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Normal Versus Hypocaloric Feeding Outcomes in Septic Critically Ill Adults: A Systematic Review

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Abstract

Sepsis is a life-threatening condition characterized by a dysregulated immune response to infection, resulting in organ dysfunction, increased nutritional requirements, and potential mortality. In critically ill adults, nutritional management typically involves hypocaloric or normocaloric feeding. This systematic review synthesized evidence from 19 studies to assess the effects of these feeding strategies on mortality, length of stay (LOS), and glycemic control. Overall, no consistent differences in mortality were observed, although some subgroup analyses suggested context-specific benefits. Hypocaloric feeding was more consistently associated with shorter LOS and improved glycemic control, potentially due to reduced metabolic stress and better feeding tolerance. However, heterogeneity in study design, caloric targets, timing of nutrition initiation, insulin protocols, and patient populations limited the strength of conclusions. Current guidelines from ASPEN, SSCM, and ESPEN provide broad recommendations, emphasizing individualized nutrition, though evidence to support precise caloric targets remains insufficient. Hypocaloric feeding appears safe and may offer LOS and glycemic control benefits, though its impact on mortality remains unclear. Nutrition management should consider patient-specific comorbidities, illness severity, and baseline nutritional status. Further research with standardized protocols and varied patient populations

is needed to optimize feeding strategies in critically ill adults with sepsis.

Keywords: sepsis, critical illness, enteral nutrition, normocaloric feeding, hypocaloric feeding, caloric restriction, glycemic control, mortality

1. Introduction

Sepsis is a life-threatening medical condition resulting from a dysregulated and excessive immune response to infection (Cao et al., 2023). When microbes invade urine, blood, skin, the lungs, or other tissues, the immune system releases a surge of chemicals into the bloodstream triggering inflammation, or widespread cellular injury throughout all body tissues (Heming et al., 2021). If the immune response becomes uncontrolled, normal blood function is disrupted, which can lead to life-threatening complications (Bennett, 2015).

Severe sepsis can result in serious organ damage, including damage to the kidneys and liver (National Institutes of Health [NIH], 2014.). Septic shock, a critical condition characterized by a sudden and profound drop in blood pressure during the immune system response to infection, can lead to inadequate blood flow and oxygen delivery to vital organs (NIH, 2014.) Prolonged deprivation of blood and oxygen can cause severe organ failure, potentially necessitating amputations and increasing the risk of mortality (Taghavi et al., 2025).

The term *sepsis* originates from the Greek word *sepein*, meaning “to rot”, and was first documented in the poems of Homer over 2700 years ago (Chang et al., 2010). Although sepsis is commonly referred to as “blood poisoning,” sepsis does not actually involve poison in the bloodstream. (NIH, 2014). Instead, sepsis is the body’s dysregulated and extreme immune response to an infection, which can lead to widespread inflammation, tissue damage, organ failure, and even death (NIH, 2014). In the United States, sepsis occurs in approximately 1 to 2% of all hospitalizations, which amounts to at least 750 000 cases annually and healthcare costs exceeding 20 billion dollars every year (Balch, 2023). Roughly 80% of sepsis-related deaths could be prevented with timely intervention, as each hour of delayed treatment increases mortality risk by 4 to 9% (Balch, 2023).

Sepsis places the body under considerable physiological stress due to potential organ dysfunction, a hypermetabolic state, and an exaggerated immune response (Wischmeyer, 2018). As a result, individuals with sepsis have increased nutritional requirements (Wischmeyer, 2018). While adequate nutritional support is essential to preserve muscle mass, facilitate recovery, and support immune function, meeting a patient’s full energy needs, referred to as normocaloric feeding, may increase the risk of complications such as overfeeding and hyperglycemia (Wischmeyer, 2018).

Hypocaloric feeding, also referred to as trophic feeding, involves delivering energy below an individual’s estimated requirements, or underfeeding, and has been increasingly utilized in the management of critically ill patients (Charles et al., 2014; Zhou et al., 2021). This approach is often easier to implement in hemodynamically unstable individuals, as hypocaloric feeding can reduce metabolic stress and improve insulin resistance (Charles et al., 2014; Zhou et al., 2021). However, prolonged hypocaloric feeding can also contribute to adverse outcomes such as malnutrition, impaired wound healing, and muscle wasting

(Charles et al., 2014; Yue et al., 2024).

Current guidelines from the American Society for Parenteral and Enteral Nutrition (ASPEN) and the European Society for Clinical Nutrition and Metabolism (ESPEN) provide vague timelines for adjusting the nutritional needs of critically ill patients (Van Niekerk et al., 2020). However, both organizations recommend a progressive approach to recovery, emphasizing gradual advancement of nutritional support based on clinical status and patient tolerance (Van Niekerk et al., 2020).

Given the widespread prevalence of sepsis, its high mortality rate, and the growing economic burden it imposes, a review of the current literature on hypocaloric versus normocaloric feeding in critically ill adults with sepsis is warranted to determine which approach is most effective at improving glycemic control, reducing mortality, and shortening hospital stays (Balch, 2023). The following systematic review synthesizes recent literature and clinical data to provide a comprehensive overview of the role of nutrition strategies in the management of septic patients in order to improve patient outcomes and emphasize the need for more precise, evidence-based guidelines.

2. Methods

The following section details the systematic methodology used to identify, select, and analyze studies comparing normocaloric and hypocaloric feeding in critically ill adults with sepsis. The registration details, database selection, keywords, and search strategies will be outlined. Additionally, the inclusion and exclusion criteria, screening procedures, search results, data extraction methods, and quality assessment protocol are presented to ensure methodological transparency and adherence to standardized systematic review guidelines.

2.1 Protocol and Registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Guidelines (Page et al., 2021). This review was also prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) - ID: CRD420251088694 (Centre for Reviews and Dissemination, 2025).

2.2 Search Strategy

The search for this systematic review was conducted in June 2025 and replicated in September 2025 to ensure inclusion of recent literature. The search strategy was developed using Medical Subject Headings (MeSH) and key terms to define the population, interventions, and outcomes of interest (U.S. National Library of Medicine, 2025). Boolean operators were utilized to combine search terms (U.S. National Library of Medicine, 2025). A refined search strategy was necessary to narrow down the key terms to obtain more targeted results aligned with the research question:

> (critical illness OR sepsis OR ICU) AND (normal caloric feeding OR permissive underfeeding OR hypocaloric feeding OR trophic feeding) AND (mortality OR glycemic control OR length of stay) NOT (pediatric or infant)

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Table 1. Key MeSH Terms Used to Build the Search Strategy

Population MeSH Terms (Critically Ill Adults)	**Intervention MeSH Terms (Normocaloric Feeding)**	**Control MeSH Terms (Hypocaloric Feeding)**	**Outcomes MeSH Terms (Glycemic Control, Mortality, LOS)**
Critical Illness	Nutrition Therapy	Caloric Restriction	Glycemic Control
Sepsis	Enteral Nutrition	Hypocaloric Feeding	Blood Glucose
Intensive Care Units	Parenteral Nutrition	Underfeeding	Insulin Resistance
Critical Care	Nutrition Support	Low Energy Intake	Mortality
Adult	Caloric Intake	Permissive Underfeeding	Length of Stay
ICU	Energy Intake	Low Energy Intake	Hospital Mortality
Systematic Inflammatory Response Syndrome	Normocaloric Feeding	Dietary Energy Restriction	Patient Outcomes
Multiple Organ Failure	Isocaloric Feeding	Feeding Method	Treatment Outcomes

Note. MeSH = Medical Subject Headings; ICU = Intensive Care Unit; LOS = Length of Stay.

2.3 Eligibility Criteria

Database filters were applied, when available, to limit results to studies involving human participants, adult populations ($\geq$ 18 years), publications in English, clinical trials, randomized controlled trials (RCTs), cohort analyses, meta-analyses, and peer-reviewed academic journals published between 2020 and 2025.

Studies were eligible for inclusion if focused on critically ill adults diagnosed with sepsis or septic shock, compared normocaloric feeding to hypocaloric feeding, and reported outcomes related to glycemic control, hospital mortality, or length of hospital stay. Eligible study designs included RCTs, prospective cohort studies, clinical trials, and meta-analyses published in English within the defined timeframe.

Studies were excluded if involved non-human subjects or pediatric populations, did not report on the specified outcomes, failed to examine caloric intake as the primary nutritional intervention, or included fewer than ten participants per study group. Systematic reviews and non-peer-reviewed publications were also excluded.

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Table 2. Predetermined Inclusion and Exclusion Criteria to Identify Relevant Studies

Criteria	Inclusion	Exclusion
Age	Adults age 18 or older	Individuals under 18
Gender	Percent female versus male	N/A
Setting/Country	ICU setting, all countries	Outpatient or non-ICU setting
Health Status/Problem/Condition	Critically ill individuals with sepsis or septic shock	Non-critically ill patients or patients without sepsis
Intervention/Exposure	Full caloric feeding and hypocaloric feeding	Nutritional interventions that do not include caloric intake
Outcomes	Data on either mortality, hospital length of stay, or glycemic control	Studies without information on either mortality, glycemic control, or hospital length of stay
Study Design Preferences	RCTs, prospective cohort studies, clinical trials, meta-analyses	Systematic reviews or non-peer-reviewed trials
Size of Study Groups	At least 10 individuals	Studies with less than 10 individuals
Language	English	Languages other than English
Publication Year Range	Past 5 years (2020 to present)	2019 or older publications
Participant Population	Human participants	Animal participants

2.4 Data Extraction and Quality Assessment

To systematically collect relevant information from each study, a standardized data extraction table was developed to ensure consistency throughout the review process. The table was adapted from the Cochrane Collaboration's data collection template to align with the specific objectives and outcomes of this review (Higgins et al., 2024). Extracted data included the study title, authors, year of publication, country, study design, study purpose, setting, participant demographics (age, sex, and sample size), details of the intervention and comparison groups, outcomes measured, and key findings. Data extraction was completed by the primary author to ensure consistency and reduce variability in interpretation throughout the extraction process.

The Academy of Nutrition and Dietetics (AND) Evidence Analysis Library (EAL) Quality Criteria Checklist was utilized to assess the methodological quality and risk of bias for each included study (Academy of Nutrition and Dietetics, 2022). Studies were rated as positive, neutral, or negative based on internal validity criteria, including relevance to the research question, subject selection, group comparability, handling of dropouts, blinding, the intervention itself, outcome measures, statistical analysis, and overall risk of bias (Academy of Nutrition and Dietetics, 2022). A positive rating indicated low risk of bias, neutral signified moderate risk, and a negative rating reflected high risk of bias (Academy of Nutrition and Dietetics, 2022).

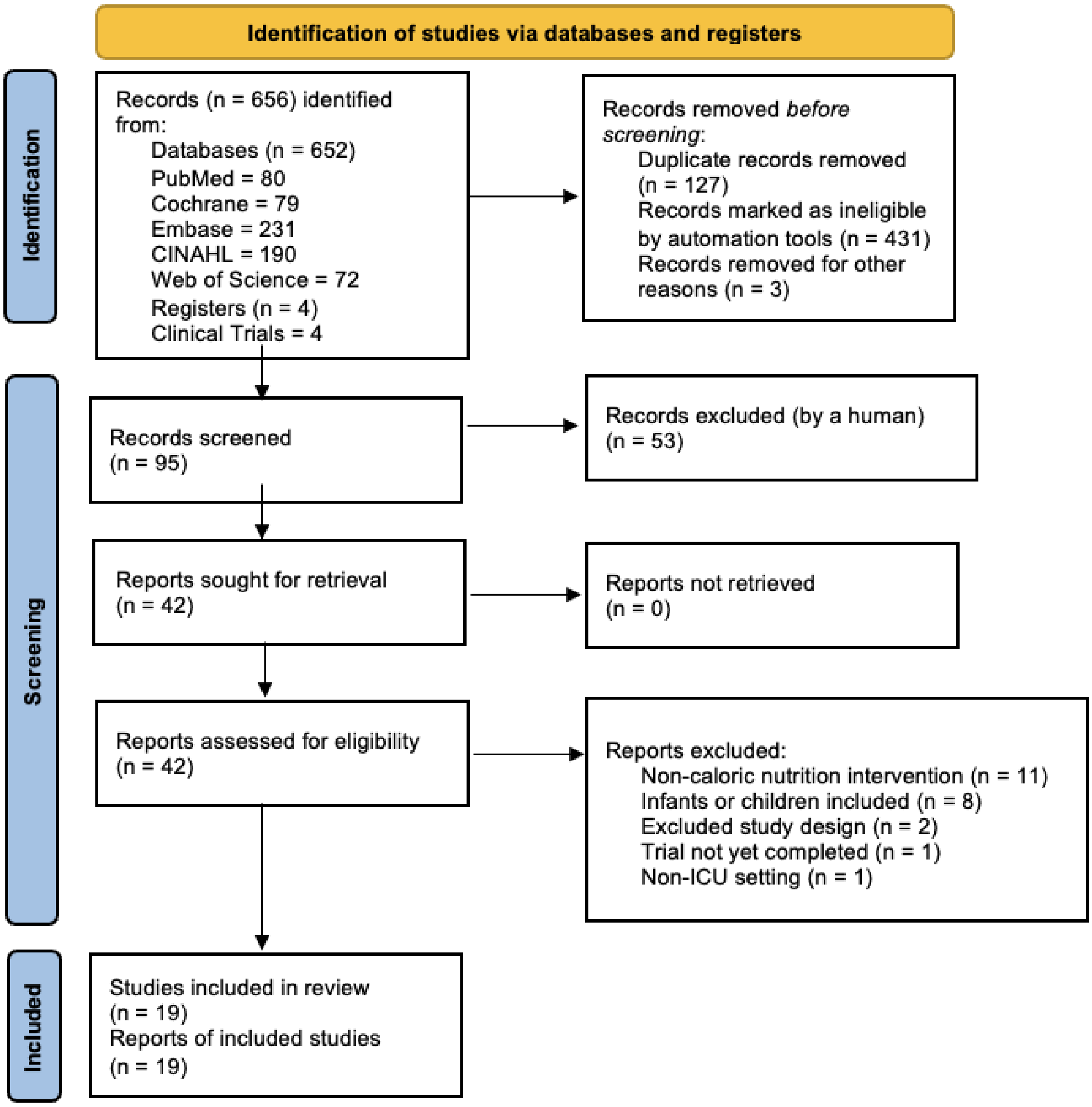

Figure 1. PRISMA 2020 Flow Diagram Utilized to Identify Studies for Inclusion

3. Results

Following the PRISMA 2020 Guidelines, 656 records were initially identified through database and register searches (Page et al., 2021). After the removal of 127 duplicate records, 431 records were removed by automated tools and three records were removed for other reasons. Ninety-five records remained for screening, with 53 records excluded, leaving 42 full-text records for assessment.

Reasons for exclusions of full-text articles included: Non-caloric interventions (n = 11), inclusion of pediatric populations (n = 8), excluded study designs (n = 2), ongoing trials (n = 1), and studies conducted outside of the ICU setting (n = 1). After applying the inclusion and exclusion criteria, 19 studies were eligible for inclusion in this systematic review. Table 3 summarizes key outcomes and quality ratings for each article. Table 3 also outlines sample sizes, study designs, and limitations taken into consideration when assigning a quality rating. The following results summarize findings related to three primary outcome categories: mortality, length of stay (LOS), and glycemic control, followed by a risk of bias and study quality assessment.

3.1 Mortality

The majority of studies, including multiple RCTs, retrospective analyses, and meta-analyses, reported no statistically significant difference in mortality between individuals receiving hypocaloric versus normocaloric feeding, suggesting caloric intake does not substantially affect the risk of death in most critically ill populations (Arabi et al., 2021; Floro et al., 2023; Kucuk et al., 2021; Li et al., 2022; Mousavian et al., 2020; Permejo eta al., 2024; Reignier et al., 2023; Singer et al., 2021; Sun et al., 2021; Viana et al., 2020; Wang et al., 2020; Xiong et al., 2021; Zhou et al., 2021). Chinnapotahala and team (2022) identified significantly lower mortality in the hypocaloric group in the ICU ($p < 0.05$), while a large meta-analysis by Yue and associates (2024) reported a reduction in mortality in the hypocaloric group in the ICU ($p = 0.02$), but no significant difference ($p = 0.51$), in mortality between groups when looking at overall, in-hospital mortality.

In contrast, other studies suggested hypocaloric feeding has the potential to cause harm. One secondary analysis of a cluster RCT reported an increased hazard of death ($p = 0.004$) with hypocaloric feeding (Lv et al., 2022). Another observational study by Matejovic and team (2022) documented no significant difference in mortality overall ($p = 0.095$); however, when patients were stratified by caloric intake, moderate caloric intake was associated with a significantly lower hazard of death (HR = 0.15; 95% CI: 0.05-0.39), suggesting the need for more detailed caloric stratification in future studies. This study should be interpreted with caution, as Matejovic and associates (2022) compared hypocaloric, normocaloric, and hypercaloric groups, unlike the rest of the studies that focused only on hypocaloric versus normocaloric feeding.

However, several studies reported benefits of various feeding regimens across specific patient subgroups. One secondary analysis of a multi-center cohort observed no overall difference in mortality ($p = 0.08$), but did report individuals with metabolic syndrome significantly ($p = 0.05$) experienced reduced mortality with normocaloric feeding (Fesen et al., 2023). Fesen and colleagues (2023) suggested metabolic phenotypes may be an important factor to consider when predicting how an individual will respond to a certain caloric intake. As a whole, the results suggest while most studies indicate no difference in mortality between hypocaloric and normocaloric groups, there is some evidence linking context-dependent associations between mortality and caloric intake. Metabolic health, timing of nutrition, comorbidities, and patient severity are all possible contributors in determining patient mortality outcomes in combination with caloric intake.

3.2 Length Of Stay (LOS) Outcomes

In contrast to mortality outcomes, findings related to hospital LOS more consistently favored a hypocaloric feeding regimen as multiple studies reported significantly shorter LOS in individuals who received reduced caloric intake (Kucuk et al., 2021; Li et al., 2022; Mousavian et al., 2020; Permejo et al., 2024; Reignier et al., 2023; Viana et al., 2020; Xiong et al., 2021). Furthermore, similar results were reported across varying populations and study designs, indicating a stronger relationship between caloric intake and LOS than between caloric intake and mortality. The largest RCT in this review, which utilized hypocaloric feeding at six calories per kilogram of body weight, reported a statistically significant ($p < 0.001$) reduction in LOS, and a meta-analysis pooling results from multiple trials also demonstrated a significantly ($p = 0.015$) shorter LOS in individuals receiving hypocaloric feeding (Permejo et al., 2024; Reignier et al., 2023).

However, several studies reported no significant difference between LOS in hypocaloric versus normocaloric groups, though some studies had limited ability to detect significant differences due to inconsistent caloric targets and underpowered samples (Chinnapotahala et al., 2022; Floro et al., 2023; Lv et al., 2022; Singer et al., 2021; Sun et al., 2021; Yue et al., 2024; Zhou et al., 2021). Two studies reported contrasting findings. Matejoic and team (2022) reported a shorter LOS in the normocaloric group ($p = 0.03$), while Wang and associates (2020) observed LOS reduction in only the lowest caloric group ($p = 0.01$), despite the benefit in reduced mortality previously seen with the moderate caloric group. The findings, in combination with feeding tolerance, metabolic efficiency, and differences in recovery, provide evidence optimal caloric feeding for minimizing LOS may differ from caloric intake shown to reduce mortality (Matejovic et al., 2022; Wang et al., 2020). Overall, the findings indicate a potential association between hypocaloric feeding and reduced LOS, although the results remain mixed due to inconsistent methodologies, caloric definitions, and small sample sizes.

3.3 Glycemic Control

In contrast to the previous two outcomes, fewer studies directly addressed glycemic control. Most studies with data on glycemic control reported hypocaloric feeding had a small, but significant difference in improving an individual’s glucose control. Several studies documented improved glycemic control with hypocaloric feeding through reductions in insulin requirements, fewer hyperglycemic events, or improved glycemic stability (Chinnapotahala et al., 2022; Li et al., 2022; Mousavian et al., 2020; Reignier et al., 2023). In particular, one large RCT observed significantly ($p < 0.001$) reduced insulin requirements in the hypocaloric group, while another reported significantly ($p < 0.05$) more rapid attainment of glycemic control with a hypocaloric feeding regimen (Mousavian et al., 2020; Reignier et al., 2023).

A retrospective study by Li and team (2022) reported significantly ($p = 0.008$) fewer hyperglycemic events in the hypocaloric group without a significant ($p = 0.33$) corresponding increase in hypoglycemic events. In contrast, other studies reported no significant differences in glycemic control between the two feeding regimens, with reported *p*-values of 0.75 (Arabi et al., 2021), 0.16 (Singer et al., 2021), 0.258 (Wang et al., 2024), and 0.616 (Zhou et al., 2021). Additionally, small sample sizes, lack of standardization in the measurement of glycemic control, and various definitions of glycemic control complicated findings (Arabi et al., 2021; Singer et al., 2021; Wang et al., 2024; Zhou et al., 2021). Baseline information about diabetes, corticosteroid use, and glycemic control reported as a secondary outcome in the studies also complicated the reporting of glycemic control outcomes and the resulting potential benefit of different feeding regimens on glycemic control.

3.4 Risk of Bias and Quality Assessment

As previously noted, the Academy of Nutrition and Dietetics (AND) Evidence Analysis Library (EAL) Quality Criteria Checklist was utilized to assess the methodological quality and risk of bias for each included study (Academy of Nutrition and Dietetics, 2022). The resulting grades for each study are included in the article summary table along with limitations reflecting the assigned rating. Various assessment criteria and the resulting grade for each study are included in the quality criteria table, reflecting limitations and strengths of each included study (see Table 4). Out of the nineteen studies, fourteen were rated as neutral due to limitations such as sample size and confounding variables. Three of the remaining studies were rated as positive largely due to their study designs, and the final two studies were rated as negative due to disparities in caloric provision and trial conclusion before completion. Overall, the quality of studies was predominantly neutral, reflecting the main trends and contrasting results seen in the review.

Table 3. Article Summary Table

Reference	**Study Design, Sample Size, and Location**	**Study Duration**	**Intervention**	**Comparison**	**Results**
Arabi et al., 2021	RCT n = 40 Riyadh, Saudi Arabia	5 to 90 days	EN with higher protein (1.2 to 2.0 g/kg)	Normocaloric EN with normal protein (0.8 g/kg)	Morality not directly analyzed in this study (Only reported by the percentage of the entire cohort, 20.5% at 90 days) Glycemic control not directly measured in this study (no significant difference in the amount of insulin administered, $p = 0.75$)
Chinnapotahala et al., 2022	RCT n = 100 Hyderabad, India	7 to 90 days	Hypocaloric feeding (15 kcal/day)	Isocaloric feeding (25 kcal/kg)	Significantly lower ICU mortality in patients in the hypocaloric group ($p < 0.05$) No significant difference in LOS ($p > 0.005$) Significantly lower hyperglycemia and insulin requirements in the

					hypocaloric group ($p < 0.005$)
Fesen et al., 2023	Secondary analysis of a multi-center RC n = 411 United States	7 to 90 days	Trophic feeds (approximately 400 kcal/day)	Full feeding (25 to 30 kcal/kg)	No significant difference in mortality in high MetS patients ($p = 0.08$) Significantly lower mortality in Non-MetS individuals who received normocaloric feeding ($p = 0.05$)
Floro et al., 2023	Retrospective study n = 104 Toronto, Canada	7 to 123 days	Lower calorie feeding (≤ 20 kcal/kg)	Higher calorie feeding (≥ 20 kcal/kg)	No significant difference in mortality ($p = 0.633$) or LOS ($p = 0.826$)
Kucuk et al., 2021	Retrospective study n = 291 Trabzon, Turkey	14 days	Hypocaloric feeding (< 70% of estimated energy needs)	Normocaloric feeding (70 to 110% of estimated energy needs)	No significant difference in mortality ($p = 0.493$) Significantly shorter LOS in individuals receiving hypocaloric feeding ($p < 0.001$)
Li et al., 2022	Retrospective study n = 3545 United States	8 to 29 days	Hypocaloric feeding (≤ 20 kcal/kg)	Normocaloric feeding (≥ 20 kcal/kg)	No significant difference in mortality ($p = 0.010$) Significantly shorter LOS in individuals receiving hypocaloric feeding ($p < 0.001$) Glycemic control was not directly measured in this study, but there were significantly fewer hyperglycemia events in the hypocaloric group ($p = 0.008$) and no significance in the number of hypoglycemic events ($p = 0.33$)
Lv et al., 2022	Secondary analysis of a cluster RCT	9 to 28 days	Hypocaloric feeding (< 70% of estimated energy	Normocaloric feeding (70 to 110% of estimated energy	Hypocaloric feeding was associated with increased mortality when compared to normocaloric feeding

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	n = 1694 Nanjing, China		needs)	needs) Hypercaloric feeding (>100% of estimated energy needs)	([HR] = 1.590, 95% [CI]: 1.162 - 2.176, *p* = 0.004] Hypercaloric feeding did not increase mortality compared to normocaloric feeding ([HR] = 1.394, 95% [CI]: 0.920 - 2.112, *p* = 0.117) No significant difference in LOS (*p* = 0.0633)
Matejovic et al., 2022	Observational study n = 1172 Europe	7 to 36 days	Low calorie feeding (<10 kcal/kg) Moderate calorie feeding (10 to 20 kcal/kg)	High calorie feeding (> 20 kcal/kg)	No significant difference in mortality (*p* = 0.095) unless grouped by caloric levels, where moderate caloric intake was associated with significantly lower mortality (HR] = 0.15, 95% [CI], [0.05, 0.39]) Significantly lower LOS in the low calorie group ([HR] = 1.12, 95% [CI], [1.02, 1.22], *p* = 0.01)
Mousavian et al., 2020	Single-blind RCT n = 58 Mashhad, Iran	7 to 28 days	Hypocaloric feeding (30% of estimated energy needs on day 1 increased to 75% of needs on day 7)	Normocaloric feeding (75% of estimated energy needs on day 1 to 90 to 100% of needs by day 7)	No significant difference in mortality (*p* = 0.640) Significantly shorter LOS in individuals receiving hypocaloric feeding (*p* = 0.046) Glucose control improved sooner in the hypocaloric group (*p* < 0.05)
Permejo et al., 2024	Meta-analysis n = 1435 Worldwide	7 to 180 days	Hypocaloric feeding (generally 12 to 15 kcal/kg)	Normocaloric feeding	No significant difference in mortality (*p* = 0.99) Significantly shorter LOS in individuals receiving hypocaloric feeding (*p* < 0.001) Data for glycemic control not pooled across studies
Reignier et al., 2023	RCT n = 3036 France	5 to 17 days	Hypocaloric feeding (6 kcal/kg)	Normocaloric feeding (25 kcal/kg)	No significant difference in morality (*p* = 0.41) Significantly lower LOS in individuals receiving hypocaloric feeding

					(*p* = 0.015) Significantly less insulin needed in individuals in the hypocaloric group (*p* < 0.001)
Singer et al., 2021	RCT n = 332 Worldwide	8 to 31 days	Tight calorie control (80 to 100% of indirect calorimetry)	Normocaloric feeding (20 to 25 kcal/kg of IBW)	No significant difference for mortality (*p* = 0.68), LOS (*p* = 0.32), or glycemic control (*p* = 0.16)
Sun et al., 2021	Prospective RCT n = 54 Nanjing, Chima	7 to 28 days	Hypocaloric feeding (30% and 60% of estimated energy needs)	Normocaloric feeding	No significant difference for mortality (*p* = 0.856) or LOS (*p* = 0.572)
Viana et al., 2020	Observational study n = 342 Porto Alegre, Brazil	7 to 41 days	Delayed hypocaloric feeding (≤ 20 kcal/kg)	Early hypercaloric feeding (≥ 20 kcal/kg)	No significant difference in mortality after adjustment ([HR] = 0.77, 95% [CI], [0.52, 1.15], (*p* = 0.159) Significantly shorter LOS in individuals receiving hypocaloric feeding (*p* = 0.012)
Wang et al., 2024	Observational study n = 179 Chengdu, China	14 days	47 dynamic indicators	N/A	No significant difference in glycemic control (*p* = 0.258)
Wang et al., 2020	RCT n = 150 Taichung, Taiwan	6 to 28 days	Trophic feeds (approximately 600 kcal/day)	Full feeding (about 25 kcal/kg)	No significant difference in mortality (*p* = 0.45) Significantly shorter LOS in individuals receiving normocaloric feeding (*p* = 0.03)
Xiong et al., 2021	Prospective RCT n = 53 Nanchang, China	7 to 28 days	Caloric capacity of 20 to 40% of ESPEN recommendations	Caloric capacity of 70 to 100% of ESPEN recommendations	No significant difference in mortality (*p* = 0.31) Significantly shorter LOS in individuals receiving hypocaloric feeding (t = -2.169, *p* = 0.036)

Yue et al., 2024	Meta-analysis n = 11 444 Worldwide	Typically 5 to 14 days Varied by study as some continued until ICU discharge or death	Permissive underfeeding (various definitions)	Full feeding (various definitions)	ICU mortality was lower in the patients with permissive underfeeding ([RR] = 0.90%; 95% [CI], [0.81, 0.99]; p = 0.02; I^2= 0%), but overall mortality and in-hospital mortality were not significantly different between the groups No significant difference in LOS (MD = 1.11, 95% [CI], [-2.16, 4.38], p = 0.51, I^2= 77%)
Zhou et al., 2021	Meta-analysis n = 6986 Worldwide	Not reported	Permissive underfeeding (various definitions)	Full feeding (various definitions)	No significant difference observed for mortality (p = 0.409), LOS (p = 0.488), or glycemic control (p = 0.616)

Table 4. Quality Criteria Table

Study	Study Design	Blinding	Sample Size	Confounder Control	Protocol Deviation	Clinical Impact	Risk of Bias
Arabi et al., 2021	🟢	🔴	🔴	🟡	🟢	🔴	🟡
Chinnapotahala et al., 2022	🟢	🟡	🟡	🔴	🟡	🟢	🟡
Fesen et al., 2023	🟡	🔴	🟢	🟡	🟡	🟡	🟡
Floro et al., 2023	🔴	🔴	🟡	🟢	🟡	🔴	🟡
Kucuk et al., 2021	🔴	🔴	🟢	🔴	🟡	🟡	🟡
Li et al., 2022	🔴	🔴	🟢	🔴	🟡	🔴	🔴
Lv et al., 2022	🟡	🔴	🟢	🟡	🟡	🟡	🟡
Matejovic et al., 2022	🟡	🔴	🟢	🟡	🟢	🟡	🟡
Mousavianet al., 2020	🟢	🟡	🔴	🟢	🟡	🟡	🟡

Permejo et al., 2024	Yellow	Yellow	Green	Yellow	Yellow	Yellow	Yellow
Reignier et al., 2023	Green	Red	Green	Green	Red	Red	Yellow
Singer et al., 2021	Green	Yellow	Red	Yellow	Red	Red	Red
Sun et al., 2021	Green	Yellow	Red	Yellow	Yellow	Yellow	Yellow
Viana et al., 2020	Yellow	Red	Yellow	Yellow	Yellow	Yellow	Yellow
Wang et al., 2024	Yellow	Red	Green	Yellow	Yellow	Yellow	Yellow
Wang et al., 2020	Green	Yellow	Yellow	Green	Green	Green	Green
Xiong et al., 2021	Green	Yellow	Red	Yellow	Yellow	Yellow	Yellow
Yue et al., 2024	Yellow	Green	Green	Green	Green	Yellow	Green
Zhou et al., 2021	Yellow	Yellow	Green	Green	Green	Yellow	Green

Note. Green = Low risk (positive), Yellow = Moderate risk (neutral), and Red = High risk (negative).

4. Discussion

This systematic review evaluated hypocaloric versus normocaloric feeding and its effects on mortality, LOS, and glycemic control in critically ill adults. Despite heterogeneity in study design and populations, consistent patterns emerged, clarifying the clinical implications of caloric provision in the ICU.

4.1 Mortality

Across nineteen studies, the majority reported no statistically significant mortality difference between hypocaloric and normocaloric feeding (Arabi et al., 2021; Floro et al., 2023; Kucuk et al., 2021; Li et al., 2022; Mousavian et al., 2020; Permejo eta al., 2024; Reignier et al., 2023; Singer et al., 2021; Sun et al., 2021; Viana et al., 2020; Wang et al., 2020; Xiong et al., 2021; Zhou et al., 2021). This consistency across RCTs, retrospective cohort studies, and meta-analyses suggests caloric intake alone may not predominantly determine survival. However, select studies highlighted the complexity of the relationship.

Specifically, one notable RCT by Chinnapotahala and team (2022) and a meta-analysis from Yue and colleagues (2024) reported significantly lower ICU mortality with hypocaloric feeding, though despite no difference in overall in-hospital mortality. Conversely, a secondary analysis of a cluster RCT by Lv and associates (2022) identified an increased hazard of death with hypocaloric feeding, while Matejovic and colleagues (2022) reported moderate caloric intake, rather than hypocaloric or normocaloric, was associated with the lowest hazard of death. The findings emphasize the importance of including intermediate caloric groups in nutritional research.

Furthermore, findings suggested the influence patient-specific factors on mortality rather than caloric provision alone. For example, patients with metabolic syndrome were reported to have benefited from normocaloric feeding, while other patients tolerated, and even benefited from hypocaloric feeding instead (Fesen et al., 2023). Therefore, the subgroup differences examined in this review highlight additional factors, including timing of nutrition initiation, baseline nutritional risk, disease severity, and metabolic phenotypes, that must be considered in evaluating an individual's risk of mortality, rather than focusing solely on caloric intake (Fesen et al., 2023). Overall, outcomes remain context-dependent, supporting individualized nutrition strategies.

4.2 LOS Outcomes

Compared to mortality, LOS outcomes were more consistent. Multiple meta-analyses and RCTs reported significantly shorter ICU LOS with hypocaloric feeding (Kucuk et al., 2021; Li et al., 2022; Mousavian et al., 2020; Permejo et al., 2024; Reignier et al., 2023; Viana et al., 2020; Xiong et al., 2021). This association was observed across diverse populations and study designs, suggesting a more direct relationship between LOS and caloric intake (Permejo et al., 2024; Reignier et al., 2023). Reduced LOS associated with hypocaloric feeding may be related to improved glycemic stability, feeding tolerance, and reduced metabolic stress, which collectively lower complication risk (Charles et al., 2014; Umphonsathien et al., 2022).

Despite more consistent findings with LOS, the findings are not without contradiction. Several studies reported no significant LOS difference, often citing methodological implications, inconsistent caloric delivery, or insufficient power (Chinnapotahala et al., 2022; Floro et al., 2023; Lv et al., 2022; Singer et al., 2021; Sun et al., 2021; Yue et al., 2024; Zhou et al., 2021). Matejovic and team (2022) associated normocaloric feeding with reduced LOS, while Wang and colleagues (2020) found LOS benefits only at the lowest caloric intake, despite improved mortality with moderate intake.

The discrepancies reinforce the complexity of caloric intake, with comorbidities, protein intake, and gastrointestinal function also influencing outcomes (Matejovic et al., 2022; Wang et al., 2020). Overall, the evidence suggests reduced LOS with hypocaloric feeding. However, variability across the studies continues to support the need for further studies with standardized protocols and more consistent caloric target definitions and implementation.

4.3 Glycemic Control

Fewer studies directly evaluated glycemic control, but those that did noted improved glycemic control with hypocaloric feeding. (Chinnapotahala et al., 2022; Li et al., 2022; Mousavian et al., 2020; Reignier et al., 2023). Glycemic control was measured differently in the studies, as insulin requirements, hyperglycemic episodes, and attainment of target glucose levels were all utilized. Li and team (2022) reported a glycemic benefit with hypocaloric feeding and noted this benefit was not associated with an increase in hypoglycemic events.

Therefore, hypocaloric feeding was recommended as a feeding method for metabolic stability without accompanying risks.

Unfortunately, the strength of the conclusions is limited due to variations in insulin protocols and glycemic outcomes being measured as either secondary or even tertiary measures. Furthermore, as with varying definitions of caloric targets, the studies did not have a consistent definition of glycemic control. As glycemic control was rarely a primary outcome, confounding variables such as corticosteroid use and diabetes were not controlled for. Few studies also reported no significant difference in glycemic outcomes with either feeding method, further limiting the conclusion that hypocaloric feeding is beneficial for glycemic control in all patient populations (Arabi et al., 2021; Singer et al., 2021; Wang et al., 2024; Zhou et al., 2021).

Overall, glycemic stability is critical for preventing complications such as infection or poor wound healing (Dasari et al., 2021; Zhou et al., 2024). While hypocaloric feeding may contribute to glycemic stability in critically ill populations, the evidence remains limited, largely due to inconsistent findings not assessing glycemic control as a primary outcome in the few existing studies.

4.4 Findings Compared to Current Guidelines

Unfortunately, published guidelines vary widely, as the American Society for Parenteral and Enteral Nutrition and the Society of Critical Care Medicine (ASPEN/SCCM) 2022 Guidelines recommend twelve to twenty-five calories per kilogram each day for patients during the first seven to ten days in the ICU (Compher et al., 2022). This large range encompasses both a hypocaloric and normocaloric feeding regimen. The European Society for Clinical Nutrition and Metabolism (ESPEN) 2023 Guidelines recommend an early phase, or one to three days at or greater than seventy percent of an individual’s energy requirements (Singer et al., 2023). Then, after day three, ESPEN 2023 Guidelines recommend eighty to one-hundred percent of an individual’s needs (Singer et al., 2023). Individuals’ needs are to be calculated with indirect calorimetry, though the lack of equipment/facilities or time constraints limits the feasibility of indirect calorimetry in most hospital settings (Lakenman et al., 2024).

Due to the limited evidence and overly generalized guidelines, clinical judgment needs to be utilized, as without adequate research, definitive guidance is unavailable. Without additional data, guidelines will remain broad and insufficiently equipped to provide support for navigating individual patient variability, complicating the determination of appropriate feeding regimens.

4.5 Risk of Bias and Quality Assessment

Most studies received a neutral quality rating (n = 14; 74%). Common limitations of the studies included lack of blinding, retrospective study designs, small sample sizes, and inadequate adjustment for confounding variables. Three studies were rated positive (n = 3; 16%), and the remaining two studies were rated as negative (n = 2; 10%) due to early trial discontinuation or extreme caloric inconsistencies.

Inconsistent caloric targets complicated comparison across studies. The inconsistencies hinder the identification of optimal nutrition strategies and limit the translation of findings into clinical recommendations. Protocol deviation, fluctuations in nutrition delivery, and homogenous populations also limit the applicability of the results to real-world populations. Finally, discrepancies in study durations, reported outcomes, and limited baseline data also limit generalizability and the overall quality of the evidence.

4.6 Strengths

This systematic review followed the PRISMA 2020 Guidelines in selecting studies and extracting data, which strengthened the methodological rigor and ensured a transparent and reproducible article selection process (Page et al., 2021). Additionally, the use of the EAL QCC to assess quality and risk of bias enhanced the validity of the evidence synthesis by systematically evaluating methodological quality (Academy of Nutrition and Dietetics, 2022). Following the PRISMA 2020 Guidelines also allowed inclusion of diverse studies conducted in ICU settings across the globe, thereby improving the generalizability of the findings (Page et al., 2021). Focusing on three primary outcomes, or mortality, LOS, and glycemic control, further streamlined comparisons across studies.

4.7 Limitations

Variation in study design, outcome measures, and definitions of caloric groups limited generalizability and comparison across studies. Additionally, underpowered studies, caloric intake reported without macronutrient breakdown, and differing timeframes for nutrition initiation complicated the interpretation of outcomes. While this review focused on critically ill adults, the exclusion of non-ICU and pediatric populations also limits the overall applicability of the findings.

4.8 Applications for Practitioner

Findings suggest hypocaloric feeding may be a safe and potentially beneficial approach in regards to better patient outcomes in critically ill adult patients. Hypocaloric feeding may result in reduced LOS and improved glycemic control without increasing mortality risk. However, due to the lack of consistent benefits of hypocaloric feeding on mortality, routine use of a hypocaloric feeding regimen is not recommended.

Furthermore, an individual’s caloric needs should not be determined solely by caloric targets. A nutritional assessment should also include consideration of the patient’s comorbidities, current illness severity, baseline nutritional status, and tools such as the Nutrition-Focused Physical Exam (NFPE) to provide clinically relevant findings to inform individualized patient care (Academy of Nutrition and Dietetics, n.d.). Consideration of individual factors is also essential for effectively implementing the Nutrition Care Process, or NCP, which is the standardized model developed by the Academy of Nutrition and Dietetics to support evidence-based practice and improve quality of care for all patients (Academy of Nutrition and Dietetics, n.d.). Furthermore, in the ICU setting, interdisciplinary communication among dietitians, nursing staff, physicians, and pharmacists is necessary when both implementing and monitoring nutrition in critically ill patients (Holdoway et al., 2022).

4.9 Future Research Directions

Although the studies examined caloric strategies for critically ill adults, gaps in the literature prevent the development of standardized, evidence-based feeding protocols. Future research should focus on multicenter, adequately powered, randomized trials with standardized definitions of hypocaloric and normocaloric feeding. Blinding where feasible, control of confounders, and consistent reporting of patient outcomes, including glycemic control, mortality, and length of stay, are recommended. Additionally, studies should collect and report baseline nutritional status to improve comparability. Addressing these gaps will strengthen evidence to inform protocol development.

5. Conclusion

Overall, this systematic review identified no definitive mortality benefit in critically ill adults receiving hypocaloric versus normocaloric feeding, though certain subgroups may respond differently. Hypocaloric feeding was more consistently associated with reductions in LOS and improvements in glycemic control. However, the overall quality of the evidence was neutral, as there was considerable variation across studies. Further research with defined protocols, caloric targets, timing, and the collection of baseline data is required to inform evidence-based feeding regimens for critically ill adults in the ICU. Current findings suggest feeding regimens should be individualized and considered alongside other potential influencing factors such as comorbidities, baseline nutritional status, and ongoing treatments.

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Authors' contributions

LR and KH were responsible for the study design and LR for data collection. LR drafted the manuscript, and KH revised multiple drafts. All authors read and approved the final manuscript.

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