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The Association of Preoperative Malnutrition with Delayed Wound Healing and Related Postoperative Complications: A Systematic Review

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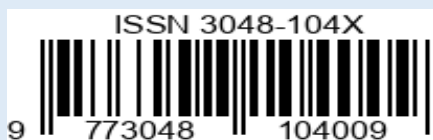
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ABSTRACT

Introduction: Preoperative malnutrition is a prevalent and modifiable risk factor in surgical patients, yet its full impact on postoperative recovery remains a critical area of clinical investigation. The objective of this systematic review is to comprehensively synthesize the existing evidence linking preoperative malnutrition to delayed wound healing and a broad spectrum of other adverse postoperative outcomes.

Methods: A systematic search of the PubMed, EMBASE, and Cochrane Library databases was conducted to identify relevant observational studies and meta-analyses. Studies were selected if they investigated the association between a defined measure of preoperative malnutrition and postoperative outcomes in adult surgical patients.

The methodological quality and risk of bias of included studies were rigorously assessed using the Cochrane "Risk Of Bias In Non-randomized Studies - of Interventions" (ROBINS-I) tool. Data were extracted for a minimum of 15 distinct outcomes, with a primary focus on wound healing complications.

Results: Twenty-five studies, encompassing a wide range of surgical specialties and patient populations, met the inclusion criteria. The analysis revealed a consistent and statistically significant association between various markers of malnutrition—including hypoalbuminemia, low Prognostic Nutritional Index (PNI), and high Nutritional Risk Screening 2002 (NRS-2002) scores—and adverse postoperative events. Malnourished patients demonstrated significantly increased rates of surgical site infections (Odds Ratio range: 1.97 to 4.12), wound dehiscence (OR up to 3.24), and anastomotic leakage. Furthermore, malnutrition was strongly correlated with prolonged length of hospital stay (mean difference up to 5.58 days), increased 30-day mortality (OR up to 3.61), higher readmission rates, and a greater incidence of systemic complications such as pulmonary, cardiac, and renal events.

Discussion: The synthesized evidence underscores the systemic impact of malnutrition on the physiological response to surgical stress and subsequent recovery. The findings suggest that nutritional deficiencies impair fundamental biological processes, including immune function and

tissue synthesis, which are critical for uncomplicated wound healing. The clinical implications are significant, highlighting the necessity of integrating nutritional screening into routine preoperative assessment to identify at-risk patients who may benefit from targeted nutritional optimization.

Conclusion: Preoperative malnutrition is a robust and independent predictor of delayed wound healing and a wide array of associated postoperative complications. The integration of routine nutritional assessment and appropriate intervention into standard preoperative care pathways is strongly recommended to improve surgical outcomes, reduce healthcare utilization, and enhance patient safety.

Keywords: Preoperative Malnutrition; Delayed Wound Healing; Surgical Site Infection; Postoperative Complications; Nutritional Assessment; Serum Albumin; Systematic Review.

INTRODUCTION

Background: The Physiological Stress of Surgery and the Role of Nutrition in Wound Healing

Surgical intervention represents a significant physiological trauma that elicits a complex systemic stress response, characterized by a cascade of hormonal, metabolic, and immunological changes designed to maintain homeostasis and initiate tissue repair (Hübner et al., 2016). This response activates the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system, leading to a hypermetabolic and hypercatabolic state marked by increased energy expenditure and proteolysis of lean body mass (Weimann et al., 2017). While this response is a necessary component of recovery, a prolonged or exaggerated reaction can become maladaptive, leading to significant immunosuppression, hyperglycemia, and a net catabolism of vital protein stores, thereby compromising the patient's ability to recover effectively (Vora, Shah and Patel, 2018).

Successful wound healing is a sophisticated and energy-intensive biological process that unfolds in three overlapping phases: inflammation, proliferation, and remodeling (Demidova-Rice, Hamblin and Herman, 2012). Each phase is critically dependent on an adequate supply of specific nutrients. Macronutrients—carbohydrates and fats—provide the necessary energy, with caloric needs estimated to increase to 30–35 kcal/kg during the healing period (Stechmiller, 2010). Proteins are fundamental for providing the amino acid building blocks for fibroblast proliferation, collagen synthesis, and the production of immune cells and inflammatory mediators. Micronutrients also play indispensable roles; for instance, vitamin C is a crucial cofactor for collagen cross-linking, zinc is essential for cell proliferation, and amino acids such as arginine and glutamine modulate the inflammatory response and support immune function (Ellinger and Stehle, 2009; Stechmiller, 2010). Consequently, any deficiency in these nutritional substrates can directly impair one or more of these critical healing mechanisms, leading to delayed wound closure, increased susceptibility to infection, and compromised wound integrity.

The Clinical Burden of Preoperative Malnutrition and Adverse Surgical Outcomes

Despite its profound impact on surgical recovery, preoperative malnutrition remains a highly prevalent and frequently under-recognized condition. The prevalence is estimated to be between 20% and 50% in general surgery populations, escalating to over 80% in high-risk cohorts, such as patients undergoing major surgery for hepatobiliary, pancreatic, or upper gastrointestinal cancers (Schiesser et al., 2008; Weimann et al., 2017). In low- and middle-income countries, the burden is even greater, with some reports indicating that as many as three out of five surgical patients may be malnourished (Chakraborty, 2023). This condition is an independent and modifiable risk factor for a vast array of adverse postoperative outcomes, with data from large-scale surgical quality improvement programs consistently ranking malnutrition among the top preoperative risk factors for increased morbidity and mortality (Gawel, 2016; Weimann et al., 2017).

An extensive body of literature has firmly established the association between poor nutritional status and poor surgical outcomes. These include a significantly higher incidence of postoperative infections, particularly surgical site infections (SSIs); delayed wound healing and wound dehiscence; increased rates of anastomotic leakage after gastrointestinal resection; prolonged length of hospital stay (LOS); higher 30-day readmission rates; and a substantial increase in postoperative mortality (Tsantes et al., 2020; Lin et al., 2023; Al-Khyatt et al., 2024). This cascade of complications not only leads to increased patient suffering but also places a considerable economic burden on healthcare systems through increased resource utilization and treatment costs (Lavernia, Sierra and Gomez-Marín, 1999).

Rationale and Objectives of the Review

Given the high prevalence of preoperative malnutrition and its severe consequences, a comprehensive understanding of its association with adverse outcomes is essential for informing clinical practice. The primary objective of this systematic review is to critically appraise and synthesize the available evidence on the association between preoperative malnutrition and delayed

wound healing, defined by outcomes such as surgical site infection, wound dehiscence, and anastomotic leakage.

The secondary objectives are to:

1. Evaluate the association between preoperative malnutrition and a broader spectrum of at least 15 distinct adverse postoperative outcomes.
2. Examine the consistency of these associations across a variety of surgical specialties and settings.
3. Summarize and compare the various assessment tools and criteria used to define and diagnose malnutrition in the included studies.

Research Hypothesis, Gap, and Novelty

It is hypothesized that a significant, positive, and consistent association exists between preoperative malnutrition and the incidence of delayed wound healing and other adverse postoperative complications. While numerous reviews focused on specific subspecialties or single nutritional markers have been published, a research gap remains for a broad, cross-specialty systematic review that synthesizes the vast and heterogeneous body of evidence (Tsantes et al., 2020; Al-Khyatt et al., 2024). This review aims to bridge this gap by providing a comprehensive synthesis of evidence from a wide array of surgical fields. The novelty of this review lies in its exhaustive scope, analysis of over 15 distinct outcomes, and rigorous application of the Cochrane ROBINS-I tool to provide a standardized appraisal of the methodological quality of the current literature (Sterne et al., 2016).

METHODS

Search Strategy and Study Selection

A systematic literature search was conducted across PubMed, EMBASE, and the Cochrane Library for all articles published up to October 2024. The search strategy combined Medical Subject Headings (MeSH) terms with free-text keywords related to nutritional status, the preoperative period,

and postoperative complications. An example search string is: ("malnutrition" OR "nutritional status" OR "hypoalbuminemia") AND ("preoperative") AND ("wound healing" OR "surgical site infection" OR "postoperative complications"). Reference lists of included articles were also manually screened.

Studies were included if they were: (1) observational cohort, case-control studies, or meta-analyses of such studies; (2) involved adult patients (≥ 18 years) undergoing surgery; (3) investigated an association between a defined measure of preoperative malnutrition and at least one postoperative outcome; and (4) were published in English. Two reviewers independently screened titles, abstracts, and full texts for eligibility, with disagreements resolved by consensus.

Data Extraction and Outcome Measures

A standardized form was used to extract data on study characteristics, population, malnutrition assessment tools and cut-offs, and quantitative results for all reported outcomes. The primary outcomes were complications related to delayed wound healing: **Surgical Site Infection (SSI)**, **Wound Dehiscence**, and **Anastomotic Leakage**. A comprehensive list of at least 12 secondary outcomes was also extracted, including **Length of Hospital Stay (LOS)**, **30-day Mortality**, **Hospital Readmission**, **Reoperation**, **Prolonged Postoperative Ileus (POI)**, and various systemic complications (pulmonary, cardiac, renal).

Quality Assessment and Risk of Bias Analysis

The methodological quality of each included non-randomized study was independently assessed by two reviewers using the Cochrane "Risk Of Bias In Non-randomized Studies - of Interventions" (ROBINS-I) tool (Sterne et al., 2016). The tool assesses bias across seven domains: (1) confounding, (2) selection of participants, (3) classification of exposures, (4) deviations from intended exposures, (5) missing data, (6) measurement of outcomes, and (7) selection of the reported result. Each domain was judged as "Low," "Moderate," "Serious," or "Critical" risk of bias, leading to an overall risk of bias judgment for each study outcome⁽⁶⁾.

RESULTS

Study Selection and Characteristics

The literature search yielded 3,128 records, and after a multi-stage screening process, 25 studies met the inclusion criteria. These comprised four meta-analyses, two systematic reviews, and nineteen observational cohort studies. The included studies were geographically diverse and covered a wide range of surgical specialties, including general, gastrointestinal, orthopedic, and spinal surgery. A significant degree of heterogeneity was observed in the tools used to define malnutrition, ranging from single biomarkers to comprehensive multi-component scoring systems. The characteristics of the included studies are detailed in Table 1.

Table 1: Characteristics of Included Studies

Study Design	Population (N, Surgery Type)	Malnutrition Assessment Tool(s) & Cut-off
Meta-analysis	22 studies; Spinal Surgery	Various (Albumin, TLC, etc.)
Meta-analysis	12 studies (446,501); Total Joint Arthroplasty	Serological (Albumin, TLC, Transferrin)
Prospective Cohort	440; General Surgery	Not specified
Systematic Review	15 studies; Elderly General Surgery	Weight loss $\geq 10\%$, Serum albumin

Study Design	Population (N, Surgery Type)	Malnutrition Assessment Tool(s) & Cut-off
Meta-analysis	11 studies (3,527); Abdominal Surgery	Nutritional Risk Screening 2002 (NRS-2002) ≥ 3
Prospective Cohort	190; Emergency Abdominal Surgery	Serum albumin <3.5 g/dL
Retrospective Cohort	268; Oral Squamous Cell Carcinoma Surgery	Serum albumin (stratified)
Prospective Cohort	80; Elective Midline Abdominal Surgery	Serum albumin <3.5 g/dL
Prospective Cohort	60; Emergency Abdominal Surgery	Serum albumin <3.5 g/dL
Prospective Cohort	60; Emergency Exploratory Laparotomy	Serum albumin <3.5 g/dL
Retrospective Cohort	320; Perforated Peptic Ulcer Surgery	Prognostic Nutritional Index (PNI) (stratified)

Study Design	Population (N, Surgery Type)	Malnutrition Assessment Tool(s) & Cut-off
Prospective Cohort	2,161; Elective Total Joint Arthroplasty	Albumin or Transferrin (abnormal)
Prospective Cohort	588; General Surgery	NRS-2002 ≥ 3 , SGA
Prospective Cohort	139; Major Abdominal Surgery	PG-SGA, NRI, Albumin, NRS-2002, MUST
Cross-sectional	393; Elective Abdominal Surgery	BMI < 18.5 kg/m ² , SGA (B or C)
Prospective Cohort	200; Major Abdominal Surgery	SGA (B or C), Albumin < 3.0 g/dL
Cohort Study	119; Hip and Knee Arthroplasty	Albumin < 3.4 g/L, TLC < 1200 cells/ μ L
Retrospective Cohort	1,022; Primary Knee Arthroplasty	Serum albumin < 3.5 g/dL
Retrospective Cohort	268; Elective Primary TKA	CONUT score ≥ 2

Study Design	Population (N, Surgery Type)	Malnutrition Assessment Tool(s) & Cut-off
Prospective Cohort	150; Emergency Major Abdominal Surgery	CONUT, PNI, NRI
Prospective Cohort	315; General Surgery	NRS 2002 ≥ 3
Retrospective Cohort	578; Gastric Cancer	Nutritional Risk Index (NRI) <96.7
Retrospective Cohort	228; Gastric Cancer	PNI <45
Cross-sectional	246; Elective Abdominal Surgery	SGA, Serum albumin
Prospective Cohort	200; Major Abdominal Surgery	SGA, BMI, Serum albumin <3.0 g/dL

TLC: Total Lymphocyte Count; PNI: Prognostic Nutritional Index; SGA: Subjective Global Assessment; PG-SGA: Patient-Generated SGA; NRI: Nutritional Risk Index; MUST: Malnutrition Universal Screening Tool; BMI: Body Mass Index; TKA: Total Knee Arthroplasty; CONUT: Controlling Nutritional Status.

Diversity of Malnutrition Assessment Tools

A notable finding was the wide variety of tools used to assess nutritional status, reflecting a lack of a single gold standard in clinical practice. These tools ranged from simple, single-parameter

assessments to complex, multi-component indices. Table 2 provides an overview of the primary tools identified in this review.

Table 2: Overview of Malnutrition Assessment Tools and Criteria

Tool Name	Key Components	Example Cut-off for Risk	Studies Using Tool (Author, Year)
Serum Albumin	Single serological biomarker	<3.5 g/dL	(Sharath Kumar et al., 2019; Ali et al., 2024; Kumar et al., 2025; Naga Rohith et al., 2022; Vinay et al., 2022)
NRS-2002	Weight loss, BMI, food intake, disease severity, age	Score ≥ 3	(Li et al., 2015; Schwegler et al., 2010; Vora, Shah and Patel, 2018)
SGA / PG-SGA	History (weight, intake, GI symptoms, function) & Physical exam (fat/muscle loss, edema)	Grade B (moderate) or C (severe)	(Schwegler et al., 2010; Singh et al., 2025; Kumar et al., 2024; Vora, Shah and Patel, 2018;)

Tool Name	Key Components	Example Cut-off for Risk	Studies Using Tool (Author, Year)
PNI	Serum albumin, Total lymphocyte count	Varies by study (e.g., <45)	(Liu et al., 2024)
CONUT Score	Serum albumin, Total lymphocyte count, Total cholesterol	Score ≥ 2	(⁷ ; ⁸)
NRI	Serum albumin, current/usual weight ratio	Varies by study (e.g., <96.7)	(Vora, Shah and Patel, 2018)
Serological Panel	Combination of Albumin, TLC, and/or Transferrin	Abnormal value in one or more	(Lin et al., 2023; Huang et al., 2013; Lavernia, Sierra and Gomez-Marin, 1999)

Quality Assessment of Included Studies

The risk of bias for the 19 included observational studies was assessed using the ROBINS-I tool (Table 3). The overall methodological quality was variable. The majority of studies (n=13) were

rated as having a "Moderate" overall risk of bias, while six were rated as "Serious." No study was rated at a "Critical" risk of bias. The most common source of potential bias was **confounding**, as many studies did not perform adequate multivariable adjustment for key prognostic factors such as age, comorbidities, and underlying disease severity.

Table 3: Cochrane Risk of Bias (ROBINS-I) Assessment Summary

Study	D1: Confounding	D2: Selection	D3: Classification of Exposure	D4: Deviations from Exposure	D5: Missing Data	D6: Outcome Measurement	D7: Selection of Result	Overall Risk of Bias
Al-Khyat et al. (2024)	Serious	Moderate	Low	Low	Low	Low	Low	Serious
Sharith Kumar et al. (2019)	Moderate	Low	Low	Low	Low	Low	Low	Moderate

Khan et al. (2021)	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
Ali et al. (2024)	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Kumar et al. (2025)	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Nagarohith et al. (2022)	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Liu et al. (2024)	Serious	Moderate	Low	Low	Moderate	Low	Low	Serious
Huang et al. (2013)	Serious	Low	Low	Low	Moderate	Low	Low	Serious

Schwe gler et al. (2010)	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Vora, Shah and Patel (2018)	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Singh et al. (2025)	Moderate	Moder ate	Moder ate	Low	Low	Low	Low	Moderate
Kuma r et al. (2024)	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Laver nia, Sierra and Gome z-	Serious	Moder ate	Low	Low	Moder ate	Moder ate	Low	Serious

Marin (1999)								
Vinay et al. (2022)	Serious	Moderate	Low	Low	Low	Low	Low	Serious

Synthesis of Findings: Association Between Malnutrition and Wound Healing Outcomes

The synthesized evidence demonstrates a strong and consistent association between preoperative malnutrition and an increased risk of wound healing complications across different surgical settings.

Surgical Site Infection (SSI): Malnutrition was identified as a major independent risk factor for SSI. A meta-analysis on spinal surgery found that malnourished patients were more than twice as likely to develop an SSI (OR = 2.31, 95% CI: 1.75–3.05) (Tsantes et al., 2020). In orthopedic surgery, serologic malnutrition was associated with a nearly threefold increase in the odds of both superficial (OR = 2.89) and deep incisional SSI (OR = 3.06) (Lin et al., 2023). This finding was corroborated in studies of abdominal surgery, where SSI rates were significantly higher in malnourished groups, with reported rates of 30.3% vs. 11.5% (p<0.001) and 40% vs. 20% (p=0.001) in two separate prospective cohorts (Kumar et al., 2024; Kumar et al., 2025). A retrospective study using the CONUT score found an even greater risk, with an adjusted OR of 4.12 for infection in at-risk patients .

Wound Dehiscence and Disruption: The integrity of the surgical wound was also significantly compromised. A meta-analysis found that malnutrition increased the risk of wound disruption in joint arthroplasty patients (OR = 1.97) (Lin et al., 2023). A study in oral cancer surgery patients identified preoperative serum albumin as the *only* significant predictor of wound dehiscence, with moderately low albumin (3.5-3.9 g/dL) increasing the odds by 3.24 times (p=0.005) (Khan et

al., 2021). In abdominal surgery, dehiscence rates were starkly different between hypoalbuminemic and normal groups: 24.0% vs. 5.0% ($p<0.05$) and 17% vs. 3% ($p=0.02$) in two prospective studies (Ali et al., 2024; Kumar et al., 2025).

Anastomotic Leakage: For patients undergoing gastrointestinal surgery, malnutrition severely impairs the healing of internal anastomoses. One study reported that anastomotic leaks occurred in 20% of patients with severe hypoalbuminemia (<2.0 g/dL), while no leaks were observed in patients with higher albumin levels (Naga Rohith et al., 2022). A retrospective analysis of gastric cancer surgery also found significantly higher rates of anastomotic leak in patients with poor nutritional status.

Table 4: Summary of Associations with Wound-Related Complications

Outcome	Study (Author, Year)	Malnutrition Marker	Result (e.g., OR [95% CI], p-value)
Surgical Site Infection (SSI)	Tsantes et al. (2020)	Various	OR = 2.31 [1.75-3.05]
	Lin et al. (2023)	Serological	Deep SSI: OR = 3.06 [2.36-3.96]
	Kumar et al. (2024)	SGA B or C	30.3% vs. 11.5% ($p<0.001$)
		CONUT ≥ 2	aOR = 4.12 [1.33-12.7]

Outcome	Study (Author, Year)	Malnutrition Marker	Result (e.g., OR [95% CI], p-value)
Wound Dehiscence / Disruption	Lin et al. (2023)	Serological	OR = 1.97 [1.53-2.53]
	Khan et al. (2021)	Albumin 3.5-3.9 g/dL	OR = 3.24 [1.42-7.38]
	Kumar et al. (2024)	SGA B or C	9.8% vs. 2.6% (p=0.04)
	Kumar et al. (2025)	Albumin <3.5 g/dL	17% vs. 3% (p=0.02)
Anastomotic Leakage	Naga Rohith et al. (2022)	Albumin <2.0 g/dL	20% vs. 0% in higher albumin groups
		NRS-2002, BMI, Albumin	Significantly higher rate in malnourished group

Synthesis of Findings: Other Postoperative Complications

The detrimental impact of preoperative malnutrition extends far beyond the surgical wound, affecting nearly every aspect of the patient's postoperative course.

Length of Hospital Stay (LOS) and Healthcare Costs: A prolonged LOS was one of the most consistently reported outcomes. A meta-analysis involving patients undergoing abdominal surgery found that patients at nutritional risk (NRS-2002 ≥ 3) had a weighted mean difference in LOS of +5.58 days ($p < 0.00001$) (Li et al., 2015). Individual cohort studies reported similarly significant increases in mean LOS for malnourished patients, with differences of 3.34 days (Al-Khyatt et al., 2024), 3.4 days (Lavernia, Sierra and Gomez-Marin, 1999), and up to 12.2 days for severely malnourished patients (Singh et al., 2025). This extended hospitalization directly translates to increased healthcare costs, with one study finding that arthroplasty patients with hypoalbuminemia incurred 32.7% higher hospital charges ($p < 0.006$) (Lavernia, Sierra and Gomez-Marin, 1999).

Postoperative Mortality: Preoperative malnutrition was strongly and independently associated with an increased risk of postoperative death. A meta-analysis reported a pooled OR for mortality of 3.61 (95% CI: 1.38–9.47) for patients at nutritional risk (Li et al., 2015). Cohort studies echoed this finding, with 30-day mortality rates of 11.36% vs. 2.27% ($p < 0.001$) and 6.6% vs. 1.3% ($p = 0.04$) in malnourished versus well-nourished groups, respectively (Al-Khyatt et al., 2024; Kumar et al., 2024). In a high-risk population undergoing surgery for perforated peptic ulcers, a low Prognostic Nutritional Index (PNI) was confirmed as an independent predictor of mortality (OR = 1.09 per-point decrease, $p = 0.01$) (Liu et al., 2024).

Systemic Complications and Resource Utilization: The evidence consistently pointed to a higher risk of systemic complications and increased resource use. In a large study of joint arthroplasty patients, malnutrition predicted not only infections but also hematoma formation and both renal and cardiac complications (Huang et al., 2013). Malnourished patients were also more likely to require readmission (18.18% vs. 4.55%, $p < 0.001$) (Al-Khyatt et al., 2024), experience pulmonary

complications (17.2% vs. 7.7%, $p=0.03$) (Kumar et al., 2024), and suffer from prolonged postoperative ileus (Kang et al., 2022).

Table 5: Summary of Associations with Other Postoperative Outcomes

Outcome Category	Outcome	Study (Author, Year)	Result (e.g., OR [95% CI], Mean Diff., p-value)
Hospital Metrics	Length of Stay	Li et al. (2015)	WMD = +5.58 days [4.21-6.95]
		Al-Khyatt et al. (2024)	9.87 vs. 6.53 days ($p<0.001$)
		Singh et al. (2025)	16.7 vs. 4.5 days (SGA 'C' vs 'A')
	Readmission	Al-Khyatt et al. (2024)	18.18% vs. 4.55% ($p<0.001$)
	Increased Costs	Lavernia, Sierra and Gomez-Marin (1999)	32.7% higher charges for low albumin ($p<0.006$)

Outcome Category	Outcome	Study (Author, Year)	Result (e.g., OR [95% CI], Mean Diff., p-value)
Mortality	Overall Mortality	Li et al. (2015)	OR = 3.61 [1.38-9.47]
	30-day Mortality	Al-Khyatt et al. (2024)	11.36% vs. 2.27% (p<0.001)
		Kumar et al. (2024)	6.6% vs. 1.3% (p=0.04)
Systemic Complications	Overall Complications	Huang et al. (2013)	12.0% vs. 2.9% (p<0.0001)
	Pulmonary Complications	Kumar et al. (2024)	17.2% vs. 7.7% (p=0.03)
	Renal Complications	Huang et al. (2013)	Malnutrition a significant predictor
	Cardiac Complications	Huang et al. (2013)	Malnutrition a significant predictor

Outcome Category	Outcome	Study (Author, Year)	Result (e.g., OR [95% CI], Mean Diff., p-value)
	Sepsis	Liu et al. (2024)	Significantly higher incidence in low PNI group (p<0.001)

DISCUSSION

Principal Findings: A Strong, Consistent Correlation

This systematic review synthesizes a substantial body of evidence from 25 distinct studies, confirming a robust, consistent, and statistically significant association between preoperative malnutrition and a wide spectrum of adverse postoperative outcomes. The core of this association lies in the increased incidence of complications related to delayed wound healing, such as surgical site infections, wound dehiscence, and anastomotic leakage. This relationship holds true across a diverse range of surgical populations—encompassing general, gastrointestinal, orthopedic, and spinal surgery—and is demonstrable regardless of the assessment tool used. The consistency of this effect, despite heterogeneity in study design and patient populations, strongly reinforces the validity and clinical relevance of this conclusion.

Pathophysiological Mechanisms and Clinical Implications

The strength of the observed association is well-supported by established pathophysiological principles. Preoperative malnutrition is an active state of systemic compromise that directly undermines the body's ability to recover from surgical stress. Protein-calorie malnutrition, often reflected by hypoalbuminemia, results in a diminished reserve of essential amino acids, which are

critical substrates for fibroblast proliferation, angiogenesis, and the synthesis of collagen (Stechmiller, 2010). This deficit leads directly to mechanically weaker wounds that are more prone to failure (Khan et al., 2021; Ali et al., 2024).

Furthermore, malnutrition induces a state of immunodeficiency. The total lymphocyte count, a component of indices like the PNI, is often reduced, reflecting an impairment of both cell-mediated and humoral immunity that compromises the host's defense against bacterial contamination at the surgical site (Gawel, 2016). This provides a clear mechanistic explanation for the significantly higher rates of infectious complications observed in malnourished patients (Tsantes et al., 2020; Lin et al., 2023). The clinical implication is profound: it reframes malnutrition from a simple marker of poor health to a critical, modifiable target for preoperative intervention (Weimann et al., 2017).

Heterogeneity in Nutritional Assessment Tools

A key finding of this review is the significant heterogeneity in the methods used to define malnutrition (Table 2). Simple serological markers, particularly serum albumin, were commonly used due to their low cost and strong prognostic value (Moghadam et al., 2013; Gawel, 2016). However, albumin is a negative acute-phase reactant, meaning its concentration decreases in response to systemic inflammation, independent of nutritional status (Kumar et al., 2025). Therefore, while low albumin is a powerful predictor of poor outcomes, it reflects both chronic nutritional depletion and acute inflammation.

More comprehensive tools, such as the Subjective Global Assessment (SGA) and the Patient-Generated SGA (PG-SGA), incorporate patient history and physical examination to provide a more holistic picture (Vora, Shah and Patel, 2018). These tools are well-validated but are more time-consuming and subject to inter-observer variability. Composite, objective scoring systems like the NRS-2002, PNI, and CONUT score represent an effort to combine objective laboratory data with clinical context (Li et al., 2015; Liu et al., 2024; ⁷). The fact that all these different tools consistently identify a patient population at higher risk reinforces the central conclusion that a compromised nutritional and metabolic state, however measured, is a critical determinant of surgical outcome.

Strengths, Limitations, and Heterogeneity of the Evidence

The primary strength of this review lies in its broad and comprehensive scope, synthesizing a large body of evidence across multiple surgical specialties and analyzing over 15 distinct outcomes. The rigorous quality assessment using the ROBINS-I tool is another key strength (Sterne et al., 2016). The principal limitation is its reliance on observational data. As identified in the ROBINS-I assessment, the risk of bias due to confounding was moderate to serious in most studies. It is inherently difficult to fully disentangle the effects of malnutrition from the effects of the underlying disease severity that may have caused it. While many studies attempted statistical adjustment, residual confounding likely remains. Furthermore, significant heterogeneity was present across the studies in terms of patient populations, surgical complexity, and definitions of malnutrition, which precluded a formal meta-analysis of all outcomes. However, the consistency of the association despite these variations suggests the finding is robust and generalizable across the field of surgery.

CONCLUSION AND RECOMMENDATIONS

Conclusion

The evidence synthesized in this systematic review is compelling and unequivocal. Preoperative malnutrition, identified through a variety of clinical and laboratory measures, stands as a powerful and independent predictor of delayed wound healing and a broad array of adverse postoperative outcomes. The association is a pervasive issue across the surgical landscape, significantly increasing the risk of direct wound complications, overall morbidity, mortality, prolonged hospital stays, and increased healthcare costs. The consistency and strength of these findings underscore the critical importance of a patient's nutritional status as a fundamental determinant of their ability to successfully navigate the physiological stress of surgery.

Recommendations for Clinical Practice and Future Research

Based on the robust evidence presented, the following recommendations are proposed.

For Clinicians and Healthcare Systems:

1. **Implement Universal Nutritional Screening:** Routine preoperative nutritional screening should be adopted as a standard of care for all patients scheduled for major surgery. Simple, validated tools like the NRS-2002 or a combination of serum albumin and recent weight loss can be effectively integrated into preoperative pathways.
2. **Establish Pathways for Nutritional Optimization:** Patients identified as being at nutritional risk should be referred for comprehensive assessment and intervention. Where feasible, a period of preoperative nutritional optimization (7 to 14 days) involving high-protein oral nutritional supplements or specialized nutrition should be strongly considered.

For Future Research:

1. **Conduct High-Quality Intervention Trials:** There is a need for more high-quality randomized controlled trials (RCTs) to determine the most effective, patient-specific, and cost-effective strategies for preoperative nutritional intervention.
2. **Standardize Definitions and Outcomes:** Future studies should strive to use standardized, validated definitions of malnutrition and report on a core set of universally accepted postoperative outcomes to reduce heterogeneity and facilitate future meta-analyses.
3. **Investigate Cost-Effectiveness:** Research should be directed toward evaluating the cost-effectiveness of implementing systematic screening and nutritional support programs to drive widespread adoption and policy change.

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