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The effect of glutamine supplementation on mortality, length of hospital stay, and systemic infections in burn patients: A systematic review and meta-analysis of randomized controlled trials

Pengaruh suplementasi glutamin dalam mortalitas, lama rawat inap, dan infeksi sistemik pada pasien luka bakar: Tinjauan sistematis dan meta-analisis uji klinis acak terkontrol

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Abstract

Background: The clinical benefits of glutamine supplementation in patients with burn injuries remain uncertain. Although glutamine has been proposed to support immune function and recovery, its effects on major clinical outcomes are inconsistent.
Objectives: This systematic review and meta-analysis evaluated the effects of glutamine supplementation on hospital length of stay, all-cause mortality, and systemic infectious complications in patients with burn injuries.
Methods: PubMed/MEDLINE, Scopus, and the Cochrane Library were searched through July 26, 2026, for randomized controlled trials comparing glutamine supplementation with placebo or standard care. The review was registered in PROSPERO (CRD420261461723). Pooled estimates were calculated using random-effects models.
Results: Eleven randomized controlled trials involving 1,662 participants were included. No statistically significant reductions were detected in hospital length of stay (mean difference, −3.22 days; 95% CI, −7.62 to 1.19), all-cause mortality (odds ratio, 0.92; 95% CI, 0.69–1.23), or systemic infectious complications (odds ratio, 0.97; 95% CI, 0.75–1.25). Heterogeneity was substantial for hospital length of stay (I^2 = 89%).
Conclusions: The pooled findings did not demonstrate a clear benefit of routine glutamine supplementation for these outcomes in patients with burn injuries. Interpretation remains limited by heterogeneity and uncertainty in the included evidence.

Keywords:
Burns, glutamine, hospitalization, meta-analysis, randomized controlled trials

Abstrak

Latar Belakang: Manfaat klinis suplementasi glutamin pada pasien luka bakar masih belum pasti. Meskipun glutamin diduga mendukung fungsi imun dan pemulihan, pengaruhnya terhadap luaran klinis utama belum menunjukkan hasil yang konsisten.

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Tujuan: Tinjauan sistematis dan meta-analisis ini mengevaluasi pengaruh suplementasi glutamin terhadap lama rawat inap, mortalitas semua penyebab, dan komplikasi infeksi sistemik pada pasien luka bakar.
Metode: Penelusuran PubMed/MEDLINE, Scopus, dan Cochrane Library dilakukan hingga 26 Juli 2026 untuk mengidentifikasi uji klinis acak terkontrol yang membandingkan suplementasi glutamin dengan plasebo atau perawatan standar. Tinjauan ini terdaftar di PROSPERO (CRD420261461723). Estimasi gabungan dihitung menggunakan model efek acak.
Hasil: Sebanyak 11 uji klinis acak terkontrol dengan 1.662 peserta diikutsertakan. Tidak ditemukan penurunan yang bermakna secara statistik pada lama rawat inap (selisih rerata, −3,22 hari; IK 95%, −7,62 hingga 1,19), mortalitas semua penyebab (rasio odds, 0,92; IK 95%, 0,69–1,23), maupun komplikasi infeksi sistemik (rasio odds, 0,97; IK 95%, 0,75–1,25). Heterogenitas lama rawat inap tergolong tinggi (I^2 = 89%).
Kesimpulan: Hasil gabungan tidak menunjukkan manfaat yang jelas dari suplementasi glutamin rutin terhadap luaran tersebut pada pasien luka bakar. Interpretasi masih dibatasi oleh heterogenitas dan ketidakpastian bukti yang tersedia.

Kata Kunci:
Glutamin, lama rawat inap, luka bakar, meta-analisis, uji klinis acak

Introduction

Severe burn injury induces profound and sustained systemic inflammation, oxidative stress, and immune dysfunction (Jeschke et al., 2020). These physiological disturbances may contribute to worse outcomes. Consequently, nutritional therapy is a fundamental component of comprehensive burn care. Beyond meeting energy and protein requirements, recent research has increasingly focused on targeted nutritional interventions that may modulate the metabolic, inflammatory, and immune responses associated with severe burn injury (Clark et al., 2017; Nunez & Clark, 2023).

Glutamine is an amino acid that serves as a key metabolic substrate for rapidly dividing cells (Cruzat et al., 2018). Under normal physiological conditions, endogenous glutamine synthesis is generally sufficient to meet metabolic demands. However, under conditions of severe metabolic stress, including major burn injury, glutamine requirements may exceed endogenous production, resulting in a relative deficiency. This condition renders glutamine conditionally essential. Glutamine supplementation has been proposed to support intestinal barrier integrity, glutathione synthesis, antioxidant defense, nitrogen metabolism, and immune function, providing a plausible biological rationale for its use in patients with severe burns (Abbasi et al., 2024; Achamrah et al., 2017; Ortiz-Reyes et al., 2023; Tao et al., 2024).

Despite this biological rationale, the clinical benefits of glutamine supplementation in patients with burn injuries remain uncertain. Randomized controlled trials have reported inconsistent findings regarding clinically important outcomes, including infectious complications, hospital length of stay, and mortality. Several earlier studies suggested potential benefits of glutamine supplementation, particularly in shortening hospitalization. In contrast, a subsequent large randomized trial has questioned these findings and challenged the routine administration of supplemental glutamine in critically ill and burn populations (Heyland et al., 2022). Variations in patient characteristics, burn severity, route and dose of glutamine administration, duration of supplementation, timing of intervention, and background nutritional therapy may contribute to the heterogeneity of the reported effects.

Previous meta-analyses have reached differing conclusions, and their estimates may depend on the trials included, intervention characteristics, and outcome definitions. Incorporating large contemporary randomized trials is particularly important when assessing mortality and infectious outcomes. A focused synthesis of the evidence is therefore clinically relevant.

Tao et al. (2024) synthesized 22 randomized trials; however, differing eligibility criteria, information sources, and outcome definitions can produce substantially different evidence bases. The present review included enteral and parenteral supplementation and focused on three outcomes: hospital length of stay, all-cause mortality, and systemic infectious complications. Evidence certainty was also assessed using the GRADE approach. Its contribution is therefore a focused evaluation of the magnitude and certainty of these associations, rather than the inclusion of the largest possible number of trials.

This systematic review and meta-analysis aimed to evaluate the effects of glutamine supplementation on hospital length of stay, all-cause mortality, and systemic infectious complications in patients with burn injuries.

Methods

Study Design and Reporting Guidelines

The methodology and reporting of this systematic review and meta-analysis followed the recommendations outlined in the PRISMA 2020 guidelines (Page et al., 2021). Before study selection and data extraction began, its protocol was registered in PROSPERO (CRD420261461723).

Eligibility Criteria

Studies were eligible if they (1) were randomized controlled trials, (2) enrolled patients with burn injuries, (3) compared glutamine supplementation with placebo or standard nutritional care without additional glutamine, and (4) reported at least one prespecified outcome: hospital length of stay, all-cause mortality, or systemic infectious complications.

Observational and nonrandomized studies, case reports and case series, review articles, and conference abstracts without adequate outcome data were excluded. Animal and in vitro studies were also excluded. Studies of multicomponent interventions were ineligible when the independent contribution of glutamine could not be determined.

Information Sources and Search Strategy

PubMed/MEDLINE, Scopus, and the Cochrane Library were searched from database inception through July 26, 2026. Only English- or Indonesian-language publications were eligible. The database-specific search strategies were as follows. PubMed/MEDLINE: ("Burns"[MeSH] OR burn*[Title/Abstract] OR "burn injury"[Title/Abstract] OR "thermal injury"[Title/Abstract]) AND ("Glutamine"[MeSH] OR glutamine [Title/Abstract] OR "glutamine supplementation"[Title/Abstract]). Scopus: TITLE-ABS-KEY (burn OR "burn injury" OR "thermal injury") AND TITLE-ABS-KEY (glutamine OR "glutamine supplementation"). Cochrane Library: ([mh Burns] OR burn*,ab,kw OR "burn injury",ab,kw OR "thermal injury",ab,kw) AND ([mh Glutamine] OR glutamine,ab,kw OR "glutamine supplementation",ab,kw).

Randomized-trial filters were applied when available in the respective databases. Reference lists of eligible trials and relevant systematic reviews were manually screened for additional studies. Trial registries and gray literature databases were not searched, and forward citation searching was not performed.

Study Selection

Retrieved records were managed in Rayyan, and duplicates were removed before screening. Two reviewers independently assessed titles and abstracts. Potentially eligible reports and those that could not be excluded confidently were assessed in full text. Disagreements were resolved by discussion and, when necessary, adjudication by a third reviewer.

Data Extraction

Two reviewers independently extracted study-level information using a prespecified framework. Extracted characteristics included first author, publication year, geographic setting, study design, sample size, patient characteristics, and burn severity, including the percentage of total body surface area (TBSA) affected. Intervention details included the route, dose, and duration of glutamine supplementation; comparator characteristics; follow-up duration; and outcomes of interest.

The primary outcomes assessed were hospital length of stay, all-cause mortality, and systemic infectious complications. Numerical outcome data were collected according to their measurement scale. For continuous variables, group-level estimates of central tendency and dispersion were obtained as means and standard deviations (SDs), while binary outcomes were captured as event counts together with the corresponding number of participants in each study arm. Where studies presented continuous variables using medians accompanied by interquartile ranges or minimum–maximum values, these summary statistics were converted to approximate means and SDs (Wan et al., 2014). If the required data could not be derived from the published information, the study was excluded from the quantitative synthesis of that specific outcome.

Risk of Bias Assessment

Two reviewers independently assessed the risk of bias in the included trials using the original

Cochrane Risk of Bias tool (RoB 1). Overall risk was classified as low if every domain was judged low risk, high if any domain was judged high risk, and unclear if at least one domain was judged unclear and none was judged high risk. Disagreements were resolved through discussion or third-reviewer adjudication.

Certainty of Evidence

Evidence certainty was assessed using the GRADE approach (Table 2). Certainty was rated very low for hospital length of stay because of risk of bias, substantial inconsistency (I^2 = 89%), and imprecision. Mortality and systemic infectious complications were each rated as moderate-certainty evidence because of imprecision.

Table 2. GRADE summary of findings

Outcome	Studies (participants)	Effect estimate	Main GRADE concerns	Certainty
Hospital length of stay	9 (1,578)	MD −3.22 days (95% CI −7.62 to 1.19)	Risk of bias, serious inconsistency (I^2=89%), imprecision	Very low ⊕◯◯◯
All-cause mortality	6 (1,437)	OR 0.92 (95% CI 0.69–1.23)	Imprecision	Moderate ⊕⊕⊕◯
Systemic infectious complications	6 (1,467)	OR 0.97 (95% CI 0.75–1.25)	Imprecision	Moderate ⊕⊕⊕◯

Outcomes

Hospital length of stay was analyzed as a continuous outcome and summarized using mean differences (MDs) and 95% confidence intervals (CIs). All-cause mortality and systemic infectious complications were summarized using odds ratios (ORs) and 95% CIs. Definitions of systemic infectious complications were retained as reported in the individual trials because diagnostic criteria differed across studies.

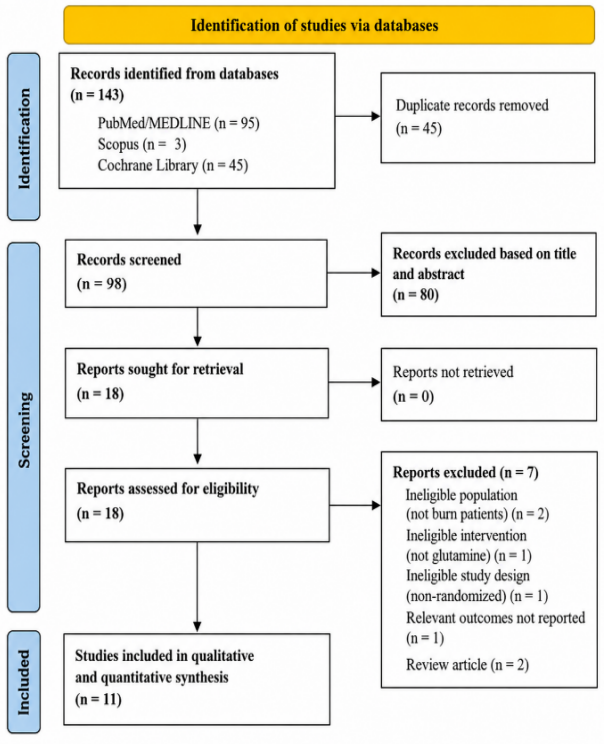


Figure 1. PRISMA flow diagram of study selection.

Study Selection

The search identified 143 records: 95 from PubMed/MEDLINE, 45 from the Cochrane Library, and three from Scopus. After removal of 45 duplicates, 98 records remained for screening. Of these, 80 were excluded, leaving 18 reports for full-text assessment. Seven reports were excluded (five for lack of relevance and two review articles). Eleven trials were included in the review (Figure 1).

Statistical Analysis

Quantitative analyses were conducted using Review Manager (RevMan), version 5.4 (The Cochrane Collaboration). Continuous outcomes measured on a common scale were pooled as mean differences (MDs), and binary outcomes were pooled as odds ratios (ORs).

Between-study heterogeneity was assessed using Cochran's Q statistic and quantified using I^2. A random-effects model was specified a priori for all analyses because clinical variation was anticipated in burn severity and glutamine dose, route, and duration. Between-study variance (τ^2) was estimated using the DerSimonian–Laird method. Exploratory assessment of potential sources of heterogeneity was planned where the available data permitted.

Funnel plots were not constructed because fewer than 10 studies contributed to each outcome, limiting their interpretability.

Results

Study Characteristics

The 11 trials were published between 2001 and 2022 and included 1,662 participants: 829 received glutamine and 833 received placebo or standard care. Trial sample sizes ranged from 26 to 1,200 participants. Reported settings included China, Egypt, India, Romania, Canada, the United Kingdom, the United States, and a multinational trial conducted in 14 countries.

Most trials reportedly enrolled patients with moderate-to-severe burns, generally involving at least 20% of total body surface area. Supplementation was typically initiated within 24–72 hours of injury or admission. Weight-based doses ranged from 0.35 to 0.57 g/kg/day, most often approximately 0.50 g/kg/day; two trials used fixed daily doses of 17–26 g. Five trials administered glutamine enterally and six parenterally.

Supplementation generally continued for 7–14 days, although some protocols continued treatment until a clinical milestone, such as wound healing, skin grafting, or discharge. Considerable variation was observed in burn severity, timing, dose, administration route, and duration (Table 1). The small number of trials limited the feasibility of reliable subgroup analyses and meta-regression by administration route, dose, burn severity, or study size. Consequently, possible sources of clinical heterogeneity could not be adequately evaluated.

Hospital Length of Stay

Nine trials involving 1,578 participants contributed to the analysis of hospital length of stay. The pooled estimate favored glutamine numerically but was imprecise and not statistically significant (MD, −3.22 days; 95% CI, −7.62 to 1.19; p = 0.15). Between-study heterogeneity was substantial (I^2 = 89%; p < 0.00001; Figure 2).

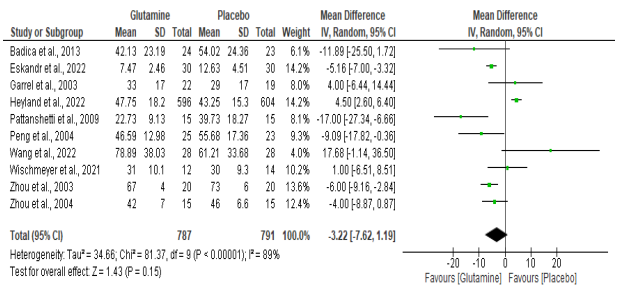


Figure 2. Forest plot of glutamine supplementation and hospital length of stay in patients with burns.

Mortality

Six trials involving 1,437 participants contributed to the mortality analysis. There were 110 deaths among 715 glutamine recipients and 118 among 722 controls. No statistically significant difference in all-cause mortality was detected (OR, 0.92; 95% CI, 0.69–1.23; p = 0.59; I^2 = 41%; Figure 3).

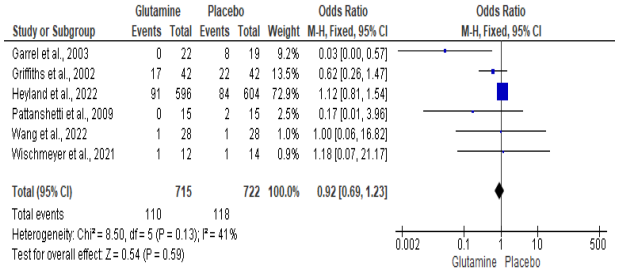


Figure 3. Forest plot of glutamine supplementation and all-cause mortality in patients with burns.

Systemic Infectious Complications

Six trials involving 1,467 participants contributed to the analysis of systemic infectious complications. Events occurred in 156 of 730 glutamine recipients and 160 of 737 controls. The pooled estimate did not show a statistically significant difference (OR, 0.97; 95% CI, 0.75–1.25; p = 0.81; I^2 = 35%; Figure 4).

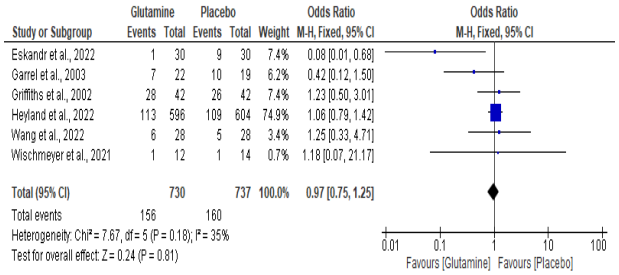


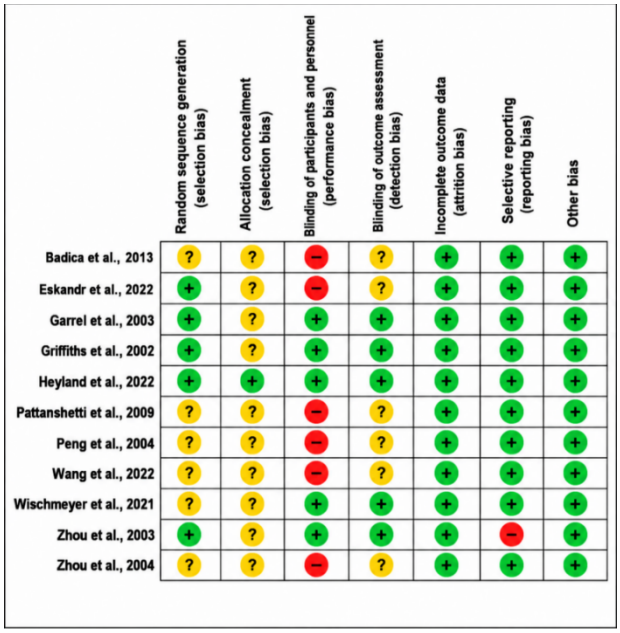
Figure 4. Forest plot of glutamine supplementation and systemic infectious complications in patients with burns.

Risk of Bias Assessment

Risk-of-bias judgments varied across trials. Incomplete outcome data were generally assessed as low risk, whereas several reports provided insufficient information on random-sequence generation or allocation concealment, resulting in unclear risks of selection bias.

Blinding of participants and personnel was absent or inadequately reported in several trials, raising concerns about performance bias. Blinding of outcome assessors was also unclear in some studies. More recently published trials generally

received more favorable ratings than several smaller, older trials (Figure 5).



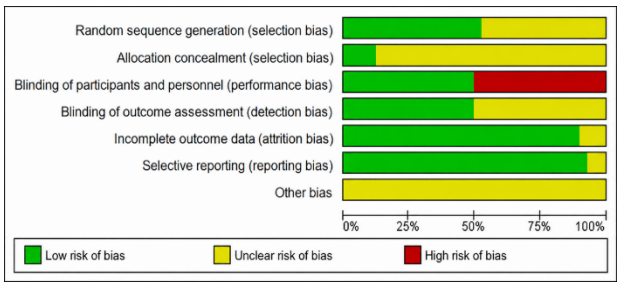


Figure 5. Risk-of-bias assessment of the randomized controlled trials included in the review.

Table 1. Characteristics of randomized controlled trials included in the systematic review and meta-analysis

Study and setting	Study characteristics	Glutamine intervention	Participants and age
Heyland et al. (2022); 14 countries; RCT	TBSA >20%; admission ≤72 h after injury	0.50 g/kg/day; enteral; administered until 7 days after the last skin-grafting procedure, discharge from the acute care unit, or 3 months after admission	Glutamine: n=596, 49.7 ± 18.1 years; Placebo: n=604, 49.1 ± 17.8 years
Wang et al. (2022); China; RCT	TBSA 30–70%; admission ≤24 h after injury	0.50 g/kg/day; parenteral; 14 days	Glutamine: n=28, 37.5 ± 9.9 years; Placebo: n=28, 37.7 ± 11.6 years
Eskandr et al. (2022); Egypt; RCT	TBSA 20–60%; admission ≤72 h after injury	0.50 g/kg/day; parenteral; 7 days	Glutamine: n=30, 30.3 ± 9.0 years; Placebo: n=30, 30.5 ± 7.5 years
Pattanshetti et al. (2009); India; RCT	TBSA 20–60%; admission ≤72 h after injury	0.50 g/kg/day; enteral; until complete wound healing or after skin grafting	Glutamine: n=15, 33.9 ± 0.0 years; Placebo: n=15, 29.1 ± 9.2 years
Peng et al. (2004); China; RCT	TBSA 30–75%; admission ≤48 h after injury	0.50 g/kg/day; enteral; 14 days	Glutamine: n=25, 36.5 ± 11.4 years; Placebo: n=23, age NR
Cucereanu-Bădică et al. (2013); Romania; RCT	TBSA >25%; admission ≤72 h after injury	0.50 g/kg/day; parenteral; at least 24 days	Glutamine: n=24, 34.2 ± 10.2 years; Placebo: n=23, 30.5 ± 11.9 years
Garrel et al. (2003); Canada; RCT	TBSA 30–80%; time to admission NR	26 g/day; enteral; at least 10 days	Glutamine: n=22, 38.0 ± 7.0 years; Placebo: n=19, 38.0 ± 18.0 years
Griffiths et al. (2002); United Kingdom; RCT	TBSA NR; time to admission NR	17–24 g/day; parenteral; at least 5 days	Glutamine: n=42, 65 (45–72) years; Placebo: n=42, 63 (54–72) years
Zhou et al. (2003); China; RCT	TBSA 50–80%; time to admission	0.50 g/kg/day; enteral; 12 days	Glutamine: n=20, 43.7 ± 3.8 years; Placebo:

	NR		n=20, 40.0 ± 4.3 years
Zhou et al. (2004); China; RCT	TBSA 30–50%; time to admission NR	0.35 g/kg/day; parenteral; 12 days	Glutamine: n=15, 34.6 ± 7.8 years; Placebo: n=15, 33.4 ± 8.1 years
Wischmeyer et al. (2001); United States; RCT	TBSA >25%; admission ≤72 h after injury	0.57 g/kg/day; parenteral; at least 7 days	Glutamine: n=12, 30 ± 22 years; Placebo: n=14, 39 ± 16 years

Abbreviations: NR, not reported; RCT, randomized controlled trial; SD, standard deviation; TBSA, total body surface area. Ages are presented as means ± SDs or medians (interquartile ranges), as reported in the original studies.

Discussion

The pooled analyses did not demonstrate statistically significant reductions in hospital length of stay, all-cause mortality, or systemic infectious complications with glutamine supplementation. Although the mean difference for hospital length of stay numerically favored glutamine, its confidence interval included both benefit and no benefit, and between-study heterogeneity was substantial. The findings therefore do not establish that glutamine improves these patient-centered outcomes in an unselected burn population.

These findings differ from several earlier meta-analyses that reported favorable effects of glutamine supplementation. Made et al. (2022) found that enteral glutamine supplementation was associated with shorter hospital stay and a lower incidence of positive wound cultures (Made et al., 2022). Similarly, Mortada et al. (2023), in a meta-analysis of seven RCTs involving 328 patients, reported significant reductions in mortality and infectious morbidity (Mortada et al., 2023).

Differences from earlier reviews may reflect variation in eligibility criteria, patient populations, burn severity, intervention dose and route, treatment duration, and trial size. The large contemporary randomized trial contributed substantial weight to the evidence base. However, available data do not establish whether discrepancies across reviews are caused by trial size, publication bias, or other methodological differences.

More recent evidence has produced less consistent results. Yue et al. (2024) evaluated six RCTs involving 1,398 patients receiving enteral glutamine and found no significant reductions in mortality or overall infectious morbidity, although hospital length of stay was reduced by approximately nine days (Yue et al., 2024). In contrast, the present analysis identified only a numerical reduction in hospital length of stay that did not reach statistical significance. One possible explanation is the substantial heterogeneity among the trials included in our analysis, suggesting that the effect of glutamine on hospitalization may vary considerably according to patient characteristics and treatment protocols.

Our findings are more consistent with the systematic review and trial sequential meta-analysis by Ortiz-Reyes et al. (2023). Their analysis of 10 RCTs involving 1,577 patients found no significant effects of enteral or intravenous glutamine on mortality, infectious complications, or other major clinical outcomes (Ortiz-Reyes et al., 2023). Notably, apparently favorable effects on mortality and infection were observed primarily in single-center studies but were not reproduced in multicenter trials. Trial sequential analysis suggested that some positive findings from smaller single-center studies could have resulted from type I error. These observations support the possibility that the discrepancy between early and contemporary evidence is related partly to study size and methodological quality.

Tao et al. (2024) subsequently reported a mixed pattern of findings after synthesizing 22 randomized trials involving 2,170 patients. Glutamine supplementation was associated with shorter hospitalization, improved wound healing, and reduced wound infection, but did not significantly reduce non-wound infections, in-hospital mortality, or intensive care unit length of stay (Tao et al., 2024).

Several methodological differences complicate comparisons with Tao et al. (2024). That review searched additional resources, including Embase, Google Scholar, Wanfang, and ClinicalTrials.gov, and evaluated a broader range of outcomes, including wound healing and wound infection. The present review was limited to three databases and three prespecified outcomes. More comprehensive searching and different outcome

definitions could explain some differences in the included evidence. Both reviews, however, reported no statistically significant reduction in mortality.

Yue et al. (2024) focused on enteral glutamine, whereas the present review considered enteral and parenteral administration. Differences in search coverage, intervention route, outcome definitions, and trial eligibility can affect pooled estimates. Such differences should be addressed explicitly before drawing conclusions about the comparative findings of these reviews.

The considerable heterogeneity observed for hospital length of stay is clinically plausible. The included trials differed substantially in burn severity, timing of supplementation, route of administration, glutamine dose, and treatment duration (Ortiz-Reyes et al., 2023; Tao et al., 2024). Most trials administered approximately 0.5 g/kg/day, although weight-based doses ranged from 0.35 to 0.57 g/kg/day, while other studies used fixed daily doses. Treatment duration ranged from several days to several weeks or was determined by clinical milestones such as wound healing or skin grafting. In addition, both enteral and parenteral routes were represented. Differences in route, dose, and timing may therefore contribute to variability in clinical response, particularly in view of the dynamic metabolic alterations associated with critical illness and severe burn injury (Nunez & Clark, 2023; Singer et al., 2023).

Hospital length of stay is also influenced by numerous factors that are not necessarily related to the biological effects of glutamine. Patients with severe burns may require repeated surgery, skin grafting, wound care, rehabilitation, or prolonged treatment of complications, while discharge practices may vary substantially between institutions (Żwierełło et al., 2023). Therefore, the numerical reduction observed in this analysis cannot be interpreted as definitive evidence of clinical benefit. Future trials may benefit from incorporating more standardized outcomes such as time to definitive wound closure, intensive care unit-free days, or duration of mechanical ventilation.

The lack of a statistically significant mortality benefit is also biologically plausible. Mortality after severe burn injury is determined by multiple interacting factors, including age, burn extent, inhalation injury, organ dysfunction, and sepsis (Rehan et al., 2023; Zeaiter et al., 2025). Consequently, modulation of a single nutritional substrate may be insufficient to produce a measurable survival effect in a heterogeneous population of critically ill patients. Differences in baseline mortality risk and contemporary burn management across the included studies may have further contributed to variability in treatment effects.

Similarly, glutamine supplementation was not associated with a statistically significant reduction in systemic infectious complications. This result is notable because infection prevention has historically been one of the principal proposed benefits of glutamine. Glutamine may support intestinal barrier integrity, lymphocyte proliferation, macrophage activity, and glutathione synthesis, providing a plausible mechanistic basis for an anti-infective effect. Nevertheless, beneficial effects reported in several early small trials were not consistently reproduced when larger contemporary studies were incorporated into pooled analyses (Wischmeyer et al., 2001; Zhou et al., 2003). This suggests that favorable effects on immunological or biochemical pathways may not necessarily translate into a clinically meaningful reduction in systemic infection.

These findings should also be considered within the evolving concept of pharmaconutrition in critical illness. Earlier nutritional paradigms generally viewed glutamine depletion as a deficiency that could be corrected through supplementation. However, more recent evidence suggests that nutrient metabolism during critical illness is substantially more complex, with the effects of nutritional interventions influenced by disease phase, organ function, nutritional status, timing, dose, and route of administration (Cruzat et al., 2018; Singer et al., 2023). Contemporary critical care nutrition has therefore increasingly emphasized targeted and individualized nutritional strategies rather than uniform supplementation across heterogeneous critically ill populations (Singer et al., 2023). In patients with severe burns, recent randomized and pooled evidence similarly suggests that the clinical response to glutamine is not uniform across patient populations and treatment settings (Heyland et al., 2022; Ortiz-Reyes et al., 2023).

Strengths of this review include its focus on randomized trials, inclusion of a large multinational trial, and assessment of clinically relevant outcomes. Important limitations include substantial

heterogeneity for hospital length of stay, variability in dose, route, timing, duration, burn severity, and background nutrition, and differing definitions of systemic infection. Searching only three databases, excluding trial registries and gray literature, and restricting publication language may have omitted eligible studies. Small sample sizes and incomplete reporting in several older trials also limited risk-of-bias assessment. Data were insufficient for robust subgroup analyses or meta-regression, and funnel plots were not considered informative because each outcome included fewer than 10 studies.

On the evidence as reported, routine glutamine supplementation cannot be recommended solely to shorten hospitalization or reduce mortality or systemic infectious complications in unselected patients with burns. Future research should examine whether well-defined subgroups respond differently and should standardize dose, route, timing, treatment duration, and relevant clinical and nutritional characteristics.

Conclusion

In this meta-analysis, glutamine supplementation was not associated with statistically significant reductions in hospital length of stay, all-cause mortality, or systemic infectious complications among patients with burn injuries.

The highly heterogeneous estimate for hospital stay warrants caution. Future studies should use consistent intervention protocols and prespecified, clinically meaningful outcomes.

Conflicts of Interest

The authors reported no conflicts of interest.

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