	post pyloric feeding during surgical procedures after protocol introduced in 2010
Carmichael et al.[52]	enteral feeding held for >50% of surgeries for mechanically ventilated patients	enteral feeding continued for ≥ 50% of surgeries for mechanically ventilated patients
	86% intragastric feeding the entire time, 7% post pyloric feeding the entire time, 7% transitioned from intragastric to post pyloric feeding. Mode of feeding not reported for separate control and intervention groups.	
Sunderman et al.[36]	nil control	post pyloric enteral feeding during surgical procedures
Sutanto et al.[58]	n = 1 patient was own control	Different lengths of perioperative fasting times: 1. 4 hours 45 min 2. 9 hours 3. 12 hours 30 minutes 4. 26 hours 40 minutes

3.2.3 Outcome Measures

Table 4 indicates the range of outcomes measured in the included studies. Predetermined primary outcome measures of this systematic review included: mortality, length of acute care hospital stay, wound infection, time to wound healing/wound closure and occurrence of aspiration pneumonia.[48] Secondary outcomes for investigation included: energy intake, protein intake, patient-reported wellbeing and satisfaction (including hunger, thirst, nausea and vomiting), and nitrogen balance. Other secondary outcomes considered for inclusion included length of ventilator support time, supplemental albumin, antibiotic days, length of stay per %third degree burn, clinical sepsis, bacteraemia, ratio of intensive care unit days per %TBSA burn, total number of intensive care days, admit/discharge weight, skeletal muscle mass, time to mobilisation, and any other relevant outcomes.[48]

When investigating the primary outcome measures, it was noted that none of the studies reported on the outcome of time to wound healing/wound closure. Mortality was reported as an outcome in two studies and[34,35] length of stay was reported in five of the included studies.[34-37,52] The incidence of wound infection was reported in three studies.[34,35,37] All of the studies,[34-38,52] except the case report,[58] reported on aspiration events as an outcome measure and pneumonia was reported separately in two of the research papers.[34,35]

There was also a range of secondary outcome measures reported. Caloric provision was reported, using varying methodology, in five of the included studies.[34,35,37,38,52] One study

reported on percentage of protein achieved.[34] Only the case report evaluated patient wellbeing (including nausea, vomiting, hunger, thirst, malaise and fatigue) associated with perioperative fasting/feeding.[58] Nitrogen balance was also reported in a singular study, which was the case series.[36] Four studies reported on the number of ventilator days.[34,35,37,52] There were eight additional secondary outcomes reported which were mostly only in singular papers and included: supplemental albumin, antibiotic days, length of stay per %third degree burn, clinical sepsis, bacteraemia, number of ICU days, ratio of ICU days/%TBSA burn, and admit/discharge weight. No study reported on either skeletal muscle mass or time to mobilisation.[48]

Table 4: Summary of outcome measures from included studies

Study	Primary outcomes	Secondary outcomes
Jenkins et al.[35]	• mortality • length of stay • pneumonia • aspiration	• cumulative caloric balance • ventilator days • supplemental albumin • antibiotic days • length of stay/%third degree burn • clinical sepsis
Pearson et al.[38]	• aspiration	• caloric intake on the day of surgery
Imeokparia et al.[37]	• length of stay • wound infection • aspiration	• calories gained/lost per kilogram of weight • ventilator days • number of ICU days
Varon et al.[34]	• mortality • length of stay • wound infection • aspiration • pneumonia	• % of calories achieved • % protein achieved • ventilator days • number of ICU days • ratio of ICU days/%TBSA burn • bacteraemia
Carmichael et al.[52]	• length of stay • aspiration	• % of caloric goals met • ventilator days
Sunderman et al.[36]	• mortality • length of stay • aspiration	• nitrogen balance • admit/discharge weight
Sutanto et al.[58]	• aspiration	Pre-operative patient-reported • nausea • vomiting • hunger • thirst Post-operative patient-reported • nausea • vomiting • malaise • fatigue

3.3 Methodological quality of included studies

3.3.1 Critical appraisal of randomised controlled trials

The results for the critical appraisal scores of the two randomised controlled trials (RCT's) included in this systematic review are presented in Table 5.[35,38] Only one of the RCT's clearly described their method of randomisation, which was via a computer-generated random number list and therefore identified as true randomisation for participant and intervention groups.[38] Concealment of treatment groups was not possible for either study given that the intervention involved either short perioperative fasting or perioperative enteral feeding and this would be extremely difficult to conceal.[35,38] Both of the RCT's reported matching of intervention and control groups for patient demographics and %TBSA burn with no significant differences between groups at baseline.[35,38] Blinding of participants and those delivering treatment did not occur in either of the RCT's, since perioperative feeding/fasting is an obvious intervention and therefore presents a logistical challenge to blind treatments.[35,38] Neither study reported on whether the outcome assessors were blind to treatments assigned.[35,38] Both of the included RCT's indicated they had identical treatment of groups (other than the intervention of interest), complete follow-up of patients, analysis of participants in the groups to which they were randomised, identical measurement of outcomes and reliable outcome measurements (questions 7-11).[35,38] Statistical analysis also scored positively in the two RCT's.[35,38] Trial design was deemed appropriate in one of the RCT's[35] however the other study[38] lacked detail in reporting of the overall perioperative fasting time and also only reported on two outcome measures. As a result, it was given an unclear rating as to whether the study design was appropriate.

Table 5: Critical appraisal scores of randomised controlled trials

	Checklist question													
Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Total
Jenkins et al.[35]	U	N	Y	N	N	U	Y	Y	Y	Y	Y	Y	Y	8
Pearson et al.[38]	Y	N	Y	N	N	U	Y	Y	Y	Y	Y	Y	U	8
%	50	0	100	0	0	0	50	100	100	100	100	100	50	

N: No, N/A: Not applicable, U: Unclear, Y: Yes. Values are indicative of Y (Yes) responses.
JBI critical appraisal checklist for randomized controlled trials.[46] Q1: Was true randomization used for assignment of participants to treatment groups?; Q2: Was allocation to treatment groups concealed?; Q3: Were treatment groups similar at the baseline?; Q4: Were participants blind to treatment assignment?; Q5: Were those delivering treatment blind to treatment assignment?; Q6: Were outcomes assessors blind to treatment assignment?; Q7: Were treatment groups treated identically other than the intervention of interest?; Q8: Was follow-up complete, and if not, were strategies to address incomplete follow-up utilized?; Q9: Were participants analysed in the groups to which they were randomized?; Q10: Were outcomes measured in the same way for treatment groups?; Q11: Were outcomes measured in a reliable way?; Q12: Was appropriate statistical analysis used?; Q13: Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

3.3.2 Critical appraisal of retrospective cohort studies

There were three retrospective cohort studies included in this systematic review.[34,37,52] The critical appraisal scores for these retrospective cohort studies are presented in Table 6.

Only one of the cohort studies indicated the control and intervention groups were recruited from a similar population and there were nil statistically significant differences in baseline demographics or TBSA burn between the groups.[52] The second of the cohort studies clearly stated the control and intervention groups were from different populations, since the recruitment date of the control group was prior to recruitment of the intervention group.[34] This paper did state the control and intervention groups were comparable in baseline demographics and TBSA burn size. The third cohort study did not have similar populations in the control and intervention groups because the intervention group had significantly larger TBSA burn involvement than the control group.[37] In addition, this research paper was unclear as to whether the two groups were recruited from the same population. Their database search was conducted within a set timeframe and participants were subsequently stratified into control and intervention groups. There was, however, comment of a new protocol being implemented during the assessment period which provided a contrast opportunity. Details were not clear as to whether this new protocol resulted in the intervention group being from a later timeframe.

All three of the retrospective cohorts were appraised to have met the criteria for the question of whether exposure was measured similarly to assign people to both exposed and unexposed groups (question two).[34,37,52]

The measurement of exposure was deemed to be measured in a valid and reliable way in two of the studies.[34,37] One of the studies had a questionable method of measurement of exposure which was either enteral nutrition held for more than 50% of surgical procedures or enteral nutrition continued for at least 50% of procedures while mechanically ventilated.[52] It was therefore given an unclear rating for question three.

Unclear ratings were given to the three retrospective cohort studies for whether confounding factors were adequately identified and measured.[34,37,52] Although all three studies did report on baseline demographics being similar in control and intervention groups, there were other potential confounding factors which could not be assessed as being adequately identified. Examples included: changes in clinical practice over time,[34] the influence of the intervention group having significantly larger TBSA involvement[37] and differences between patients receiving enteral feeding through all operations compared to those who had enteral feeding during just over 50% of operations.[52]

Similarly, strategies to deal with confounding factors were either not stated or unclear in all of the cohort studies.[34,37,52] Of particular note was one of the studies had a major confounding factor and there was no adjustment within either the in study design or in data analysis to deal with this confounding factor.[37]

The three cohort studies were appraised as having the groups/participants free of the outcome at the start of the study.[34,37,52] Outcomes were also all measured in a valid and reliable way in all cohort studies, though there was some variability in the way the outcome of aspiration was measured.[34,37,52] The follow-up time was sufficient in all studies.[34,37,52]

Only one of the cohort studies reported on the occurrence of patient deaths and therefore this was the only study which was assessed to have complete follow-up.[34] Although the drop-out rate in the other two studies was likely to be low, absolute reporting could not be verified because it was not clearly stated.[37,52]

None of the studies discussed strategies to address incomplete follow-up. discussed strategies to address incomplete follow-up.[34,37,52] Statistical analysis was identified as appropriate in all studies.[34,37,52]

Table 6: Critical appraisal scores of retrospective cohort studies

	Checklist question											
Citations	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total
Imeokparia et al.[37]	N	Y	Y	U	N	Y	Y	Y	U	U	Y	6
Varon et al.[34]	N	Y	Y	U	U	Y	Y	Y	Y	U	Y	7
Carmichael et al.[52]	Y	Y	U	U	U	Y	Y	Y	U	U	Y	6
%	33	100	66	0	0	100	100	100	33	0	100	

N: No, N/A: Not applicable, U: Unclear, Y: Yes. Values are indicative of Y (Yes) responses.
JBI critical appraisal checklist for Retrospective Cohort Studies[59]. Q1: Were the two groups similar and recruited from the same population? Q2: Were the exposures measured similarly to assign people to both exposed and unexposed groups? Q3: Was the exposure measured in a valid and reliable way? Q4: Were confounding factors identified? Q5: Were strategies to deal with confounding factors stated? Q6: Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? Q7: Were the outcomes measured in a valid and reliable way? Q8: Was the follow-up time reported and sufficient to be long enough for outcomes to occur? Q9: Was follow up complete, and if not, were the reasons to loss to follow up described and explored? Q10: Were strategies to address incomplete follow up utilized? Q11: Was appropriate statistical analysis used?

3.3.3 Critical appraisal of case series studies

There was only one retrospective case series study included in this systematic review. Critical appraisal scores of this case series are presented in Table 7.[36] Overall, the study was deemed to be of high methodological quality, as evidenced by critical appraisal score answers being yes, to all 10 appraisal criteria.

Table 7: Critical appraisal scores of case series studies

	Checklist question										
Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Total
Sunderman et al.[36]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10
%	100	100	100	100	100	100	100	100	100	100	

N: No, N/A: Not applicable, U: Unclear, Y: Yes. Values are indicative of Y (Yes) responses. JBI critical appraisal checklist for case series studies.[59] Q1: Were there clear criteria for inclusion in the case series? Q2: Was the condition measured in a standard, reliable way for all participants included in the case series? Q3: Were valid methods used for identification of the condition for all participants included in the case series? Q4: Did the case series have consecutive inclusion of participants? Q5: Did the case series have complete inclusion of participants? Q6: Was there clear reporting of the demographics of the participants in the study? Q7: Was there clear reporting of clinical information of the participants? Q8: Were the outcomes or follow up results of cases clearly reported? Q9: Was there clear reporting of the presenting site(s)/clinic(s) demographic information? Q10: Was statistical analysis appropriate?

3.3.4 Critical appraisal of case report studies

Table 8 provides the critical appraisal scores for the one included case report study.[58] This study did not score well during critical appraisal. Most (75%) of the checklist questions received either a no or unclear. Despite these low critical appraisal scores, the decision was made to still include the case report because it was the only one that reported wellbeing outcomes such as hunger, thirst, nausea and vomiting.

The patient demographics and size of injury were clearly described but there was no timeline of patient history or progress. Similarly, the clinical condition of the patient was presented but lacked details as to both the amount of partial and full-thickness burns and also the location of the burn on the patient's body. There were no diagnostic tests or assessment methods detailed in the paper however potentially it was not essential in this particular circumstance. The intervention, treatment procedures and post-intervention clinical condition were assessed as not being clearly described and not easy to interpret. Adverse events (aspiration and differences in blood glucose levels) were mentioned however there were no details provided on how these were measured. A takeaway lesson was provided by the case report authors but would have been more beneficial if greater details were provided, based on the results of the case study.

Table 8: Critical appraisal scores of case report studies

	Checklist question								
Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Total
Sutanto et al.[58]	Y	N	U	U	N	N	U	Y	2
%	100	0	0	0	0	0	0	100	

N: No, N/A: Not applicable, U: Unclear, Y: Yes. Values are indicative of Y (Yes) responses.
JBI critical appraisal checklist for case report studies[59]. Q1: Were patients' demographic characteristics clearly described? Q2: Was the patient's history clearly described and presented as a timeline? Q3: Was the current clinical condition of the

patient on presentation clearly described? Q4: Were diagnostic tests or assessment methods and the results clearly described? Q5: Was the intervention(s) or treatment procedure(s) clearly described? Q6: Was the post-intervention clinical condition clearly described? Q7: Were adverse events (harms) or unanticipated events identified and described? Q8: Does the case report provide takeaway lessons?

3.4 Review of findings/results

Primary outcomes

There were five primary outcome measures which were identified in the included papers. These were mortality, wound infection, length of stay, aspiration and pneumonia.

3.4.1 Mortality

Mortality was reported as an outcome measure in three of the included studies and the results are presented in Table 9.[34-36] One of the studies which reported on mortality was a randomised controlled trial,[35] one was a retrospective cohort[34] and one was a case series.[36]

The randomised controlled trial by Jenkins et al. compared their paediatric patients who had post pyloric enteral feeding withheld during surgery (control) to patients who had post pyloric enteral feeding continued during surgery (intervention).[35] The control and intervention groups were similar with respect to patient demographics and %TBSA burn but the intervention group had a higher percentage of third-degree (full thickness) burns. Jenkins et al. reported four deaths out of the 40 patients (10%) in the control group and five deaths out of the 40 patients (12%) in the intervention group.[35] The difference in mortality was reported as not statistically significant but the p-value could not be ascertained from the paper. Potential confounding factors were the intervention group (which had slightly higher mortality) had significantly more surgical procedures ($p<0.03$) as well as deeper burns compared to the control.

The retrospective cohort study by Varon et al. also reported on mortality their adult patients with major burns.[34] In this study, the control group had post pyloric enteral feeding withheld 8 hours prior to surgery and 2 hours post-surgery. The intervention group received post pyloric enteral feeding continuously during their surgical procedures. Patient demographics and %TBSA burn were comparable between the control and intervention groups. This study reported the control group experienced four deaths out of the 16 patients (25%) and the intervention group experienced three deaths out of 17 patients (18%). The difference in mortality between the two groups was reported as not statistically significant ($p=0.69$). A potential bias in this research was the intervention group (who had slightly lower mortality) was from a later timeframe compared to the control group.

Sunderman et al.[36] conducted a case series and was the third of the included studies which reported on the mortality rate of patients who received post pyloric enteral feeding during surgical procedures. This research reported 18 deaths out of 434 burns patients (4.1% of patients). This paper did not have a control group therefore nil useful conclusions could be made as to whether perioperative feeding influenced mortality rates in this study.

A meta-analysis could not be conducted for the outcome of mortality. The study by Jenkins et al. was the only paper which had potential to be included however the numbers were so low, it was determined there would be no value conducting a meta-analysis on just one small study.[35] Varon et al.'s research paper could not be included in a meta-analysis because the control and intervention groups were from different timeframes.[34]

Table 9: Mortality outcome summary of findings

Study	Control	Intervention	Statistically significant difference in outcome?	Comment
Jenkins et al.[35]	• feeding withheld during surgery* • mortality = 4 patients • n=40 • mean TBSA burn=36.2% • mean age = 7.4 years • mean no. surgeries = 3.2	• feeding during surgery* • mortality = 5 patients • n=40 • mean TBSA burn=36.2% • mean age = 7.5 years • mean no. surgeries = 4.0	no *p-value not given*	intervention group had significantly higher % of full-thickness burns, more surgical procedures and more antibiotic therapy
Varon et al.[34]	• feeding withheld during surgery** • mortality = 4 patients • n=16 • mean TBSA burn= 45.7% • mean age = 49.8 years • mean no. surgeries = 7.3	• feeding during surgery** • mortality = 3 patients • n=17 • mean TBSA burn= 42.6% • mean age = 41.6 years • mean no. surgeries = 7.4	no p= 0.69 *(p <0.05 considered significant)*	control was from an earlier timeframe
Sunderman et al.[36]	• nil control	• feeding during surgery • mortality = 18 patients • n = 434 patients • mean TBSA burn= 51.3% • Mean age = 6.4 years • Mean no. surgeries = 8.4	N/A	nil useful conclusion on the influence of intraoperative feeding on mortality

**Control and intervention groups were similar in age, % TBSA burn, male/female ratio, incidence of smoke inhalation and postburn day of admission.*

*** Control and intervention groups comparable in baseline demographics of age, male/female ratio and % TBSA burn.*

3.4.2 Wound infection

Three of the included studies reported on the incidence of wound infections in burns patients who experienced perioperative fasting compared to those who received intraoperative feeding.[34,35,37] One of these studies was a randomised controlled trial[35] and the other two were retrospective cohorts.[34,37] Table 10 presents the results of wound infection from each of these studies.

Jenkins et al. reported their control group (who experienced perioperative fasting, n=40) experienced nine wound infections and the intervention group (who received post pyloric enteral feeding during theatre, n=40) experienced two wound infections.[35] They reported the difference in results was statistically significant. Criteria for identification of wound infection was a positive wound culture of greater than 105 micro-organisms per gram of tissue, systemic antibiotics, or graft loss, or any combination of these. A potential confounding factor was the intervention group (who had fewer wound infections) also had more antibiotic therapy.

The retrospective cohort published by Imeokparia et al.[37] reported their paediatric patient control group (perioperative enteral feeding withheld) had four patients with wound infections (n=13, 30.8%). In contrast, the intervention group (received continuous post pyloric enteral feeding) had six patients with wound infections (n=17, 35.3%). This difference was reported as not statistically significant. The criteria for determining wound infection was not provided in the article. A potential influencing factor in this study was the intervention group (who had slightly more wound infections) also had significantly higher %TBSA burn than the control group.

Varon et al.'s[34] retrospective cohort also reported on wound infection and found their control group (perioperative enteral feeding withheld) experienced 12 wound infections overall (75%) and the intervention group (continuously fed during surgery) experienced 10 wound infections (59%). The slightly lower occurrence of wound infections in the intervention group was reported as not statistically significant different compared to the control. The method for identifying wound infection was not explained in this study. A potential influencing factor in this research paper was the intervention group was from a later timeframe than the control group.

Table 10: Wound infection

Study	Control	Intervention	Statistically significant difference in outcome?	Comment
Jenkins et al.[35]	• feeding withheld during surgery* • 9 patients with wound infections • n = 40 • mean TBSA burn = 36.2% • mean age = 7.4 years • mean no. surgeries = 3.2	• feeding during surgery* • 2 patients with wound infections • n = 40 • mean TBSA burn = 36.2% • mean age = 7.5 years • mean no. surgeries= 4.0	yes (p<0.02)	intervention group had deeper burns, more surgical procedures and more antibiotic therapy
Imeokparia et al.[37]	• feeding withheld during surgery*** • 4 patients with wound infections • n =13 • mean TBSA burn = 21.8% • mean age = 9.3 years • mean no. surgeries = 2.3	• feeding during surgery*** • 6 patients with wound infections • n=17 • mean TBSA burn = 32.4% • mean age = 6.3 years • mean no. surgeries = 4.4	no (p = 1.00)	intervention group had significantly larger %TBSA
Varon et al [34]	• feeding withheld during surgery** • 12 wound infections • n=16 • mean TBSA burn = 45.7 % • mean age = 49.8 years • mean no. surgeries = 7.3	• feeding during surgery** • 10 wound infections • n=17 • mean TBSA burn 42.6% • mean age = 41.6 years • mean no. surgeries = 7.4	no (p = 0.46) *(p <0.05 considered significant)*	populations were from different timeframes

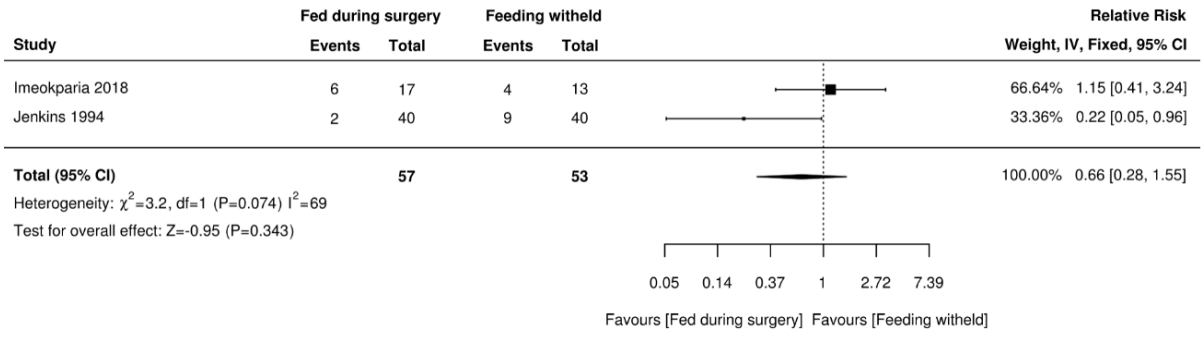
**Control and intervention groups were similar in age, % TBSA burn, male/female ratio, incidence of smoke inhalation and postburn day of admission.*

*** Control and intervention groups comparable in age, male/female ratio and % TBSA burn.*

**** Control and intervention groups were similar in age, male/female ratio, mechanism of injury, and number of operations but intervention group had larger % TBSA burn.*

Figure 2 depicts the meta-analysis relating to perioperative feeding and the outcome of wound infection. Only two studies[35,37] could be included in this meta-analysis. The research by Varon et al.[34] could not be included because the control and intervention populations were from different timeframes. The meta-analysis shows little to no evidence that feeding during surgery reduces the rate of wound infection compared to those that have feeding withheld (RR = 0.66, 95% CI 0.28 – 1.55).

Figure 2: Meta-analysis of intraoperative feeding vs perioperative fasting on wound infection.



3.4.3 Length of stay

Five out of the seven included studies reported on whether they could identify a relationship between perioperative enteral feeding and length of acute hospital stay.[34-37,52] The results are summarised in Table 11. One of these studies was a randomised controlled trial,[35] three were retrospective cohorts,[34,37,52] and one was a case series.[36]

The randomised control trial by Jenkins et al. reported their control group (perioperative fasting) had a shorter length of stay compared to the intervention (received intraoperative enteral feeding).[35] The control group had a mean length of stay 1.6 days shorter but the difference between the two groups was reported as not statistically significant. There was however, a lack of homogeneity between the control and intervention groups, with the intervention group having deeper burns and more surgical procedures than the control.

The three retrospective cohorts reported varying results in the length of stay of their patient groups who experienced perioperative fasting compared to intraoperative post pyloric enteral feeding. Imeokparia et al. reported their control group (perioperative fasting) had a shorter length of stay compared to the intervention (intraoperative enteral feeding) and they reported the difference was statistically significant (control group mean length of stay 17.7 days shorter).[37] The patients in the intervention group did however have a larger %TBSA burns compared to the control group.

In contrast, the retrospective cohort by Varon et al. reported the control group (perioperative fasting) had a mean length of stay which was 5.3 days longer than the intervention group (post pyloric enteral feeding during theatre).[34] This difference between intervention and control groups was reported as not statistically significant. Of note is the intervention group was from a later timeframe compared to the control, which has the potential to influence these results.

The third retrospective cohort which reported on length of stay was by Carmichael et al. however the control and intervention groups were presented differently. This study only included mechanically ventilated burns patients who were stratified into a control group (patients who had enteral feeding withheld for >50% of surgeries) and an intervention group (patients who had enteral feeding continued for ≥ 50% of surgeries).[52] In this study, the mean length of stay was 27 days longer in the control compared to the intervention group. The difference in length of stay was reported as not statistically significant.

Sunderman et al. also reported on the length of stay of their paediatric burns patients who received intraoperative post pyloric enteral feeding.[36] This retrospective case series reported

their patients had a mean length of stay of 46.8 days (± SD 26.6). Since this case series did not have a comparator, no comment can be made on the influence of perioperative nutrition on length of stay in this patient group.

Table 11: Length of stay

Study	Control	Intervention	Statistically significant difference in outcome?	Comment
Jenkins et al.[35]	• feeding withheld during surgery* • mean LOS = 32.6 days • n = 40 • mean TBSA burn = 36.2% • mean age = 7.4 years • mean no. surgeries = 3.2	• feeding during surgery* • mean LOS = 34.2 days • n = 40 • mean TBSA burn = 36.2% • mean age = 7.5 years • mean no. surgeries= 4.0	No (p value not given)	intervention group had mean LOS 1.6 days longer intervention group had deeper burns and more surgical procedures
Imeokparia et al.[37]	• feeding withheld during surgery*** • mean LOS = 29.9 • n =13 • mean TBSA burn = 21.8% • mean age = 9.3 years • mean no. surgeries = 2.3	• feeding during surgery*** • mean LOS = 47.6 days • n=18 • mean TBSA burn = 32.4% • mean age = 6.3 years • mean no. surgeries = 4.4	yes P value = 0.03 *(≤0.05 significant)*	intervention group had a significantly larger %TBSA (p = 0.032). intervention group on average had 17.7 days longer LOS
Varon et al.[34]	• feeding withheld during surgery** • mean LOS = 57.9 days • n = 16 • mean TBSA burn = 45.7% • mean age = 49.8 years • mean no. surgeries = 7.3	• feeding during surgery** • mean LOS = 52.6 days. • n = 17 • mean TBSA burn = 42.6% • mean age = 41.6 years • mean no. surgeries = 7.4	*No* p= 0.66 *(p<0.05 considered significant)*	intervention group had on average 5.3 days shorter LOS. populations were from different timeframes
Carmichael et al.[52]	• feeding held for >50% of surgeries**** • mean LOS = 86 days • n = 30 • mean = 46% TBSA • mean age = 41 years	• feeding continued for ≥ 50% of surgeries**** • mean LOS = 59 days • n = 15 • mean = 41% TBSA burn • mean age = 37 years	no P = 0.36 (P <0.05 considered significant)	Ventilated patients only LOS mean = 27 days less in intervention group
Sunderman et al.[36]	• nil control	• mean LOS = 46.8 days (± SD 26.6). • feeding during surgery • n = 434 patients • mean TBSA burn=51.3% • Mean age = 6.4 years • Mean no. surgeries = 8.4	N/A	nil useful conclusion on the influence of intraoperative feeding on length of stay

**Control and intervention groups were similar in age, % TBSA burn, male/female ratio, incidence of smoke inhalation and postburn day of admission.*

*** Control and intervention groups comparable in age, male/female ratio and % TBSA burn.*

**** Control and intervention groups were similar in age, male/female ratio, mechanism of injury, and number of operations but intervention group had larger % TBSA burn.*

*****Control and intervention groups had no significant difference in age, ratio male/female, and mean %TBSA.*

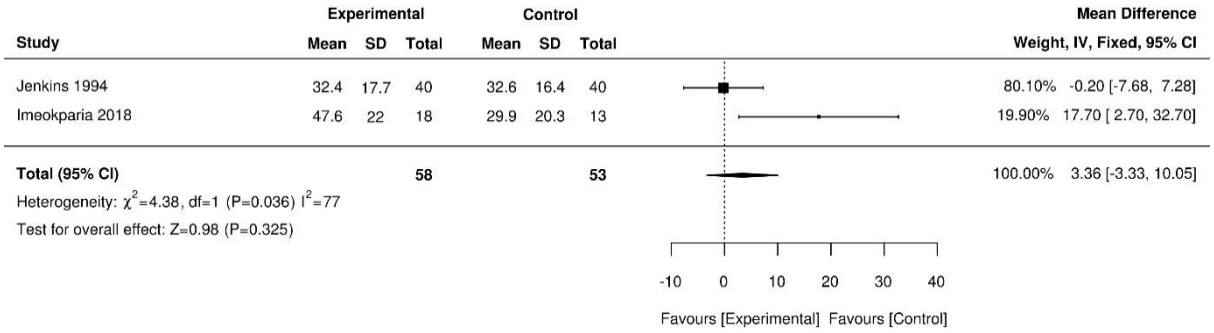
Meta-analysis was completed on the influence of intraoperative post pyloric feeding compared to fasting on length of stay and the results are shown in Figure 3.

Only two studies could be included in this meta-analysis.[35,37] The paper by Varon et al. could not be included due to the control and intervention groups coming from different timeframes.[34] Carmichael et al's research did not have a comparable intervention and controls

to the other studies in the meta-analysis and therefore was excluded.[52] The case series by Sunderman et al. could not be included because there was no control group.[36]

The meta-analysis shown in Figure 3 indicates little to no evidence that intraoperative feeding reduces length of stay in burns patients when compared to patients who have enteral feeding withheld during the perioperative period (RR = 3.36, 95% CI = -3.33 - 10.05). An additional note is the high level of heterogeneity, as indicated by an I^2 of 77.

Figure 3: Meta-analysis of the influence of intraoperative feeding vs fasting on length of stay



3.4.4 Aspiration

The incidence of aspiration was the most common primary outcome assessed in the included studies, with all seven studies including aspiration events as an outcome measure.[34-38,52,58]

Table 12 summarises the reported results relating to aspiration from each of the studies. There were no reported occurrences of aspiration events in any of the study participants, despite a range of interventions. The patients in four of the studies received post pyloric feeding during surgical procedures.[34-37] One study included patients who received either post pyloric feeding (86%) or intragastric feeding (7%) or transitioned from gastric to post pyloric feeding (7%), but all of their patients were intubated and mechanically ventilated.[52] One study reported on patients who received nasogastric feeding and short perioperative fasting.[38] One study, the case report, did not report whether their patient had intragastric or post pyloric feeding while only having a relatively short preoperative fasting period.[58] Although there was variation in the feeding and fasting methods between the included studies, the consistent result was of no aspiration events in any patients, regardless of perioperative feeding method.

A meta-analysis was not conducted for the outcome of aspiration relating to perioperative feeding since there was nil aspiration reported in any intervention or control groups.

Table 12: Aspiration events

Study	Control	Intervention	Aspiration outcome
Jenkins et al.[35]	feeding withheld during surgery* n = 40	post pyloric intraoperative enteral feeding n = 40	"Nil patient in either group suffered aspiration"
Pearson et al.[38]	Intragastric feeding up until 4 hours prior to surgery n = 11	intragastric feeding up until 1 hour prior to surgery n = 7	"There was no evidence of perioperative aspiration in any of the patients during their surgical procedures"
Imeokparia et al.[37]	feeding withheld during surgery*** n =13	post pyloric intraoperative enteral feeding n=18	"Neither study group had patients with aspiration events in the perioperative feeding period"
Varon et al.[34]	feeding withheld during surgery** n = 16	post pyloric intraoperative enteral feeding n = 17	"There were no intraoperative aspiration events or regurgitation events in either group"
Carmichael et al.[52]	feeding held for >50% of surgeries**** n=30	feeding continued for ≥ 50% of surgeries n= 15	"There were no documented aspiration events during any of the operative procedures reviewed"
Sunderman et al.[36]	Nil control	post pyloric intraoperative enteral feeding n= 434	"There were no documented incidences of clinically evident aspiration among the group"
Sutanto et al.[58]	Nil control	Enteral feeds up until 1 hour 30 minutes prior to surgery n = 1	"The aspiration which is a possible risk during anaesthesia induction, surgery, extubation and immediate post-operative period in non-fasting patients was not seen in our patient"

**Control and intervention groups were similar in age, % TBSA burn, male/female ratio, incidence of smoke inhalation and postburn day of admission.*

*** Control and intervention groups comparable in age, male/female ratio and % TBSA burn.*

**** Control and intervention groups were similar in age, male/female ratio, mechanism of injury, and number of operations but intervention group had larger % TBSA burn.*

*****Control and intervention groups had no significant difference in age, ratio male/female, and mean %TBSA.*

There was some variability in the definition of aspiration. Table 13 summarises the definitions each study used to identify aspiration events. Common themes in definitions were whether enteric tube feeds were suctioned from endotracheal tubes and changes in patient oxygenation levels. Although there were some common themes as to how aspiration was defined, there was no consistent and standardised methods of diagnosis. A lack of a clear definition of aspiration makes it difficult to adequately compare across studies.

Table 13: Definitions used to identify aspiration events.

Study	Definition of aspiration
Jenkins et al.[35]	Aspiration not clearly defined. Closest definition was: "patients were closely monitored by anaesthesia personnel during the surgical procedure for tube position, gastric reflux and aspiration"
Pearson et al.[38]	"the appearance of new infiltrates on a postoperative chest roentgenogram, notes in the anaesthetic record that indicated the occurrence of aspiration, and unexplained postoperative fever or hypoxia."
Imeokeparia et al.[37]	"examination of the anaesthetic record, any diagnosis of aspiration pneumonia, along with any need for supplemental oxygen after discharge from the post-anaesthesia recovery unit. Supplemental oxygen was used as an indicator of aspiration as hypoxia is sensitive sign of pneumonia or pneumonitis."
Varon et al.[34]	"enteric contents or tube feeds were suctioned from endotracheal tube by flexible suction catheter or bronchoscopy or if visual evidence of regurgitation occurred coincident with an acute change in ventilatory status or oxygenation."
Carmichael et al.[52]	"(1) if enteric contents or tube feeds were suctioned from the endotracheal tube by flexible suction catheter during the procedure or (2) if there was evidence of regurgitation that coincided with an acute change in oxygenation or ventilator status, as documented by the anaesthesiologist."
Sunderman et al.[36]	"if enteric contents or tube feeding were suctioned from the endotracheal tube or if visualized regurgitation occurred with an acute change in respiratory status during the perioperative period."
Sutanto et al.[58]	Nil definition provided.

3.4.5 Pneumonia

Only two of the included studies reported on pneumonia as an outcome measure.[34,35] One of the studies was the randomised controlled trial by Jenkins et al.[35] and the other was the retrospective cohort by Varon et al.[34] Table 14 summarises the results reported on the occurrence of pneumonia in the patients who received intraoperative post pyloric enteral feeding compared to those who experienced perioperative fasting.

Jenkins et al. reported five out of 40 patients (12.5%) developed pneumonia in the control group (feeding withheld during operative procedures) and nine out of 40 patients (22.5%) developed pneumonia in the intervention group (received intraoperative post pyloric enteral feeding).[35] This difference was reported as not statistically significant. The criteria for pulmonary infection was "a positive sputum culture with consistent radiographic changes and systemic antibiotic therapy" (page 201). As mentioned previously, the intervention group in this study had deeper burns, more surgical procedures and more antibiotic therapy which has the potential to influence the results outcomes.

Varon et al. also reported a lower occurrence of pneumonia in their control group compared to the intervention group.[34] This paper identified 14 out of 16 patients (87.5%) developed

pneumonia in the control group (had enteral feeding withheld during surgical procedures), compared with 16 out of 17 patients (94.1%) who developed pneumonia in the intervention group (continued to receive post pyloric enteral feeding during surgical procedures). The definition of pneumonia used by Varon et al. was "culture-positive pneumonia" (page 300) however nil further details were provided.[34] This paper has the potential bias of the intervention group coming from a later timeframe than the control.

Table 14: Pneumonia in control vs intervention groups

Study details	Control	Intervention	Statistically significant difference?	Comment
Jenkins et al.[35]	• feeding withheld during surgery* • 5 patients with pneumonia • n = 40 • mean TBSA burn = 36.2% • mean age = 7.4 years • mean no. surgeries = 3.2	• feeding during surgery* • 9 patients with pneumonia • n = 40 • mean TBSA burn = 36.2% • mean age = 7.5 years mean no. surgeries= 4.0	No (p value not stated)	intervention group had deeper burns, more surgical procedures and more antibiotic therapy
Varon et al.[34]	• feeding withheld during surgery** • 14 patients with pneumonia • n=16 • mean TBSA burn = 45.7 % • mean age = 49.8 years • mean no. surgeries = 7.3	• feeding during surgery** • 16 patients with pneumonia • n=17 • mean TBSA burn 42.6% • mean age = 41.6 years • mean no. surgeries = 7.4	No (p= 0.60)	control was from an earlier timeframe

**Control and intervention groups were similar in age, % TBSA burn, male/female ratio, incidence of smoke inhalation and postburn day of admission.*

*** Control and intervention groups comparable in age, male/female ratio and % TBSA burn.*

A meta-analysis could not be completed for the influence of intraoperative feeding compared to fasting on pneumonia. Only the study by Jenkins et al. had results appropriate for a meta-analysis however numbers were deemed too small to be of any value.[35] Similar to reported previously, Varon et al.'s populations were not homogenous and could not be included in a meta-analysis.[34]

Secondary outcomes

3.4.6 Calorie intake

Five of the included studies[34,35,37,38,52] provided details on whether perioperative enteral feeding influenced the number of Calories patients received. Two studies were RCT's[35,38] and three were retrospective cohorts.[34,37,52] Table 15 summarises the Caloric delivery outcomes reported in the included studies.

Each study reported on Caloric provision differently, therefore are difficult to compare the studies as a combined group. There was however a consistent theme that indicated patients who received perioperative enteral feeding received substantially more Calories compared to

those who experienced perioperative fasting. Graphical displays of the results of Calorie provision from each study are presented within the narrative descriptions of results.

Table 15: Caloric delivery

Study details	Control	Intervention	Statistically significant
Jenkins et al.[35]	• feeding withheld during surgery* • cumulative Caloric balance = -7899 ±3123 • n = 40 • mean TBSA burn = 36.2% • mean age = 7.4 years • mean no. surgeries = 3.2	• feeding during surgery* • cumulative Caloric balance = +2673±2147 • n = 40 • mean TBSA burn = 36.2% • mean age = 7.5 years • mean no. surgeries= 4.0	Yes Feeding witheld group = significant and consistent Calorie deficit (p<0.006).
Pearson et al.[38]	• fasting 4 hours prior to theatre • 15% of Caloric goals achieved on day of surgery • n = 11 • mean TBSA burn= 41% • mean age = 39 years	• fasting 1 hour prior to theatre • 30% of Caloric goals achieved on day of surgery • n =7 • mean TBSA burn = 47% • mean age 46 year	Yes (p = 0.01, p of <0.05 considered significant)
Imeokparia et al.[37]	• feeding withheld during surgery*** • lost a mean of 119.1 Calories per kg weight • n =13 • mean TBSA burn = 21.8% • mean age = 9.3 years • mean no. surgeries = 2.3	• feeding during surgery*** • gained mean 144.4 Calories per kg of weight • n = 18 • mean TBSA burn = 32.4% • mean age = 6.3 years • mean no. surgeries = 4.4	Not determined: p value/statistical significance not stated.
Varon et al.[34]	• feeding withheld during surgery** • 73.2±18.4% of target Calories • n=16 • mean TBSA burn = 45.7 % • mean age = 49.8 years • mean no. surgeries = 7.3	• feeding during surgery** • 97.5 ±13. % of target Calories • n=17 • mean TBSA burn 42.6% • mean age = 41.6 years • mean no. surgeries = 7.4	Yes p-value 0.001 – statistically significant
Carmichael et al.[52]	• feeding held for >50% of surgeries**** • 69% of mean Caloric needs met • n = 30 • mean = 46% TBSA mean age = 41 years	• feeding continued for ≥ 50% of surgeries**** • 81% of mean Caloric needs met • n = 15 • mean = 41% TBSA burn mean age = 37 years	Yes (p=0.01) p-value of <0.05 considered significant.

**Control and intervention groups were similar in age, % TBSA burn, male/female ratio, incidence of smoke inhalation and postburn day of admission.*

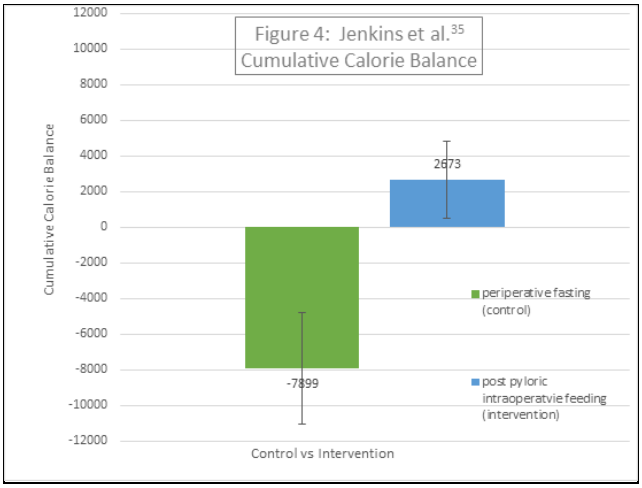
*** Control and intervention groups comparable in age, male/female ratio and % TBSA burn.*

**** Control and intervention groups were similar in age, male/female ratio, mechanism of injury, and number of operations but intervention group had larger % TBSA burn.*

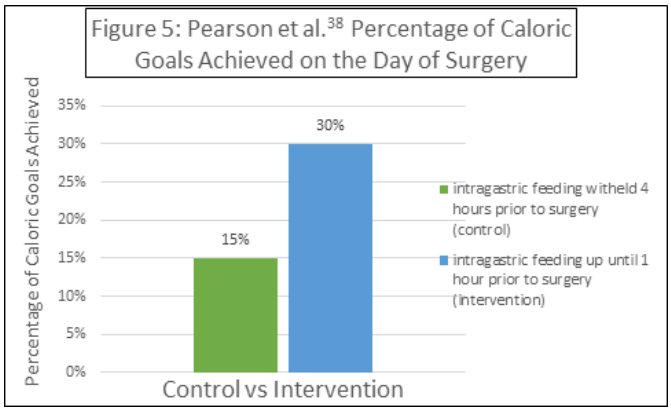
*****Control and intervention groups had no significant difference in age, ratio male/female, and mean %TBSA.*

Jenkins et al. reported the control group (patients who experienced perioperative fasting) demonstrated a consistent Calorie deficit throughout the study period (P<0.01) compared with the intervention group (received post pyloric intraoperative enteral feeding).[35] The differences in Caloric provision between the two groups was reported as statistically significant.

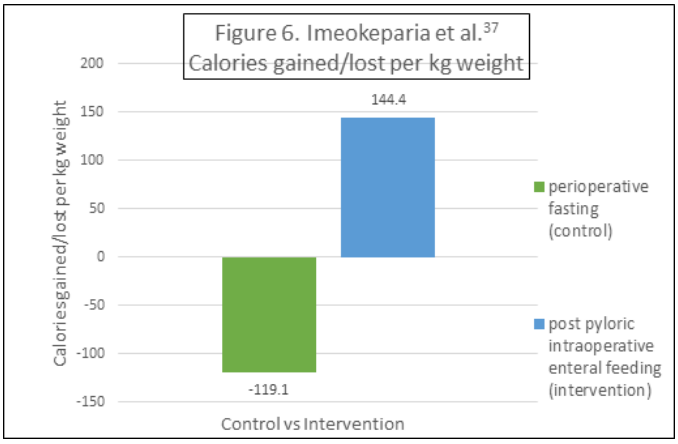
Figure 4 shows the cumulative Caloric balance reported by Jenkins et al.[35]



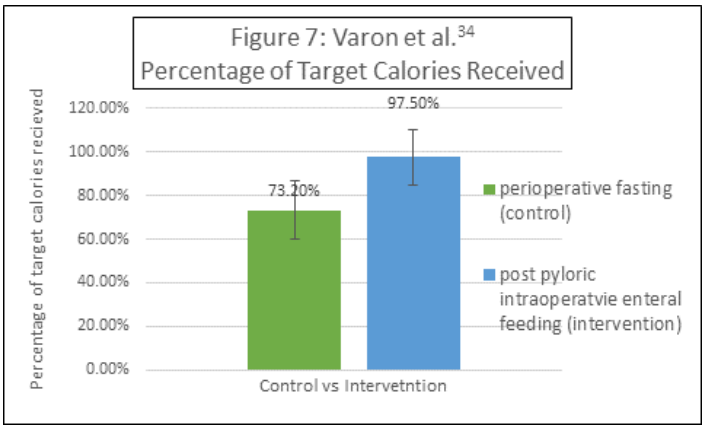
Pearson et al. had multiple phases within their research paper, however one arm compared patients who had intragastric enteral feeding withheld 4 hours prior to surgery to patients who had intragastric feeding stopped 1 hour prior to surgery.[38] This study only reported on fasting time before anaesthesia, not total fasting time They found the control group (who were fasted for 4 hours prior to surgical intervention) received 15% of Caloric goals achieved on day of surgery and the intervention group (fasted for only 1 hour prior to surgery) achieved 30% of Caloric goals on the day of surgery. Pearson et al. reported the difference in the amount of goal Calories achieved on the day of surgery between the control and intervention groups was statistically significant. The results are presented in Figure 5.[38]



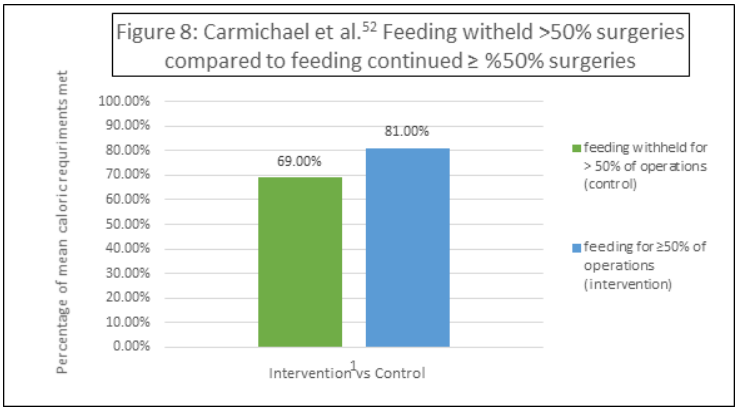
Imeokparia et al. reported on Calories gained/lost per kilogram of weight in their paediatric patients. Figure 6 graphically represents the results.[37] This research identified their control group (experienced perioperative fasting) had a mean of 119 Calories lost per kilogram of weight. In contrast, the intervention group (perioperative post pyloric enteral feeding) had a mean of 144 Calories gained per kilogram of weight. This paper did not report on any statistical significance of the differences between the control and intervention group with respect to Calories gained/lost per kg of weight.



The study by Varon et al. reported on percentage of goal Calories achieved in patients who experienced perioperative fasting compared with those who received intraoperative post pyloric enteral feeding.[34] Varon et al. also found the control group (perioperative fasting) received significantly fewer of the goal Calories (mean 73.2% Calories achieved) compared to the intervention group (post pyloric feeding during surgery) (mean 97.5% Calories achieved). Figure 7 is a graphical representation on the results.[34]



Carmichael et al. also reported on the percentage of goal Calories achieved. Figure 8 represents a graph of their results.[52] This paper included only intubated, mechanically ventilated burns patients who either had feeding withheld for >50% of surgeries or continued for ≥50% of surgeries. The method of enteral feeding included both intragastric and post pyloric tube placement. This paper reported the control group (feeding withheld for > 50% of surgical procedures) received 69% of mean Caloric requirements overall and the intervention group (received enteral feeding for ≥50% of operations) received 81% of mean Caloric requirements overall. The intervention group was reported to have met significantly more of their mean Caloric requirements compared to the control group.



A meta-analysis was not appropriate due to these differences in reporting of Caloric delivery. Although there were differences in how data was collected and reported, the consistent theme is patients who received either intraoperative enteral feeding or shorter fasting times, received substantially more Calories compared to those who did not receive perioperative feeding or short fasting.

3.4.7 Ventilator days

Four of the included studies (one RCT[35] and three retrospective cohorts)[34,37,52] reported on days patients received ventilatory support and the results are presented in Table 16.

Jenkins et al. and Varon et al. reported longer mean number of ventilator days in their control groups (experienced perioperative fasting) compared to the intervention (received post pyloric feeding during surgical procedures).[34,35] Similarly, Carmichael et al. reported a trend towards a greater number of ventilator days in the control group (enteral feeding held for >50% of surgeries) compared to the intervention group (enteral feeding continued for ≥ 50% of surgical procedures).[52]

In contrast, Imeokparia et al. reported a lower number of ventilator support days in the control group (perioperative fasting) compare to the intervention group (post pyloric enteral feeding during theatre.[37] This could potentially be explained in the larger %TBSA burn in this study's intervention group.

Table 16: Ventilator days

Study	Control	Intervention	Statistically significant
Jenkins et al.[35]	• feeding withheld during surgery* • mean ventilator days 7.1 ± 1.7^ • n = 40 • mean TBSA burn=36.2% • mean age = 7.4 years • mean no. surgeries = 3.2	• feeding during surgery* • mean ventilator days 4.1 ± 1.1^ • n = 40 • mean TBSA burn=36.2% • mean age = 7.5 years • mean no. surgeries = 4.0	No (p value not given)
Imeokparia et al.[37]	• feeding withheld during surgery** • mean ventilator days 1.5 ± 5.0^^ • n =13 • mean TBSA burn = 21.8% • mean age = 9.3 years • mean no. surgeries = 2.3	• feeding during surgery** • mean ventilator days 9.8 ± 8.4^^ • n=18 • mean TBSA burn = 32.4% • mean age = 6.3 years • mean no. surgeries = 4.4	Yes P= 0.0041 (≤0.05 considered significant)
Varon et al.[34]	• feeding withheld during surgery*** • mean ventilator days 44.5 ± 44^^ • n = 16 • mean TBSA burn = 45.7 % • mean age = 49.8 years • mean no. surgeries = 7.3***	• feeding during surgery*** • mean ventilator days 32.6 ± 25.6^^ • n = 17 • mean TBSA burn 42.6% • mean age = 41.6 years • mean no. surgeries = 7.4	No P =0.34 (<0.05 considered significant)
Carmichael et al.[52]	• feeding held for >50% of surgeries**** • Mean ventilator days = 42 ± 55^^ • n=30 • mean = 46% TBSA • mean age = 41	• feeding continued for ≥ 50% of surgeries**** • mean ventilator days = 24 ± 45^^ • n= 15 • mean = 41% TBSA burn • mean age = 37	No (p value = 0.29 and P < 0.05 considered significant)

**Control and intervention groups were similar in age, % TBSA burn, male/female ratio, incidence of smoke inhalation and postburn day of admission.*

*** Control and intervention groups comparable in age, male/female ratio and % TBSA burn.*

**** Control and intervention groups were similar in age, male/female ratio, mechanism of injury, and number of operations but intervention group had larger % TBSA burn.*

*****Control and intervention groups had no significant difference in age, ratio male/female, and mean %TBSA.*

^ = Standard error of mean presented

^^ = Standard deviation presented

Figure 9: Meta-analysis of the influence of intraoperative feeding vs fasting on ventilator days

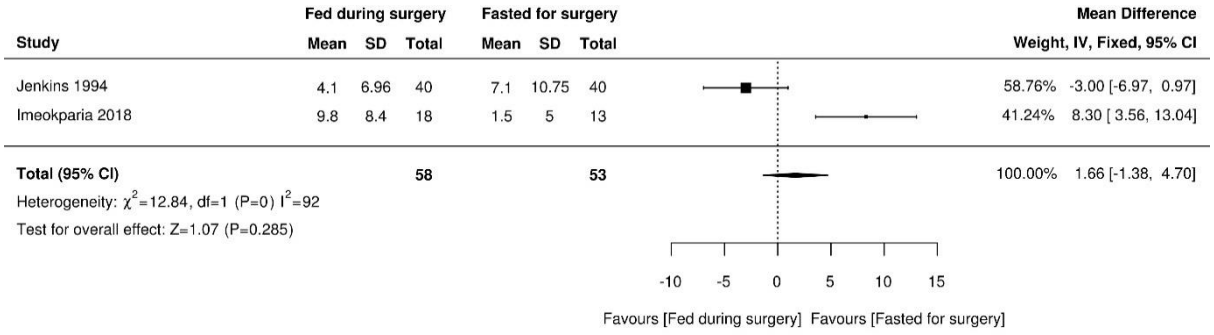


Figure 9 represents the meta-analysis on the influence of intraoperative feeding compared to fasting on ventilator days. Only two of the studies could be included in the meta-analysis.[35,37] As reported earlier, Varon et al. was not included due to their two patient groups being from differing timeframes.[34] Carmichael et al.'s study also could not be used in the meta-analysis since they reported results differently to the other research papers.[52] The meta-analysis which included the two remaining studies indicates little to no evidence that intraoperative feeding

reduces length of mechanical ventilation in burns patients when compared to patients who have enteral feeding withheld during the perioperative period (RR = 1.66, 95% CI = -1.38 - 4.70).[35,37] An additional note is the high level of heterogeneity, as indicated by an I^2 of 92.

As has been reported previously, the results of the meta-analyses need to be interpreted with caution, since Jenkin's et al.'s intervention group had substantially higher percentage of full thickness burns and significantly more surgical procedures.[35] Imeokparia et al.'s intervention groups also had larger %TBSA burns.[37]

3.4.8 Wellbeing measures: nausea, vomiting, thirst, hunger, malaise and fatigue.

Only one of the included studies reported on the impact of perioperative feeding on wellbeing measures such as nausea, vomiting, thirst, hunger, malaise and fatigue.[58]

This single case report was of low quality, as determined by critical appraisal score, however was included in this systematic review because of the unique and patient-centred reporting method. This paper reported on a 26-year-old male with 67% TBSA burn. Weight = 45kg, height = 163cm, BMI = 16.9 (underweight). The patient experienced varying perioperative fasting times, ranging from 1 hour 30 minutes before surgery to 14 hours 45 minutes before surgery. Perioperative wellbeing outcomes were then recorded.

Table 17 summarises the results reported in this case study. Overall, perioperative enteral nutrition increased satisfaction including less hunger, thirst, postoperative nausea and vomiting compared with extended fasting.

Table 17: Wellbeing signs and symptoms reported in one included study[58]

Method of fasting	Total fasting time	Wellbeing signs and symptoms
Enteral nutrition up until 1 hr 30 minutes before surgery	4 hours 45 min	preoperative nausea and vomiting but nil hunger, thirst
		postoperative nausea but nil vomiting, malaise or fatigue
Enteral nutrition up until 3 hours 45 minutes before	9 hours	Nil preoperative nausea, vomiting, hunger or thirst
		Postoperative nausea and vomiting but nil malaise or fatigue
Enteral nutrition up until 1 hour 35 minutes before surgery	12 hours 30 minutes	Nil preoperative nausea, vomiting, hunger or thirst
		postoperative nausea, vomiting, malaise and fatigue
Oral diet up until 14 hours 45 minutes before surgery	26 hours 40 minutes	preoperative hunger and thirst
		postoperative nausea, vomiting, malaise and fatigue

3.4.9 All other secondary outcomes

There were a number of other secondary outcomes measured within the included studies. "Other" secondary outcomes included: supplemental albumin, antibiotic days, length of stay/%third degree burn, clinical sepsis, bacteraemia, ratio of ICU days/%TBSA burn, number of ICU days, nitrogen balance, amount of goal protein provided, admit/discharge weight. Table 18 summarises the results reported in each of these studies. Overall, there was no consistency as to whether intraoperative perioperative feeding improved the outcomes measured, with most studies showing very small differences in outcomes.

Supplemental albumin, antibiotic days, length of stay per % of third degree burns and clinical sepsis were reported by Jenkins et al.[35] This study found the control group (who were fasted during the perioperative period had:

- significantly more supplemental albumin,
- significantly fewer antibiotic days,
- a non-significant longer mean length of stay per % third-degree burn, and
- a non-significant fewer number of patients with clinical sepsis

compared to the intervention group who received intraoperative post pyloric feeding.

Bacteraemia, ratio of ICU days per %TBSA burn and % of goal protein received were reported by Varon et al.[34] This research paper found no significant difference in bacteraemia between the group who had perioperative enteral feeding withheld compared to the group who received intraoperative post pyloric feeding. They also found the ratio of ICU days per %TBSA burn was moderately shorter (non-significant) in the control group (perioperative fasting) compared to the intervention group (received intraoperative post pyloric feeding) (ratio of 1.18 in control compared with 1.73 in intervention). Varon et al. also reported the patients in their control group had significantly less % of goal protein achieved compared to the intervention (mean 70.6% in perioperative fasting group compared with mean 98.1% protein achieved in intraoperative feeding group).[34]

The number of days spent in intensive care was reported by two studies, and there were varying results.[34,37] Imeokparia et al. found the control group who experienced perioperative fasting had significantly fewer ICU days compared to the intervention group who received intraoperative post pyloric feeding.[37] In contrast, Varon et al. found the control group had a non-significant greater mean number of ICU days compared to the group who received intraoperative post pyloric feeding.[34]

Nitrogen balance and admit/discharge weight was reported in the case series published by Sunderman et al.[36] This study found patients who received intraoperative post pyloric

(N=434) maintained an average of 3.1 ±2.8 daily nitrogen balance and also maintained their weight within ±10% of their recorded admission weight. There was no control as a comparator in this research paper.

Table 18: Summary of "other" secondary findings

Outcome measure	Study	Result
Supplemental albumin	Jenkins et al.[35]	control group required more supplemental albumin (p <0.04) compared to intervention which received intraoperative post pyloric feeding
Antibiotic days	Jenkins et al.[35]	control group had fewer mean antibiotic days compared with intervention group, which received intraoperative post pyloric feeding (control mean 4.1 days vs intervention mean 7.7 days^)(p<0.05)
Length of stay per %third degree burn	Jenkins et al.[35]	control group had longer mean length of stay per % third degree burn compared with intervention group which received intraoperative post pyloric feeding (control mean 2.0 days vs interention mean 4.5 days)
Clinical sepsis	Jenkins et al.[35]	control group had fewer patients with clinical sepsis, compared with intervention group (8/40, 20% patients with sepsis in control vs 10/40, 25% patients in intervention group)
Bacteraemia	Varon et al.[34]	control had 7/16 (44%) patients with bacteraemia vs intervention who had 8/17 (47%) patients with bacteraemia (p = 1.000)
Ratio of ICU days/%TBSA burn	Varon et al.[34]	control group had fewer ICU days/%TBSA burn compared with intervention (mean 1.18 days in control vs mean 1.73 days in intervention (p = 0.81)
Number of ICU days	Imeokparia et al.[37]	control group had fewer ICU days (mean 4.3 days in control group vs mean 22.4 days in intervention)
	Varon et al.[34]	control group had greater ICU days than intervention (control mean 48.5 days vs intervention mean 45 days, p = 0.772)
% goal protein achieved	Varon et al.[34]	control group achieved mean 70.6% goal protein vs intervention group achieved mean 98.1%
Nitrogen balance	Sunderman et al.[36]	Nil control Patients who received intraoperative post pyloric (N=434) maintained an average of 3.1 ±2.8 daily nitrogen balance
Admit/discharge weight.	Sunderman et al.[36]	Nil control 68% (259 of 381) of patients who received intraoperative post pyloric feeding maintained their weight within ±10% of their recorded admission weight

3.5 GRADE Summary of Findings

Table 19 is the GRADE summary of findings (Grading of Recommendations Assessment, Development and Evaluation) for seven of the outcome measures. The approach of GRADE classifies findings based not only on study design but also considers other factors such as risk of bias, publication bias, inconsistency, indirectness, imprecision of evidence, effect sizes, dose-response relationships, and confounders of findings.[45] This GRADE process classifies the quality of the evidence (certainty) into one of four scores: high, moderate, low and very low.[45] GRADEPro software was used in the development of this table.[44] The results presented Table 19 indicates the certainty of evidence was very low for all of the seven outcome measures. Studies were downgraded for a range of factors including risk of bias, inconsistency, indirectness and imprecision. The reasons for the downgrading of certainty of evidence is outlined in explanations a - m within the table.

Table 19: GRADE summary of findings table

Summary of findings:

Perioperative feeding compared to perioperative fasting for either children (less than 18 years) or adults (greater than or equal to 18 years) who have sustained an acute burn injury and undergone surgical management of their burn

Patient or population: either children (less than 18 years) or adults (greater than or equal to 18 years) who have sustained an acute burn injury and undergone surgical management of their burn
Setting: medical facilities treating patients with acute burns
Intervention: perioperative feeding
Comparison: perioperative fasting

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with perioperative fasting	Risk with perioperative feeding				
Mortality follow up: mean 34 days	100 per 1,000	**125 per 1,000** (34 to 366)	**OR 1.29** (0.32 to 5.19)	80 (1 RCT)	⨁◯◯◯ VERY LOW a,b,c,d	
Wound infection follow up: mean 56 days	245 per 1,000	**157 per 1,000** (66 to 365)	**RR 0.64** (0.27 to 1.49)	111 (2 observational studies)	⨁◯◯◯ VERY LOW c,e,f,g,h	
Length of stay follow up: mean 56 days		mean difference **3.36 days higher** (3.33 lower to 10.05 higher)	-	111 (2 observational studies)	⨁◯◯◯ VERY LOW e,h,i	
Aspiration events follow up: mean 64 days	Although there was variability in the definition of aspiration (see results section) and also differences between studies, it should be noted that there were no reported occurences of aspiration in any study.			545 (3 observational studies)	⨁◯◯◯ VERY LOW c,e,i,j,k,l	
Pneumonia follow up: mean 34 days	125 per 1,000	**225 per 1,000** (80 to 490)	**OR 2.03** (0.61 to 6.72)	80 (1 RCT)	⨁◯◯◯ VERY LOW b,c,d,e	
Ventilator days follow up: mean 56 days		mean **1.66 days higher** (1.38 lower to 4.7 higher)	-	111 (2 observational studies)	⨁◯◯◯ VERY LOW c,e,g,i	
Calorie Intake assessed with: One study did not report on follow-up time but follow-up of other two studies reported below. follow up: mean 56 days	Although there was variablity between the studies and also each study reported on Calorie intake differently, the consistent outcome was that the patients who recieved either intraoperative post pyloric enteral feeding or short perioperative fasting, recieved a greater caloric intake compared to patients who experienced extended perioperative fasting.			129 (3 observational studies)	⨁◯◯◯ VERY LOW b,c,e,g,j,l,m	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio; **RR:** Risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Downgraded for risk of bias related to blinding. There was to nil ability to blind participants and assessors and also nil allocation concealment however this would be virtually impossible to avoid and unlikely to influence the outcome of mortality.
b. Downgraded one level for inconsistency: Jenkins included only children and adults up to 24 years.
c. Downgraded one level related to indirectness due to intervention group having statistically significantly higher % of full thickness burns and significantly more surgical procedures Jenkins et al.)
d. Downgraded one level for imprecision due to very small sample size and not enough to show a real difference in outcomes
e. Downgraded one level for risk of bias due to none of the studies having either blinding of assessors or participants. Nil allocation concealment (potential selection bias)
f. Downgraded one level for inconsistency. One study did not provide criteria for determining wound infection and the other study's criteria was as follows: a positive wound culture of greater than 105 micro-organisms per gram of tissue, systemic antibiotics, or graft loss, or any combination of these.
g. Imeokeparia downgraded for indirectness due to intervention group had a significantly larger %TBSA
h. Downgraded one level for imprecision due to very wide confidence interval in forest plot
i. Downgraded one level for inconsistency: Jenkins included children and adults up to 24 years, Imeokparia only children.
j. Downgraded for risk of bias due to Pearson et al. study having limitations in reporting of perioperative fasting times
k. Downgraded one level for indirectness due to inconsistencies in the definition of aspiration.
l. Downgraded for indirectness since Pearson had short fasting for patients receiving intragastric feeding whereas Jenkins and Imeokparia had patients who received intraoperative post pyloric feeding.
m. Downgraded for imprecision due to different reporting methods between studies of Caloric intake.

Chapter 4: Discussion

4.1 General discussion

A systematic review on the safety and effectiveness of perioperative enteral feeding in burns is important because it summarises the findings of relevant studies and provides evidence to guide clinical practice. Despite the limitations in the quality of the included studies, this systematic review has the potential to contribute to the quality of available evidence and inform clinical practice in the management of patients with burn injuries.

Results from the synthesis of included studies primarily indicate that perioperative feeding is both safe, in that there were no aspiration events, and also effective, in that the groups who received perioperative feeding consistently received higher Calorie intakes. There were however limitations in the quality, sample sizes and homogeneity of the included studies. The study limitations have impacted on the certainty of findings of this systematic review, which is outlined in the GRADE summary of findings table (Table 19).

A similar systematic review published by Pham et al. in March 2020 also concluded that intraoperative enteral nutrition in patients with burn injuries may improve nutritional intake without an increase in complications.[49] Although there were similarities between this systematic review and the publication by Pham et al. there are also substantial differences.[49] Firstly the systematic review by Pham et al. had no protocol published a-priori.[49] Pham et al.[49] included seven studies in their systematic review and five of these were the same as this systematic review.[34-37,52] Of the other two studies included in the systematic review by Pham et al.[49] but excluded here, one[31] was excluded during study selection because the assessors agreed it did not adequately meet inclusion criteria and only assessed patients for their first surgery. The other study[60] included by Pham et al.[49] was not burns-specific. The participants had non-specified trauma, necrotising soft tissue injury and incarcerated bowel but there was no mention of patients who had sustained burn injuries. The search limitations of this systematic review only included patients with a primary admission reason as an acute burn.

There were also other substantial differences between the systematic review by Pham et al. and this systematic review.[49] Pham et al. did not appraise the methodological quality of the included studies, or include a GRADE summary of findings but did briefly assess levels of evidence.[49] They also included the study by Varon et al. in meta-analysis however this systematic review excluded Varon et al.'s study from meta-analysis because the control and intervention were from different timeframes.[34] Pham et al.'s systematic review also lacked detailed analysis of confounding factors within studies, for example higher percentage of full thickness burns in control vs intervention.[49] This highlights the importance of defining a

robust research question, and defining inclusion and exclusion criteria, with transparent reporting in the systematic review process.

4.2 Impact of perioperative feeding in burns on mortality

Literature suggests that the mortality rate of burns patients has improved over time, due to research translation in many aspects of care including enteral nutrition, resuscitation protocols, improved infection control, early wound debridement and respiratory support.[61] A meta-analysis of RCT's in patients with major burns concluded early enteral nutrition reduces mortality and improves other key patient outcomes.[62] Continuation of enteral feeding during the perioperative period has the potential to influence mortality rate, since it potentially results in fewer enteral feeding deficits.[34-36]

There were three included studies which reported on mortality as an outcome measure.[34-36] One of these was a case series and since there was no comparator, nil conclusions could be made about the influence of intraoperative feeding on mortality in this patient group.[36] The other two studies had varying results. Jenkins et al. reported a higher mortality rate in the patients who had intraoperative and enteral feeding (5/40 in intervention compared to 4/40 in control).[35] Conversely, Varon et al. reported lower mortality in the patient group who received intraoperative enteral feeding compared with the patients who had enteral feeding withheld during surgical procedures (3/16 in intervention compared to 4/16 in control).[34]

There were major confounding factors in both of these studies which had the potential to influence results. The intervention group (intraoperative enteral feeding) in the study by Jenkins et al. had a higher percentage of full-thickness burns and more surgical procedures.[35] Research suggests greater full-thickness burn area and also the number of operative procedures are both risk factors for death in patients with burn injuries.[61,63] The confounding factor in the study by Varon et al. was the participants in the intervention group (intraoperative enteral feeding) were from a later timeframe compared to the group who experienced perioperative fasting.[34] The patients from the later timeframe may have had enhanced patient care and subsequently improved patient mortality rates. These confounding factors had the potential to influence the mortality rate outcomes, especially when looking at very small patient numbers.

If the mortality numbers of the RCT[35] and retrospective cohort study[34] are combined, there was a total of 16 deaths (eight in the control groups and eight in the intervention groups) out of 113 total participants. Neither study reported either a statistically significant difference in mortality or an ability to make any strong conclusions on the clinical impact of intraoperative feeding on burn patient mortality. Overall, it is impossible to make any conclusions regarding the effect of perioperative enteral feeding on mortality.

4.3 Impact of perioperative feeding in burns on wound infection

Wound infection in patients with burns is a serious problem because infections can cause a delay in epidermal maturation which leads to additional scar formation.[64] In addition, wound infections may result in systemic bacteraemia, sepsis and in severe cases, it can lead to multiple-organ dysfunction syndrome.[64] Mortality rates of patients with systemic infections in burns can be as high as 75%.[65] Literature suggests malnutrition is related to decreased wound tensile strength and increased wound infection rates.[66] Perioperative feeding has the potential to reduce wound infection rates, since fasting for theatre has been identified as one of the major causes of suboptimal nutrition in patients with burn injuries.[13,67,68]

There were three included studies which assessed wound infection rates of patients with burns who received post pyloric intraoperative feeding compared to those who experienced perioperative fasting.[34,35,37] These studies showed conflicting outcomes. Jenkins et al. reported fewer patients with wound infections in the intervention group (intraoperative feeding, 5.0% of patients) compared to control (perioperative fasting, 22.5% of patients).[35] Varon et al. also reported fewer wound infections in the intervention group who had intraoperative feeding (59% wound infection) compared to the control (75% wound infection).[34] In contrast, Imeokparia et al. reported a slightly greater wound infection rate in the intervention group (35.3% of patients who had intraoperative feeding) compared to the control (30.8% of patients who experienced perioperative fasting).[37]

Multiple confounding factors were identified in the studies, which could have influenced the outcome of wound infection. One potential confounding factor in the study by Jenkins et al. was the intervention group (patients who received intraoperative feeding) had substantially more antibiotic days compared to the control.[35] Antibiotics can be protective in treating underlying infections in burns, therefore the higher antibiotic days in the intervention group could have contributed to the reduced incidence of wound infections.[69] Another potential influence on outcome in the study by Jenkins et al. was the intervention group had a higher percentage of full-thickness burns.[35] Research into burn wound infection has reported patients with full-thickness burns can have higher wound colonisation than those with partial-thickness burns.[70] Even though the intervention group had fewer wound infections, compared to the control, it is theoretically possible a greater difference in wound infection rates could have been identified if both groups had comparable depths of burns.

An issue with the study by Varon et al. which may have influenced the results was the control and intervention groups were from different timeframes.[34] The control group timeframe was from 2008 to 2009, and the intervention group timeframe was from 2010 to 2013. Changes in

burn patient care over time, such as improved hygiene and wound infection preventative measures, could have resulted in fewer wound infections in the participant group from the later timeframe.

Imeokparia et al.'s study also had a substantial confounding factor. [37] The intervention group had a larger percentage TBSA burn, compared to the control group. A higher percentage TBSA burns has been associated with an increased risk of nosocomial infections in burns, therefore a potential reason for the higher wound infection in the patient group who received perioperative feeding is they had on average, larger burns.[70,71]

Overall, it is difficult to make any clear conclusions on the influence of perioperative enteral feeding on wound infections. There were small sample sizes and substantial confounding factors in each of the three included studies.[34,35,37] The range of results and low certainty of the effect of perioperative feeding on wound infections is reflected in the meta-analysis presented in chapter 3.

4.3 Impact of perioperative feeding in burns on length of stay

Burn patient management requires considerable financial resources, and length of stay has a substantial impact on cost.[72] Literature suggests there are many influences on length of stay of burns patients, most notably incidence of infection, wound depth, %TBSA and presence of inhalation injury.[73] Protocols aimed at reducing length of stay have included adequate nutrition support, early excision and grafting, a shift toward increasing outpatient management, and improved wound dressings.[72,74,75] Perioperative enteral feeding has the potential to improve the length of stay due to improvements in the adequacy of nutrition support. This potential influence of nutrition on length of stay should be viewed in the context of the many other factors which determine patients' length of stay.

Five of the included seven studies reported on length of stay,[34-37,52] however one of these studies[36] was a case series and no comment could be made on the influence on perioperative feeding on length of stay in this patient group.

There were three comparable studies which investigated post pyloric feeding being withheld during theatre compared to patients who received intraoperative post pyloric and included length of stay as an outcome measure.[34,35,37] The studies by Jenkins et al. and Imeokparia et al. found length of stay to be longer in patients who received intraoperative feeding and the study by Varon et al. found shorter length of stay in the group who received intraoperative feeding.[34,35,37] Only Imeokparia et al. found the differences in length of stay between the control and intervention groups were statistically significant. [37]

All of these studies however had substantial confounding factors which could potentially influence the patients' length of stay. The intervention group in the study by Jenkins et al. could have had a longer length of stay because this group had a higher percentage of full thickness burns and more surgical procedures compared to the control.[35] Similarly, the patients in the intervention group in the study by Imeokparia et al. had a larger %TBSA burn compared to the control, which could have influenced the intervention group's length of stay.[37] Varon et al.'s group who received intraoperative feeding and had a shorter length of stay were from a later timeframe compared to the control group.[34] Improvements in patient care and procedures over time have the potential to also contribute to shorter length of time in the group from the later timeframe.

The final included study which reported on length of stay was by Carmichael et al.[52] This research investigated mechanically ventilated patients who had enteral feeding (either intragastric or post pyloric) withheld for >50% of surgeries and compared them with patients who had enteral feeding (either intragastric or post pyloric) feeding continued for ≥ 50% of surgeries. Carmichael et al. reported the mean length of stay in the patient group who had enteral feeding continued for ≥50% of surgeries (intervention group) to be 27 days shorter than the group who had feeding withheld for >50% of surgeries (control group).[52] This study did not have major confounding factors identified between the control and intervention groups.

Overall, the varying results relating to the role of perioperative enteral feeding on length of stay make it difficult to come to any definitive conclusions. The meta-analysis (Figure 3) presented in chapter 3 also reflects conflicting evidence on the influence of intraoperative feeding versus fasting on length of stay. There were many confounding factors in the studies, along with small patient numbers and literature reports there are many potential influences on length of stay. A large-scale RCT would potentially ameliorate the challenges faced with small sample sizes and heterogeneous populations.

4.4 Impact of perioperative feeding in burns on aspiration events

One of the most clinically important results highlighted in this systematic review was the impact of perioperative feeding on aspiration events. There were no aspiration events reported in any of the studies.

Traditionally, fasting for theatre has been implemented to protect patients from aspiration events during theatre.[76] Pulmonary regurgitation of gastric contents carries with it morbidity and mortality risk.[77] Recent research has however questioned the effectiveness of extended fasting before theatre. A systematic review by Brady, Kinn and Stuart found patients given a

drink of water two to three hours preoperatively had significantly lower volume of gastric contents than the groups following a standard "fasting from midnight" regime.[26] The optimum preoperative length of time to avoid solid food remains debated however many countries have established fasting guidelines. The American Society of Anesthesiologists recommends fasting from the intake of a light meal for 6 or more hours before elective surgery and avoidance of a fatty meal for 8 hours preoperatively for adults.[17] The European Society of Anaesthesiology has similar recommendations of nil solid food for 6 hours before elective surgery in adults and children but carbohydrate-rich drinks can be consumed up to 2 hours before surgery.[78] Australian fasting guidelines are consistent with those from USA and Europe[17] of limited solid food for up to 6 hours prior to anaesthesia and clear fluids being allowed up to two hours prior to anaesthesia. None of these guidelines however discuss the recommendations of liquid enteral feeding prior to surgery. A potential reason for the absence of enteral feeding from guidelines could be the overwhelming lack of research and evidence on the topic. Research relating to post pyloric enteral feeding during surgery appears to be limited to burns. No other research was identified which reported on intraoperative feeding in non-burns patients. The limitations of research regarding the optimal fasting time to reduce aspiration risk in enterally fed patients are reflected in a paper by Segaran et al. who identified that there is a "lack of research on gastric emptying times for enteral nutrition in intubated critically ill patients, and as a consequence, there is no recognised guidance on the length of time that should elapse between stopping enteral nutrition and commencing anaesthetic procedures" (page 38).[79]

There were six out of the seven included studies in this systematic review which included aspiration as an outcome measure. Four of these studies had patients who received post pyloric enteral feeding during theatre.[34-37] One of the included studies included patients who received both intragastric and post pyloric feeding during theatre but their patient population was mechanically ventilated and had a previously secure airway.[52] Only one study had patients who underwent short fasting (enteral feeding until 2 hours prior to surgery) and had intragastric enteral feeding tubes.[38] If the patient numbers are totalled from the studies which had patients who received post pyloric intraoperative enteral feeding (Jenkins et al.,[35] Imeokparia et al.,[37] Varon et al.[34] and Carmichael et al.[52]) then overall, 509 patients received enteral feeding during surgery and nil had aspiration events. The results from the included studies indicate enteral feeding during surgery did not cause any acute adverse events in any of the three different methods of perioperative feeding (i.e. intraoperative post pyloric feeding, intraoperative intragastric or post pyloric feeding in ventilated patients, or short fasting in patients receiving intragastric feeding).

There was some diversity in the definition of aspiration, as noted in the results section. A lack of consistency in aspiration definition has the potential to reduce the reliability of the results but since there were no reported aspiration events, the influence of the diverse aspiration definitions is unlikely to be substantial. Although there were diagnostic differences between studies when identifying aspiration, there was overwhelming evidence of the safety of intraoperative feeding.

4.5 Impact of perioperative feeding in burns on pneumonia

There are many risk factors for pneumonia in burns patients. Chan et al. identified burn patients' risk factors for pneumonia to include inhalation injury, a higher %TBSA burn, face and neck burns and aged over 65 years.[80] Intraoperative gastric aspiration is also a known risk factor for pneumonitis and pneumonia.[81,82] Increased risk of anaesthesia-related aspiration can occur in patients with decreased lower oesophageal sphincter tone (can be caused by medications such as propofol, opioids, thiopental and atropine), obesity, previous oesophageal surgery, presence of oesophageal cancer, inadequate preoperative fasting, gastrointestinal obstruction and presence of a hiatus hernia.[82] Pneumonia in patients with burn injuries can therefore be due to a complex relationship between injury and risk factor.

Only two of the included studies clearly reported on pneumonia as an outcome measure.[34,35] Of some concern is both of the studies reported higher rates of pneumonia in the patient groups who received intraoperative post pyloric enteral feeding. Although there was an observed increase in pneumonia in the groups who received intraoperative feeding, in raw numbers the difference was small with 34% of the combined control groups reporting pneumonia and 44% of the combined intervention groups reporting pneumonia. The observed higher rate of pneumonia in the groups who received intraoperative post pyloric feeding is an important outcome to be aware of, but since nil aspiration events occurred in these groups, a definitive relationship between intraoperative feeding and increased incidence of pneumonia was not evident in these two studies.

One other study, by Imeokparia et al. eluded to reporting on pneumonia by stating "no perioperatively fed patients were documented to neither have persistent cough nor receive an increase in supplemental oxygen following recovery from the post anaesthesia care unit" (page 347).[37] The previous statement was considered to be insufficient to be diagnostic for pneumonia within this particular systematic review.

Of interest, is the similar systematic review by Pham et al.[49] did use the statement by Imeokparia et al.[37] of nil cough or increased post-operative oxygen as indicative for nil

pneumonia. As a result, Pham et al's.[49] systematic review reported there was nil pneumonia in either the control or intervention groups in the study by Imeokparia et al.[37]

4.6 Impact of perioperative feeding in burns on Calorie delivery

There is a wealth of literature of the importance of adequate nutrition in burns. Nutritional support is documented to preserve lean body mass, promote wound healing, reduce bacterial translocation of the gut, enhance immunologic defences, reduce the incidence of Curling's ulcers, reduce catecholamine levels and reduce mortality.[7-9] Similarly, literature indicates if burns patients are underfed, they have increased loss of lean body mass, a progressive decline of host defences, increased length of stay and increased mortality.[83] Adequate nutrition is evidently very important in burns patients but literature is scant as to whether moderate Calorie deficits associated with surgical procedures also impacts patient outcomes.

The impact of either short fasting or intraoperative feeding on Caloric intake was measured in five of the included studies.[34,35,37,38,52] There were substantial methodological differences between studies as to how they presented Caloric intake and Calorie deficits. Despite these differences, the consistent similarity was that all five of the studies identified increased Caloric delivery in the intervention groups (received either short fasting, or intraoperative post pyloric feeding).

The results from this systematic review clearly demonstrated that patients who receive either short fasting or intraoperative feeding have improved Caloric provision. There are potential clinical benefits of increased nutrition associated with either short fasting or intraoperative feeding. The flow-on effect of enhanced perioperative Caloric provision to provide clinical benefit warrants further research and investigation.

4.7 Impact of perioperative feeding in burns on ventilator days

Burns patients may require mechanical ventilation if they cannot maintain an airway or adequate oxygenation or ventilation. The predisposing factors for burns patients to require mechanical ventilation include inhalation injury, infection, sepsis, heart failure and fluid overload.[84]

There is limited research on the effect of enteral feeding on ventilator days in burns patients. One 15-year retrospective cohort study by Pantet et al. found prolonged ventilator time in patients with major burns who intentionally received a reduced energy prescription compared to other patient groups.[10] This study however could not demonstrate a direct causal

relationship between energy provision and ventilator days. Another multicentre prospective study by Mosier et al. reported length of mechanical ventilation similar for burns patients in their study who received early enteral feeding compared to late enteral feeding.[85] Overall, there are many factors that influence ventilator days in patients with burn injuries. Adequate nutrition has the potential to influence time required for ventilatory support however there is a lack of burns-specific research data on this topic.

There is marginally more research data on the clinical influence of either energy balance or nutritional status on ventilator days in general intensive care critically ill patients. Dvir et al. investigated the relationship between negative energy balance and complications in critical illness.[86] They reported negative energy balance was not correlated with the length of mechanical ventilation in their patient population. In contrast, Grippa et al. conducted a prospective cohort study of critically ill children receiving mechanical ventilation and reported a strong association between nutritional status on admission and duration of mechanical ventilation.[87] Similarly, Moisey et al. found sarcopenia (but not BMI) was associated with increased time on mechanical ventilation in their elderly ICU population.[88]

Although there is limited research on the impact of perioperative feeding on mechanical ventilation times in burns patients, the information gathered from research in other areas of critical illness suggests malnutrition may increase ventilation days. Enteral feeding helps prevent malnutrition in patients otherwise unable to consume an oral diet. There is insufficient evidence of the relationship between closely meeting estimated nutritional needs (e.g. reduced fasting due to perioperative feeding) on ventilator days in critically ill burn patients.

Four of the included studies reported on the number of days patients received ventilatory support but there were conflicting results on the relationship between perioperative feeding and ventilator days. Of the three studies which compared the outcomes of enteral feeding being withheld during surgery (control) to intraoperative post pyloric enteral feeding during surgery (intervention), Jenkins et al. and Varon et al. reported fewer ventilator days in the intervention group whereas Imeokparia et al. reported more ventilator support days in the intervention group.[34,35,37] Potential confounding factors of these studies are similar to those discussed earlier, specifically Jenkins et al. had patients with a higher percentage of full thickness burns in the intervention group, Varon et al.'s patients in the intervention group were from a later timeframe and Imeokparia et al. had a higher % TBSA burn in the intervention group compared to the control.[34,35,37]

The study by Carmichael et al. reported on ventilated burns patients who had enteral feeding (either intragastric or post pyloric) withheld for > 50% of surgeries compared to those who

had feeding continued for ≥50% of surgeries.[52] Carmichael et al. identified a trend towards a reduction in ventilator days in the intervention group, where enteral feeding was continued for ≥50% of surgeries.[52]

As there were conflicting results on the relationship between enteral feeding and ventilator support days, along with the range in outcome measures and the heterogeneity of the included studies, it is not possible to make any conclusions relating to the impact of perioperative feeding on days burns patients require ventilator support from the included studies.

4.8 Impact of perioperative feeding in burns on wellbeing measures

There was one included study which investigated patient wellbeing which was a case report, and it therefore received low scores during critical appraisal.[58] Despite the low-quality rating of this study, it highlights an important but often overlooked aspect of burn patient care. Sutanto et al. demonstrated nil preoperative hunger and thirst when the patient received enteral feeding up until 90 minutes, 225 minutes and 95 minutes respectively.[58] In contrast, the patient experienced preoperative hunger and thirst when they had an extended fast of oral diet withheld for 14 hours 45 minutes prior to surgery. In addition, Sutanto et al. found their patient had increasing postoperative nausea, vomiting, malaise and fatigue, as total fasting time increased.[58]

The findings from this case report of a patient with a major burn are consistent with those found in research in other surgical patients. Although there is limited research regarding the impact of reduced fasting on wellbeing in patients with burn injuries, there has been extensive research relating to the provision of carbohydrate-rich drinks just prior to general surgery. A systematic review conducted by Bilku et al. reported "preoperative carbohydrate drinks improved patient wellbeing after surgery significantly, especially hunger, thirst, malaise, anxiety and nausea" (page 21).[18] Similarly, the systematic review conducted by Noba and Wakefield found perioperative carbohydrate drinks had a substantial positive effect on "postoperative discomfort especially: nausea, vomiting, hunger, thirst, dry mouth, weakness, tiredness, malaise, fatigue, anxiety and depression" (page 3113).[89]

Unfortunately, the lack of burns-specific research on the impact of either short fasting or intraoperative post pyloric feeding on burn patient wellbeing results in an inability to make definitive recommendations but, based on current literature, it does seem likely that reducing fasting times in burns patients and providing either preoperative enteral nutrition or carbohydrate drinks closer to surgery could improve the patient's thirst, hunger, nausea, vomiting, malaise and fatigue.

4.9 Impact of perioperative feeding in burns on other outcome measures

There were many other secondary outcomes reported within the included studies, however most were only measured in one of the studies.

Results from one study indicated that the intervention group required less supplemental albumin and had shorter length of stay per percentage of third-degree burn and less bacteraemia. [35] The same study by Jenkins et al. also found the intervention group had more mean antibiotic days, and more patients with clinical sepsis.[35] There were conflicting outcomes with respect to ICU days with one study showing their intervention group had more ICU days[37] and another study finding the intervention group had fewer ICU days.[34] Overall, there was no consistency as to whether intraoperative perioperative feeding improved the other secondary outcomes with any differences in outcome measures being small. Confounding factors in the studies such as intervention groups having either deeper burns, were from a later timeframe or had larger percentage of burns further decrease the certainty of any findings.

5. Impact of any assumptions and limitations

The primary assumption of this systematic review is the belief that the participant total body surface area (TBSA) burns were correctly calculated, for all included patients. Clinicians utilise a number of methods to estimate percentage of TBSA burn injury. These include: the Rule of Palm, the Rule of Nines and the Lund and Brower chart.[90] Literature reports conventional methods of estimating size of burn injury can be inaccurate, especially in the obese patient.[91,92] Although these methods of estimating burn size have the potential to be inaccurate, and are a potential shortcoming in this systematic review, there is no way to control the reported TBSA.

A limitation of this systematic review is that it only included patients with burn injuries and did not include similar groups, such as trauma and other ICU patients who received perioperative enteral nutrition. The rationale for limiting the inclusion criteria is based on the premise that patients with burns are a unique subset of critically ill patients and are at risk of a specific set of physiological responses and complications including hypothermia, compartment syndrome, inhalation injury, infection, hyperglycaemia and hypermetabolism.[93,94] A presumption has been made that other critically ill patients (for example those who have a primary diagnosis of respiratory failure or severe neurological disorder) experience a different clinical course compared to burns patients and were therefore excluded from this systematic review.

The decision to only include patients with a primary diagnosis of burns is in contrast to the systematic review conducted by Pham et al.[49] which included a publication where there was no direct mention of the participants having burn injuries but instead the participants had non-specified trauma, necrotising soft tissue injury and incarcerated bowel.[60] The participant characteristics in the publication by McElroy et al. did not meet the inclusion criteria for this systematic review and the exclusion of similar papers in the critically ill patient population has the potential to limit the results available to be presented.[60]

Another limitation of this review is only articles published in English were investigated. The exclusion of publications other than in English has the potential of introducing bias into the results. Research literature has however suggested no evidence of bias from the use of English-language restrictions in systematic reviews in medicine.[95] This limitation was therefore deemed as having inconsequential impact on the results of the systematic review.

One of the further limitations of this research was the exclusion of published conference abstracts. There were eight conference abstracts which were identified from the database searching and cross referencing, as initially meeting inclusion criteria.[96-103] Unfortunately, this author was unable to elicit sufficient details from each of the conference abstracts in order to include them in the systematic review. The list of excluded conference abstracts is provided in Appendix 6. Attempts were made to contact authors of the research published as conference abstracts but were unsuccessful in eliciting further details. If all of these eight conference abstracts had progressed to publication, there would have been a much larger data source of information. Consequently, some primary research could not be included in this systematic review, due to inadequate detail of the results.

It should also be noted that due to the small number of included studies, a decision was made to include studies for both adults and children and assess outcome measures as a combined group. It is possible the impact of perioperative nutrition has a different influence on outcomes for adults compared to children but an assumption was made that any influence would be small. If there were a greater number of included in the systematic review, then subset analysis could have been conducted but this was not possible with only seven included studies.

6. Implications for practice

The information generated as a result of this systematic review indicates that for patients receiving post pyloric enteral feeding, there is no evidence of increased risk of aspiration if enteral feeding is continued during surgery and continuation of post pyloric enteral feeding during surgery would likely facilitate improved Caloric delivery. Reduced fasting times in

patients with burn injuries may also help improve patient wellbeing measures. The certainty of evidence however was rated very low during GRADE analysis, due to high heterogeneity, low sample sizes and inconsistencies between the available primary research studies. As a result, any decision to continue post pyloric enteral feeding during surgical procedures should be made in consultation with the multidisciplinary burns team and with the respective anaesthetists.

An important clinical question, following on from this systematic review, is whether burns patients should routinely have a post pyloric feeding tube inserted, rather than an intragastric enteral feeding tube, to facilitate safe intraoperative feeding. One potential risk of routine post pyloric feeding is the insertion of nasoduodenal/nasojejunal feeding tubes being more difficult and may take longer, therefore impeding the efficient commencement of enteral feeding. There is some research which supports this view. A systematic review by Marik and Zaloga concluded that time to initiate enteral nutrition was substantially shorter in the patients who received gastric feeding compared to those who received post pyloric feeding in critically ill medical, neurosurgical and trauma patients admitted to ICU.[104] Early enteral nutrition for burns patients is currently consistent with guidelines therefore routine post pyloric feeding, if it results in delays, may not be in the best interests of patient care.

A dilemma for clinical practice is how best to overcome the loss of nutrition of approximately 12% of estimated energy requirements associated with burns patients fasting for surgery.[16] This research has identified perioperative post pyloric enteral feeding to be a safe and effective method for minimising the nutrient deficits associated with fasting for surgery. Other research has suggested the caloric deficits could be addressed by using a "catch-up" protocol, where 24-hour volumes are targeted rather than enteral feeding at a typical hourly rate. Pham et al. found a post-operative catch-up protocol in their ventilated patients with burn injuries (n=41) eventuated in patients meeting 80% of their prescribed calories perioperatively, 69% of the time.[105] It is not within the scope of this systematic review to determine whether post pyloric intraoperative feeding compared to "catch-up" protocols are more beneficial than the other.

This systematic review was unable to conclusively answer the clinical questions of what the optimum feeding/fasting regime is for patients with burn injuries. There was insufficient evidence to demonstrate superior patient outcomes (e.g. mortality, wound infection, length of stay, ventilator days and pneumonia) of either:

- the traditional fast from midnight before surgical procedures, or
- provision of clear fluids up until 2 hours before surgery, or
- short perioperative fasting times in patients receiving intragastric enteral feeding or

- intraoperative post pyloric enteral feeding (either post pyloric or intragastric in mechanically ventilated patients).

No research could be found which investigated a relationship between perioperative clear fluids and outcomes of patients with burn injuries. Although there is very limited burns-specific literature, other research has reported that the provision of oral carbohydrate up to 2 hours prior to surgery may improve patient wellbeing, insulin resistance and glycogen stores. In the absence of burns-specific research, similarities may be drawn but cannot be conclusive until research is conducted which includes patients with burn injuries in the intervention population.

7. Implications for research

This systematic review highlighted the lack of large-scale quality research relating to the effectiveness of perioperative feeding in burns. Burns research can be challenging since populations of major burns are often small and management can vary between individual healthcare facilities and also between countries. Small sample sizes will likely cause a weak effect estimates, especially when considered with a large number of confounders. Control of confounding factors can be performed by methods such as stratification, standardisation, multivariable regression analysis and propensity score.[106]

A recommendation as a result of this systematic review is to conduct a large-scale multi-centre, multi-national research project where patients are randomly allocated to receive either standard treatment or post pyloric perioperative feeding. Outcome measures should be clearly defined and consistent and validated tools should be utilised. Ideally, a range of outcomes could be measured including wellbeing, insulin resistance, wound infection, length of stay, mortality, pneumonia, aspiration events, ventilator days and Caloric intake.

Future research would ideally include wellbeing and insulin resistance since research relating has demonstrated the benefit of perioperative oral glucose provision in gastrointestinal surgical patients.[18,25] It is possible perioperative enteral feeding could also provide improved wellbeing and reduced insulin resistance in burns patients. A recommendation for future research is to include a validated measurement of patient wellbeing as part of the assessment and, if possible, also include assessment of perioperative feeding on insulin resistance as an outcome measure. The outcome measures of wellbeing and insulin resistance may be more sensitive indicators of the effectiveness and benefit of perioperative feeding compared to outcomes such as wound infection, mortality, length of stay, ventilator day and pneumonia.

8. Conclusion

This systematic review achieved the goal of synthesising the current evidence for the effectiveness and safety of perioperative enteral nutrition in patients with burn injuries. It has demonstrated intraoperative post pyloric enteral feeding is effective in providing patients with a higher Caloric intake compared to those who are fasted during the perioperative period. There was also clear evidence presented which consistently demonstrated the safety of post pyloric feeding during surgical procedures in patients with burn injuries. There was insufficient primary research available to report on the safety and effectiveness of short fasting compared to nil fasting when patient received perioperative intragastric feeding.

Some of the included studies indicated clinical benefit of post pyloric feeding on mortality, wound infection, length of stay and ventilator days, but alternatively some studies did not. Consequently, there is insufficient evidence to make a conclusion about any relationship between post pyloric feeding and enteral feeding on mortality, wound infection, length of stay and ventilator days. There was a trend towards increased pneumonia in patients who had post pyloric feeding however there were many confounding factors and small sample sizes which makes the finding highly uncertain. Patient wellbeing was improved with reduced perioperative fasting and consistent with what is reported in literature but the included case study did not score well during critical appraisal and therefore makes clinical conclusions difficult.

The reason for lack of clarity relating to the outcomes of length of stay, wound infection, pneumonia and ventilator days can at least in part be attributed to small sample sizes and heterogeneous populations in the included studies. Further high quality, large-scale research is needed to effectively answer the question as to the clinical impact of perioperative feeding in burns.

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98. Bolton D. Continuing enteral tube feeding in burn patients requiring surgery. J Burn Care Res 2018; 39: S164.
99. Collins J and Loning M. Preoperative npo status is not required in mechanically ventilated burn patients with enteral feeding access. J Burn Care Res 2015; 36: S75.
100. Maarouf R and Feldman MJ. Implementation of Continuous Enteral Feeding and Shortened Fasting Periods in the Perioperative Burn Patient. J Burn Care Res 2018; 39(suppl_1): S70-S70.
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104. Farber MS, Moses J and Korn M. Reducing costs and patient morbidity in the enterally fed intensive care unit patient. JPEN J Parenter Enteral Nutr 2005; 29(1 suppl): S62-69.
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10. Appendices

Appendix 1: Pubmed search strategy 02022019.

Pubmed

Burns [mh] OR	"enteral nutrition"[mh] OR	"perioperative period"[mh] OR
burn*[tw] OR	"nutritional support" [mh] OR	"perioperative care" [mh] OR
"thermal injur*"[tw]	"enteral nutrition"[tw] OR	intraoperative [tw] OR
	"enteric feeding" [tw] OR	per?operative [tw] OR
	"nutritional support"[tw] OR	"preoperative fasting" [tw]
	"naso?* feeding"[tw] OR	
	"enteral feeding"[tw]	

e.g. Search

((((Burns [mh] OR burn*[tw] OR "thermal injur*"[tw])) AND ("enteral nutrition"[mh] OR "nutritional support" [mh] OR "enteral nutrition"[tw] OR "enteric feeding" [tw] OR "nutritional support"[tw] OR "naso?* feeding"[tw] OR "enteral feeding"[tw])) AND (("perioperative period"[mh] OR "perioperative care" [mh] OR intraoperative [tw] OR per?operative [tw] OR "preoperative fasting" [tw]))

Search #	Query – 01/02/2019	Number of results
#1	Burns [mh] OR burn*[tw] OR "thermal injur*"[tw]	112 206
#2	"enteral nutrition"[mh] OR "nutritional support" [mh] OR "enteral nutrition"[tw] OR "enteric feeding" [tw] OR "nutritional support"[tw] OR "naso?* feeding"[tw] OR "enteral feeding"[tw]	50 037
#3	"perioperative period"[mh] OR "perioperative care" [mh] OR intraoperative [tw] OR per?operative [tw] OR	330 960

	"preoperative fasting" [tw]	
#4	#1 and #2 and #3	65
	Remove duplicates	65

Appendix 2: Embase search strategy 02022019.

Burn/exp OR	“enteric feeding”/exp OR	“perioperative period”/exp OR
burn*	“nutritional support”/exp OR	“perioperative car*”/exp OR
	“nose feeding”/exp OR	intraoperative OR
	“enteral nutrition” OR	per?operative OR
	“enteric feeding” OR	“preoperative fast*”
	“nutritional support” OR	
	“nasogastric feeding” OR	
	“nasojejunal feeding” OR	
	“enteral feeding”	

Search #	Query 01/02/2019	Number of results
#1	'burn'/exp OR burn	99 018
#2	'enteric feeding'/exp OR 'nutritional support'/exp OR 'nose feeding'/exp OR 'enteral nutrition' OR 'enteric feeding' OR 'nutritional support' OR 'nasogastric feeding' OR 'nasojejunal feeding' OR 'enteral feeding'	57 257
#3	'perioperative period'/exp OR 'perioperative car*' OR intraoperative OR per?operative OR 'preoperative fast*'	301 861
#4	#1 AND #2 AND #3	42
	Remove duplicates	42

Appendix 3: CINAHL search strategy 02022019

SU burns OR	SU “enteral nutrition” OR	SU“perioperative care” OR
TX burn*	SU “nutritional support” OR	TX intraoperative OR
	TX “enteral nutrition” OR	TX per?operative OR
	TX “enteric feeding” OR	TX “preoperative fast*”
	TX “nutritional support” OR	
	TX “naso* feeding” OR	
	TX “enteral feeding”	

Search #	Query 01 02 2019	Number of results
#1	SU burns OR TX burn*	105 965
#2	SU “enteral nutrition” OR SU “nutritional support” OR TX “enteral nutrition” OR TX “enteric feeding” OR TX “nutritional support” OR TX “naso* feeding” OR TX “enteral feeding”	20 103
#3	SU“perioperative care” OR TX intraoperative OR TX per?operative OR TX “preoperative fast*”	194 034
#4	#1 and #2 and #3	230
	Remove duplicates	229

Appendix 4: Web of Science search strategy 02022019

TS=Burn* OR	TS =“enteral nutrition” OR	TS=“perioperative period” OR
TS= “thermal injur*”	TS =“nutritional support” OR	TS= “perioperative care” OR
	TS =“enteral feeding” OR	TS= intraoperative OR
	TS=“enteric feeding” OR	TS= per?operative OR
	TS= “naso?* feeding”	TS=”preoperative fasting”

Search #	Query 02/02/2019	Number of results
#1	TS=Burn* OR TS= “thermal injur*”	206,492
#2	TS =“enteral nutrition” OR TS =“nutritional support” OR TS =“enteral feeding” OR TS=“enteric feeding” OR TS= “naso?* feeding”	18 640
	TS=“perioperative period” OR TS= “perioperative care” OR TS= intraoperative OR TS= per?operative OR TS=”preoperative fasting”	164 076
#4	#1 and #2 and #3	15

Appendix 5: All other searches 02022019.

Cochrane Central Register of Controlled Trials

Perioperative nutrition burns

Results = 4 (one potential trial, 2 articles I already have, one irrelevant result).

clinicaltrials.gov (US Clinical Trials Register),

Search: perioperative nutrition burn = 1 result, terminated trial

Burn enteral = 8 results, one potential completed trial but no results published: a study on nutrition support in adult patients with severe burns.

www.anzctr.org.au (Australian and New Zealand Clinical Trials Register),

2 results "burns enteral" but nil relevant.

4 results "burns nutrition" but nil relevant.

www.clinicaltrialsregister.eu (European Clinical Trials Register),

1 result "burns nutrition"

2 results "burns enteral"

Nil relevant.

Mednar (Mednar.com) = 26 results, 4 relevant but I already had them. None sent to endnote.

Search perioperative enteral feeding in burns.

SumSearch 2, 8 results "burns perioperative enteral feeding" 4 studies relevant but I had them. None sent to endnote.

ProQuest Dissertations and Theses Global

https://search-proquest.com.proxy.library.adelaide.edu.au/pqdtglobal/results/A9175A74ED864A98PQ/1?accountid=8203#

searched Burns (Title) AND Perioperative (anywhere) AND nutrition (anywhere)= 7 results, one potential. All 7 exported to EndNote.

Google Scholar

https://scholar.google.com.au/scholar?hl=en&as_sdt=0%2C5&q=burn+perioperative+nutrition&oq=b

21 000 results. First 3 pages scanned. Nil new relevant papers could be found. After 3 pages the topics varied widely and it was determined unlikely to find anything new and relevant.

OpenGrey

http://www.opengrey.eu/search/request?q=burns+nutrition

4 irrelevant results

OpenDOAR http://v2.sherpa.ac.uk/opendoar/

– searched "burn" and "nutrition". One completely irrelevant result. No results for burns enteral feeding or burns perioperative nutrition.

Openthesis.org

http://www.openthesis.org/search

searched burn perioperative nutrition. 39 irrelevant results.

WHO International Clinical Trials Registry Platform (ICTRP) http://www.isrctn.com/

Searched "Burns" and got 34 results, nothing relevant.

Latin American and Caribbean Health Sciences Literature (LILACS database) searched burn AND perioperative AND nutrition. 199 results, nothing new.

AllTrials – nothing came up.

Appendix 6: Excluded articles and reasons for exclusion.

Citation (N=46)	Reason for Exclusion
1. Andel D, Kamolz LP, Donner A, Hoerauf K, Schramm W, Meissl G, et al. Impact of intraoperative duodenal feeding on the oxygen balance of the splanchnic region in severely burned patients. Burns 2005; 31(3): 302-305.	Intervention: Exclude due to only looks at first burns surgery. Does not include information about entire burns admission.
2. Atkins A and Phillips W. Delivery of Enteral Nutrition Improved After Transition to Closed Enteral Feeding System. MEDSURG Nursing 2015: 14-15.	Population: does not specifically look at burns patients.
3. Bengmark S, Andersson R and Mangiante G. Uninterrupted perioperative enteral nutrition. Clin Nutr 2001; 20(1): 11-19.	Population: does not specifically looking at burns patients
4. Bittner EA, Shank E, Woodson L and Martyn JAJ. Acute and perioperative care of the burn-injured patient. Anesthesiology 2015; 122(2): 448-464.	Intervention: doesn't look at perioperative enteral nutrition
5. Bolton D. Continuing enteral tube feeding in burn patients requiring surgery. Journal of Burn Care and Research 2018; 39: S164.	Conference abstract. Email sent to author 21/01/19 but no reply.
6. Boswick JA, Jr., Thompson JD and Kershner CJ. Critical care of the burned patient. Anesthesiology 1977; 47(2): 164-170.	Intervention: Does not talk about perioperative enteral feeding.
7. Buchanan RT and Levine NS. Nutritional support of the surgical patient. Ann Plast Surg 1983; 10(2): 159-166.	Population and Intervention: does not talk about either perioperative nutrition or burns patients
8. Carmichael H, Joyce S, Smith T, Patton L, Wagner A and Wiktor AJ. Safety and efficacy of intraoperative gastric feeding during burn surgery. Journal of Burn Care and Research 2018; 39: S30.	Conference abstract (university of Colorado, Denver). Full published article in included studies.
9. Clark DK and Marvin M. The development of an evidence-based postoperative nausea and vomiting protocol in the perioperative setting. Critical Care Nurse 2009; 29(2): e23-24.	Population and Intervention: does not include either perioperative nutrition or burns patients
10. Collins J and Loning M. Preoperative npo status is not required in mechanically ventilated burn patients with enteral feeding access. Journal of Burn Care and Research 2015; 36: S75.	Conference abstract. Insufficient information. Attempted to contact author – could not find contact email. May need to revisit.
11. Cooper A, Jakobowski D, Spiker J, Floyd T, Ziegler MM and Koop CE. Nutritional assessment: an integral part of the preoperative pediatric surgical evaluation. J	Conference abstract. Exclude based on no mention of burns.

Pediatr Surg 1981; 16(4 Suppl 1): 554-561.	
12. da Silveira GRM and Coutinho ESF. Re. More research needed in quality, quantity and timing of enteral formulas for the acutely ill. Nutrition 2014; 30(2): 240-241.	Letter the editor. Intervention: Comment on immunonutrition, not perioperative feeding.
13. Farber MS, Moses J and Korn M. Reducing costs and patient morbidity in the enterally fed intensive care unit patient. Journal of Parenteral and Enteral Nutrition 2005; 29(1): S62-S69.	Conference abstract. Intervention: Not burns-specific. Looks at immunonutrition, not perioperative nutrition.
14. Fischer C, Jenkins M, Gottschlich M, Warden G and McCall J. Perioperative enteral nutrition in the pediatric burn patients. Anesthesiology 1995; 83(3A): A1164-A1164.	Conference abstract. It appears same authors and topic from included published study.
15. Harbin KR and Norris TE. Anesthetic Management of Patients With Major Burn Injury. AANA Journal 2012; 80(6): 430-439.	Intervention: does not mention perioperative enteral feeding in burns.
16. Howard L and Ashley C. Nutrition in the perioperative patient. Annual Review of Nutrition 2003; 23(1): 263-282.	Intervention: does not talk about perioperative nutrition.
17. Huckleberry Y. Nutritional support and the surgical patient. American Journal of Health-System Pharmacy 2004; 61(7): 671-684.	Population: does not discuss burns.
18. Jethon J. [Progress in the treatment of burns]. Pol Tyg Lek 1990; 45(47-48): 943-945.	Language: not in English.
19. Kahn AM, Kross ME and Geller FM. Feeding gastrostomy for the severely burned patient. Arch Surg 1984; 119(11): 1316-1317.	Intervention: does not talk about perioperative nutrition.
20. Kefer S, Stannard D, Tarrac S, Tuthill N, Stein P, Bryan DN, et al. Reviews. Aorn J 2010; 91(3): 413-420.	Is a book review. Does not discuss the topic.
21. Khandelwal A, Aliotta R, Walfish A and Lovich-Sapola J. Impact and safety of a multidisciplinary burn perioperative fasting guideline. Journal of Burn Care and Research 2016; 37: S211.	Conference abstract. Email sent to author 2/02/2019, no reply
22. Krzak A, Taylor S, Cherry-Bukowiec JR and Wang SC. Retrospective chart review of perioperative enteral nutrition and incidence of aspiration in adult, burn patients. Journal of Burn Care and Research 2015; 36: S154.	Conference abstract. Could not find author contact details. May need to revisit
23. Lown D. Use and efficacy of a nutrition protocol for patients with burns in intensive care. Journal of Burn Care and Rehabilitation 1991; 12(4): 371-376.	Intervention: does not talk about perioperative enteral feeding.
24. Lyons M, Clemens LHE and Gottschlich	Intervention: identifies causes of feeding stoppages

MM. Energy deficits associated with nasogastric feeding in patients with burns. Journal of Burn Care and Rehabilitation 2000; 21(4): 372-374+371.	but does not investigate perioperative feeding.
25. Maarouf R and Feldman MJ. Implementation of continuous enteral feeding and shortened fasting periods in the perioperative burn patient. Journal of Burn Care and Research 2018; 39: S70.	Conference abstract. Email sent to author, 11/10/2019 – no reply.
26. MacKay D and Miller AL. Nutritional support for wound healing. Alternative Medicine Review 2003; 8(4): 359-377.	Intervention: talks about vitamins etc involved in wound healing but not burns perioperative feeding.
27. Maniatis K and Smith K. Optimal nutrient delivery: Strategies of a burn centre of excellence. Journal of Burn Care and Research 2016; 37: S264.	Conference abstract. Did not contact author due to intervention: unlikely to be of further benefit since it mostly talks about multiple different protocols improving overall outcomes and promoting best practice.
28. Medlin S. Nutrition for wound healing. British Journal of Nursing 2012: S11-15.	Participants and intervention: does not talk about perioperative nutrition in burn.
29. Mehta NM. The Quest to Preserve Muscle Mass - Lessons from Pediatric Burn Injury. Pediatr Crit Care Med 2017; 18(12): 1186-1187.	Intervention: does not investigate perioperative nutrition.
30. Mizock BA and Sriram K. Perioperative immunonutrition. Expert Review of Clinical Immunology 2011; 7(1): 1-3.	Editorial. Population: not burns-specific.
31. Musselius IS, Mikhel'son VA, Stepanenko SM, Beliaeva ID, Lazarev VV and Popova TS. Nutritional therapy in children during perioperative period. Anesteziol Reanimatol 2004; (1): 42-46.	Population: gastrointestinal pathologies, not burns.
32. Pham CH, Collier ZJ and Gillenwater J. How long are burn patients really npo in the perioperative period and can we effectively correct the caloric deficit using an enteral feeding "catch-up" protocol? Journal of Burn Care and Research 2018; 39: S21.	Conference abstract. Intervention and outcome: Does not look at perioperative feeding and their outcomes but rather investigates catch-up protocol to correct deficiencies.
33. Powers J. Guidelines for Preoperative Fasting for Hospitalized Patients. Alisa Veijo, California: American Association of Critical-Care Nurses; 2017. pp. 90-92.	Population: does not specifically look at burns patients and more of a guideline but does make some good points.
34. Rauen CA, Chulay M, Bridges E, Vollman KM and Arbour R. Seven evidence-based practice habits: putting some sacred cows out to pasture. Critical Care Nurse 2008; 28(2): 98-118.	Population: not burns patients. Also off topic. Just looks at things commonly done incorrectly.
35. Rimdeika R, Gudaviciene D, Adamonis K,	Intervention: does not look at perioperative nutrition.

Barauskas G, Pavalkis D and Endzinas Z. The effectiveness of caloric value of enteral nutrition in patients with major burns. Burns 2006; 32(1): 83-86.	
36. Rochlin DH, Sheckter C, Moshrefi S, Schenone M, Vargas V, Sproul J, et al. Volume vs. rate-based tube feeding in burn patients: Improving nutrition. Journal of Burn Care and Research 2018; 39: S177.	Conference abstract. Intervention: does not look at perioperative feeding. No need to investigate further.
37. Rose DD and Jordan EB. Perioperative management of burn patients. Aorn J 1999; 69(6): 1211-1222; quiz 1223-1230	Intervention: does not investigate perioperative feeding.
38. Shelley C, Regier B, Hendren G, Howard J, Ballew A and Reynolds J. Enteral nutrition and aspiration events in patients placed prone for burn surgery: An academic institutional review. Journal of Burn Care and Research 2018; 39: S90.	Conference abstract. Looks at prone intraoperative feeding. Email sent to author 21/01/2019 but no reply.
39. Shields BA, Brown JN, Aden JK, Salgueiro M, Mann-Salinas EA and Chung KK. A pilot review of gradual versus goal re-initiation of enteral nutrition after burn surgery in the hemodynamically stable patient. Burns 2014; 40(8): 1587-1592.	Intervention: does not specifically look at perioperative feeding but rather re-initiation of goal enteral feeding rate post theatre.
40. Sunderman C, Gottschlich M, Allgeier C, James L and Warden G. Safety and efficacy of intraoperative nutrition support in a pediatric burn unit. Journal of Burn Care and Research 2016; 37: S92.	Conference abstract. Published full article included in studies.
41. Suter PM. [Posttraumatic and postoperative catabolism: protein metabolism]. Internationale Zeitschrift fur Vitamin- und Ernahrungsforschung Beiheft 1979; 18: 119-123.	Population and intervention: does not look at perioperative feeding in burns.
42. Thakkar R, Giles S, Capello T and Fabia R. Safety and efficacy of uninterrupted perioperative enteral feeding in pediatric burn patients. Journal of Burn Care and Research 2016; 37: S208.	Conference abstract. Attempted to contact author but could not find email address. May need to recheck
43. Thomas JM and Bester K. Paediatric burns anaesthesia: The things that make a difference. Southern African Journal of Anaesthesia and Analgesia 2014; 20(5): 190-196.	Intervention: does not look at perioperative feeding.
44. Williams FN, Branski LK, Jeschke MG and Herndon DN. What, How, and How Much Should Patients with Burns be Fed? Surg Clin North Am 2011; 91(3): 609-629.	Intervention: a good article on the metabolic effects of burns but does not talk about perioperative feeding.
45. Wilmore DW. Postoperative protein sparing. World J Surg 1999; 23(6): 545-552.	Intervention: doesn't talk about perioperative feeding.

46. Wu YW, Liu J, Jin J, Liu LJ and Wu YF. [Effects of early enteral nutrition in the treatment of patients with severe burns]. Zhonghua Shao Shang Za Zhi 2018; 34(1): 40-46.	Intervention: talks about early enteral feeding but not perioperative feeding.
47. Buescher T, Becker WK, McManus WF, Bruitt BA. Perioerative enteral feeding. Proceedings from the American Burn Association 1990; 22: 162.	Found from reference cross check. Conference abstract only and not burns specific.