INPLASY

# Effects of Glutamine Supplementation on Clinical Outcomes and Nutritional Status in Patients with Cancer: A Systematic Review and Meta-Analysis

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**ADMINISTRATIVE INFORMATION**

**Support -** No support.

**Review Stage at time of this submission -** Data analysis.

**Conflicts of interest -** None declared.

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**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 September 2026 and was last updated on 18 September 2026.

## INTRODUCTION

**Review question / Objective** To undertake a systematic review and meta-analysis to examine the evidence base for the effects of glutamine supplementation on clinical outcomes and nutritional status in patients with cancer.

**Rationale** Cancer-related malnutrition is highly prevalent and worsens clinical outcomes, treatment tolerance, and quality of life. Glutamine, conditionally essential under catabolic stress, supports immune function, gut integrity, and nitrogen balance, making it a promising supportive intervention for cancer patients. However, existing evidence on glutamine in oncology remains inconclusive due to small sample sizes, heterogeneous protocols, and inconsistent outcome definitions. This systematic review and meta-analysis aims to comprehensively evaluate the effects of glutamine supplementation on clinical outcomes and nutritional status in patients with cancer. The findings may inform evidence-based nutritional recommendations and identify research gaps.

**Condition being studied** Cancer-related malnutrition and metabolic stress in patients with solid tumors or hematological malignancies. This condition is highly prevalent and clinically important because it arises from tumor-induced metabolic changes, reduced dietary intake, and treatment toxicities. It leads to immune dysfunction, increased infection risk, poor treatment tolerance, longer hospital stays, and reduced quality of life. Under catabolic stress, glutamine becomes conditionally essential because endogenous synthesis may be insufficient to meet increased demands for immune function, gut barrier integrity, and nitrogen balance. Glutamine depletion may further aggravate malnutrition and inflammation.

## METHODS

**Search strategy** The literature search strategy for this systematic review and meta-analysis covers databases in both English and Chinese, all built around three core elements—glutamine + cancer/neoplasm + clinical trial—with database-specific syntax. In PubMed, the search combines MeSH terms ("glutamine"[MeSH Terms] AND "neoplasms"[MeSH Terms]) with a clinical trial article type filter (clinicaltrial[Filter]). In MEDLINE (via EBSCO), the heading MH "Glutamine" is combined with cancer-related headings (MH "neoplasms" OR MH "cancer" OR MH "tumor" OR MH "malignan*"), restricted by the publication type PT "Clinical Trial". In Web of Science, topic searches TS=(glutamine) and TS=(cancer OR tumor OR neoplasm OR malignan*) are combined with the all-field qualifiers ALL=(clinical trial) OR ALL=(randomized controlled trial). In Scopus, the abstract search ABS(glutamine) is combined with ABS(neoplasm OR cancer OR tumor OR malignan*) and ABS("clinical trial" OR "randomized controlled trial"), limited to journal articles via LIMIT-TO (DOCTYPE, "ar"). In EMBASE, abstract fields are used: ('neoplasm':ab OR 'cancer':ab OR 'tumor':ab OR 'malignan*':ab) AND 'glutamine':ab, further restricted to clinical trials or randomized controlled trials ('clinical' AND 'trial':ab OR 'randomized' AND 'controlled' AND 'trial':ab). In CINAHL, the same abstract-field approach is applied: (AB neoplasm OR AB cancer OR AB tumor OR AB malignan*) AND (AB glutamine), restricted to (AB clinical trial) OR (AB randomized controlled trial). For the Chinese databases, the Wanfang Literature Database searches 摘要:(谷氨酰胺) [abstract: glutamine] combined with 摘要:(肿瘤) OR 摘要:(癌) [abstract: tumor OR cancer] and 摘要:(试验) [abstract: trial]; the China National Knowledge Infrastructure (CNKI) uses TKA='谷氨酰胺' combined with TKA='肿瘤' OR TKA='癌' and TKA='试验'; and the VIP Chinese Science and Technology Periodicals Database uses R=谷氨酰胺 combined with R=肿瘤 OR R=癌 and R=试验. Together, these strategies apply consistent concepts and restrictions across the English and Chinese databases.

**Participant or population** Tumor patients diagnosed clinically or confirmed by pathology (including solid tumors and hematological malignancies).

**Intervention** Glutamine or in combination with other substrates.

**Comparator** No-treatment control, or placebo product involving no additional nutritional supplementation or as the same supplementation as the intervention group without the ingredient of interest.

**Study designs to be included** Clinical trial.

**Eligibility criteria** Protocol or abstract, not report data of trails, was excluded.

**Information sources** PubMed, MEDLINE, Web of Science, EMBASE, CINAHL, Scopus, China Wanfang Literature Database, China National Knowledge Infrastructure (CNKI) and VIP Chinese Science and Technology Periodicals Database.

**Main outcome(s)** Clinical outcomes and nutritional status.

**Additional outcome(s)** Immune function and inflammatory markers.

**Data management** We conducted the data extraction and synthesis in SAS 9.4 software (SAS Institute Inc., Cary, NC, USA).

**Quality assessment / Risk of bias analysis** Risk of bias was assessed independently by two investigators according to the Version 2 of the Cochrane tool for assessing risk of bias in randomized trials (RoB 2). The risk-of-bias judgments are “low risk of bias,” “some concerns,” or “high risk of bias”, which based on, and summarize the answers to signalling questions within five distinct domains respectively (i.e. bias arising from the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of the reported result).

**Strategy of data synthesis** Meta-analyses of continuous outcomes were performed on the extracted data. For the measurement outcome measures, given the varying methods used to measure clinical outcomes and nutritional status respectively, standard mean difference (SMD) (Takeshima et al., 2014) with 95% confidence intervals (CIs) between treatment and control group were used to express intervention effect estimates. Where the mean of data was presented in the individual study, but without standard deviation (SD), SD was calculated from the reported standard error (SE) or 95% CIs . Studies reporting only median and interquartile range (IQR) were converted to mean and SD according to an established method (Luo et al., 2018, Wan et al., 2014). The hazard ratio (RR) and 95% confidence

interval (CI) were used to assess the intervention effect size for the classification outcome measures. Meta-analyses results are illustrated using a forest plot. Test for overall effect (Z score) was regarded significant at $P<0.05$.

**Subgroup analysis** Subgroup analyses will be performed according to different types and grades of complications, such as infection-related complications, oral mucositis (any grade and severe grade).

**Sensitivity analysis** Sensitivity analyses were also conducted for all outcomes by the "remove 1" technique. Such a procedure aimed to assess whether individual studies had a disproportionate effect on the results of the meta-analyses.

**Country(ies) involved** China.

**Keywords** glutamine; cancer; clinical outcomes, nutritional status, meta-analysis.

**Contributions of each author**
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