

EFFECTIVENESS OF NEUTROPENIC DIETS IN PREVENTING INFECTION AMONG CANCER PATIENTS: A REVIEW OF CURRENT EVIDENCE

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Abstract

Background: For decades, the neutropenic diet (ND) has served as a cornerstone of supportive oncology care. This paradigm is founded on the traditional premise that restricting raw produce and unpasteurized dairy minimizes the risk of food-borne infections and bacterial translocation. However, as contemporary oncology shifts toward evidence-based clinical practices, the therapeutic utility of these highly restrictive dietary protocols is under intense scrutiny.

Objective: This narrative review critically synthesizes contemporary literature to evaluate the clinical efficacy of the neutropenic diet compared to standard food safety protocols. Specifically, it assesses their relative impacts on preventing infection, reducing mortality, and maintaining the nutritional, biological, and psychological well-being of oncology patients.

Methods: A narrative analysis was conducted to synthesize findings from recent randomized controlled trials (RCTs), meta-analyses, and scoping reviews. The analysis encompasses both adult and pediatric oncology populations, with an emphasis on landmark syntheses published between 2006 and 2025.

Results: High-level evidence consistently demonstrates that the ND does not significantly reduce the incidence of febrile neutropenia, bacteremia, or mortality compared to standard food safety guidelines. This lack of superior efficacy persists even during periods of profound neutropenia, defined as an absolute neutrophil count (ANC) of less than 500 cells/ μ L. Mechanistically, removing dietary fiber leads to a systemic shift toward mucin-degrading gut bacteria. This erodes the protective inner epithelial mucus layer, increasing intestinal permeability and paradoxically facilitating the systemic translocation of opportunistic pathogens. Psychologically, the diet significantly diminishes quality of life (QoL) by inducing food-related anxiety and worsening treatment-induced anorexia.

Conclusion: International professional bodies now advocate for the liberalization of oncology diets. The transition from a "sterile plate" model to evidence-based food safety education (clean, separate, cook, chill) is heavily supported by modern data. Retiring the ND in favor of a nutrient-dense, fiber-rich approach supports both the biological barrier integrity and psychological resilience of oncology patients.

Keywords: Neutropenia, Oncology Nutrition, Neutropenic Diet, Food Safety, Febrile Neutropenia, Quality of Life, Gut Microbiome.

1. Introduction

The clinical management of cancer has seen revolutionary shifts in the 21st century, yet managing its most pervasive complication—febrile neutropenia—remains a foundational challenge in oncology care. Systemic treatments such as high-dose chemotherapy and hematopoietic stem cell transplantation (HSCT) are

engineered to eliminate rapidly dividing malignant cells. However, this cytotoxic action is non-discriminatory, frequently devastating the bone marrow's capacity to produce neutrophils. While mild neutropenia is clinically characterized by an absolute neutrophil count (ANC) dropping below 1,500 cells/ μL , the patient's clinical vulnerability peaks drastically when neutropenia becomes severe or profound, defined as an ANC of less than 500 cells/ μL . In this profound immune-compromised state, the primary immune responders are effectively depleted, allowing common environmental microbes and opportunistic pathogens within the food supply to translocate across the gut mucosa, often triggering life-threatening sepsis.

To mitigate this vulnerability, the medical community in the 1960s and 1970s pioneered the Neutropenic Diet (ND). Originally conceived as a highly restrictive "sterile diet" served within laminar-flow isolation rooms, the protocol was built on the theoretical premise that minimizing microbial ingestion would directly translate to lower infection rates. Over the decades, institutional guidelines transitioned into a "low-microbial" framework. This contemporary iteration mandates the strict avoidance of raw produce, unpasteurized dairy, and cold-cut meats, swapping them for thick-skinned fruits and meats cooked to internal temperatures exceeding 75°C. The clinical objective remains explicit: eradicate exposures to *Listeria*, *Salmonella*, and *Pseudomonas* lingering in raw or minimally processed foods.

Despite its widespread institutional adoption, a growing body of clinical evidence suggests that the ND is a tradition-bound practice rather than an evidence-based one. Recent scoping reviews, most notably by Gulliver et al. (2024), have synthesized decades of data, revealing a stark lack of correlation between strict dietary exclusion and improved patient outcomes. Multiple randomized controlled trials (RCTs) demonstrate that patients who follow standard food safety guidelines—such as the U.S. FDA frameworks emphasizing rigorous hand hygiene, cross-contamination prevention, and temperature control—experience no higher rates of infection or mortality than those subjected to the restrictive ND.

This dietary debate carries profound implications for patient recovery and survivorship. Adequate nutrition is a vital pillar of oncological resilience, yet the ND inherently compromises dietary variety. By eliminating fresh fruits, vegetables, and whole grains, the diet inadvertently restricts essential antioxidants, micronutrients, and dietary fiber at a time when metabolic demands are exceptionally high. Furthermore, the psychological burden of navigating a dense "forbidden food" list can exacerbate treatment-induced anorexia and mucositis, significantly lowering the patient's quality of life (QoL). When food is perceived as a clinical threat rather than a source of healing, the risks of protein-energy malnutrition and maladaptive eating habits escalate.

While major professional clinical societies, including the European Society for Clinical Nutrition and Metabolism (ESPEN), shift toward liberalizing oncology diets, global healthcare settings remain deeply fragmented, with many institutions continuing to enforce rigid restrictions out of historical precedent. This review critically synthesizes current literature regarding the efficacy and necessity of the neutropenic diet. By evaluating the collective impact of these dietary interventions on infection rates, nutritional status, and patient well-being, this paper seeks to determine whether the transition from exclusionary regimens to enhanced, evidence-based food safety protocols is supported by the weight of modern scientific data.

2. Review of Literature

2.1 Methods

A comprehensive search of contemporary clinical literature was performed across electronic databases including PubMed, the Cochrane Library, and Scopus to capture key data published between 2006 and 2025. Search strings utilized a combination of Medical Subject Headings (MeSH) and free-text terms, including "neutropenic diet", "low bacterial diet", "febrile neutropenia", "oncology nutrition", and "food safety guidelines". The selection process prioritized high-level evidence syntheses, including meta-analyses, systematic reviews, and randomized controlled trials evaluating both pediatric and adult oncology patients undergoing myelosuppressive therapies.

2.2 Historical Evolution of the Neutropenic Diet

The neutropenic diet emerged during the 1960s and 1970s when advances in chemotherapy and bone marrow transplantation resulted in prolonged periods of severe immunosuppression. Early clinical practice was based

largely on theoretical concerns regarding microbial contamination of food rather than direct clinical evidence. During this period, patients were frequently placed on highly restrictive “sterile diets,” and some institutions incorporated protective isolation measures such as laminar airflow rooms (Moody et al. 2006).

Over time, the concept evolved into the modern low-microbial or neutropenic diet, which restricts raw fruits and vegetables, unpasteurized dairy products, undercooked meats, raw eggs, and foods perceived to carry a higher microbial burden. Despite widespread adoption, significant variation exists among institutions regarding permitted and prohibited foods, reflecting the absence of a universally accepted definition of the neutropenic diet (Van Tiel et al. 2007; Carr and Halliday 2015).

2.3 Evidence from Randomized Controlled Trials

The clinical efficacy of neutropenic dietary restrictions has been fundamentally challenged by a series of pivotal randomized controlled trials (RCTs). Over the last two decades, these prospective studies have systematically compared restrictive dietary models against liberalized, food-safety-focused protocols to determine whether eliminating specific food groups yields any measurable clinical advantage.

The shift toward questioning traditional restrictions began to accelerate with concurrent landmark studies published in 2006. DeMille et al. (2006) evaluated hospitalized adult oncology patients, demonstrating that strict dietary restrictions failed to provide statistically significant protection against infectious complications. The investigators concluded that strict adherence to rigorous, generalized food handling practices was far more critical to patient safety than the systematic elimination of whole food groups.

Concurrently, Moody et al. (2006) investigated these parameters within a pediatric oncology cohort—a population historically viewed as highly vulnerable to opportunistic food-borne pathogens. Their trial demonstrated that children permitted a liberalized food safety approach experienced infection rates entirely comparable to those adhering to a rigid, traditional neutropenic diet. These findings provided early prospective evidence that strict dietary exclusions may be clinically unnecessary, even in highly vulnerable pediatric populations undergoing intensive myelosuppressive therapies.

Building upon these findings, Gardner et al. (2008) conducted an influential RCT focusing on adults receiving induction chemotherapy for acute myeloid leukemia (AML)—a clinical scenario characterized by prolonged, severe neutropenia. The trial directly compared a traditional cooked-food neutropenic diet with a liberalized diet that permitted fresh, well-washed fruits and vegetables. The study reported no significant differences in major infection rates, episodes of febrile neutropenia, overall mortality, or general treatment outcomes between the two arms.

Subsequent RCTs across both adult and pediatric oncology settings have consistently replicated these outcomes (Moody et al. 2018; Gupta et al. 2022; Radhakrishnan et al. 2022). The accumulated prospective data has uniformly failed to demonstrate a significant reduction in febrile neutropenia, bacteremia, or mortality associated with restrictive dietary protocols, suggesting that the “sterile plate” model offers no distinct clinical advantage over standard, rigorous food hygiene.

2.4 Findings from Systematic Reviews and Meta-Analyses

As evidence accumulated, several systematic reviews and meta-analyses synthesized the available data to determine whether neutropenic diets confer a measurable clinical benefit. Sonbol et al. (2019) conducted a systematic review and meta-analysis including six comparative studies involving 1,116 oncology patients. The authors found no statistically significant difference in infection rates between patients receiving neutropenic diets and those consuming regular diets. Rates of bacteremia, fungemia, and mortality were also comparable. Interestingly, patients undergoing hematopoietic stem cell transplantation demonstrated a slightly increased risk of infection when subjected to restrictive dietary regimens.

Building upon these findings, Ma et al. (2022) analyzed outcomes from 1,114 neutropenic patients and similarly concluded that neutropenic diets did not reduce infection incidence or mortality. Subgroup analyses

revealed consistent results across adult and pediatric populations. More recently, Gulliver et al. (2024) performed a comprehensive scoping review examining twenty-one studies involving cancer patients receiving chemotherapy or HSCT. Their review confirmed that neutropenic diets offered no meaningful advantage in preventing infection-related complications.

Furthermore, several included studies reported higher infection rates among patients following restrictive dietary protocols, raising concerns regarding the unintended consequences of dietary limitations. Collectively, these high-level evidence syntheses suggest that the neutropenic diet lacks sufficient evidence to justify routine clinical use, a consensus heavily reinforced by a wave of recent clinical guideline reviews (Ammann et al. 2025; Carlesse et al. 2025; Phillips et al. 2025).

2.5 Nutritional Implications of Dietary Restriction

Cancer-associated malnutrition remains a significant predictor of treatment intolerance, prolonged hospitalization, and reduced survival. Therefore, any dietary intervention implemented during cancer treatment should be carefully evaluated for its impact on nutritional status. Restrictive neutropenic diets often reduce the consumption of fresh fruits, vegetables, nuts, seeds, and minimally processed foods. These foods are important sources of vitamins, minerals, antioxidants, and dietary fiber (Ravasco et al. 2019). Limiting access to these nutrient-dense foods may contribute to inadequate micronutrient intake during periods of increased metabolic stress.

Studies reviewed by Gulliver et al. (2024) observed greater weight loss and larger declines in serum albumin concentrations among patients following neutropenic diets compared with those consuming liberalized diets. Reduced dietary variety may also contribute to lower energy and protein intake, increasing the risk of protein-energy malnutrition. Additionally, treatment-related symptoms such as nausea, mucositis, xerostomia, and taste alterations already present significant barriers to adequate food intake. Restrictive dietary prescriptions may further decrease food acceptability and compromise overall nutritional adequacy (Bakker et al. 2021).

2.6 Gut Microbiome and Intestinal Barrier Function

Recent advances in molecular nutrition, mucosal immunology, and microbiome research have introduced a critical mechanistic perspective that strongly challenges traditional neutropenic dietary restrictions. The human intestinal epithelium is protected by a dense, complex mucus layer composed primarily of the gel-forming mucin glycoprotein MUC2. This layer acts as a physical shield, keeping the dense community of luminal gut microbiota at a safe distance from the underlying host immune cells. Under normal dietary conditions, fermentable dietary fiber serves as the primary substrate for beneficial intestinal microorganisms. These microbes ferment the fiber to produce short-chain fatty acids (SCFAs)—predominantly acetate, propionate, and butyrate—which act as vital energy sources for colonocytes, stimulate mucin production, maintain tight junction proteins (such as claudins and occludin), and preserve epithelial integrity (Makki et al. 2018).

When a patient is placed on a restrictive neutropenic diet, the drastic reduction or total exclusion of raw fruits, vegetables, nuts, and whole grains eliminates these crucial fermentable carbohydrates. Deprived of their preferred energy source, the metabolic profile of the gut microbiota shifts dangerously. To survive, the microbial community undergoes a structural dysbiosis characterized by a stark drop in protective SCFA-producing taxa and a rapid proliferation of specialized mucus-degrading bacteria, such as *Akkermansia muciniphila* and *Bacteroides caccae*. These species possess specialized carbohydrate-active enzymes (CAZymes) that allow them to utilize host secretory mucin O-glycans as an alternative carbon source.

Consequently, prolonged fiber deprivation drives these bacteria to aggressively erode the protective inner mucin layer, significantly thinning the physical barrier between the gut lumen and the host tissue. This diet-induced thinning of the mucus layer, combined with a decline in SCFA-mediated tight junction maintenance, increases intestinal permeability (often termed "leaky gut"). In a severely immunocompromised patient, this compromised barrier facilitates the direct translocation of viable, opportunistic luminal pathogens—such as *Pseudomonas aeruginosa* and members of the *Enterobacteriaceae* family—across the epithelial monolayer and directly into the systemic circulation.

As documented by Taur et al. (2012), reduced microbial diversity and disrupted barrier states are heavily associated with poorer clinical outcomes among hematopoietic stem cell transplant recipients, including a heightened susceptibility to primary, endogenous bloodstream infections. Gulliver et al. (2024) further underscored that the traditional "sterile plate" model may paradoxically compromise the very biological barriers intended to protect the patient. Preserving gut microbiome diversity through fiber-dense, safe food options may therefore offer far superior systemic protection against infection than unproven, exclusionary dietary restrictions.

2.7 Impact on Quality of Life and Patient Experience

Quality of life is increasingly recognized as a critical component of comprehensive cancer care. Patients receiving chemotherapy frequently experience appetite loss, taste changes, fatigue, and emotional distress, all of which influence dietary intake. Research indicates that neutropenic diets may impose an additional psychological burden by creating anxiety around food choices and increasing the perception of food as a source of danger rather than nourishment (Carr and Halliday 2015). Restrictions can also interfere with cultural food practices, family meals, and social interactions, potentially reducing overall satisfaction with care.

The review by Gulliver et al. (2024) reported lower quality-of-life scores among patients prescribed highly restrictive dietary regimens. Pediatric populations appeared particularly vulnerable, as food restrictions often resulted in reduced meal enjoyment and increased caregiver stress (Beauchemin et al. 2025). These findings highlight the importance of balancing infection prevention strategies with patient-centered nutritional care.

2.8 Current Guidelines and Shifting Clinical Practice

Growing evidence against routine neutropenic dietary restrictions has prompted major professional organizations to reconsider traditional recommendations. The European Society for Clinical Nutrition and Metabolism (ESPEN) and the American Society of Clinical Oncology (ASCO) now emphasize evidence-based food safety education rather than strict food exclusions (Muscaritoli et al. 2021). Similarly, recommendations from the U.S. Food and Drug Administration (FDA) and the World Health Organization (WHO) prioritize safe food handling practices, including proper hand hygiene, prevention of cross-contamination, adequate cooking temperatures, and safe food storage. Current evidence increasingly supports a liberalized dietary approach that promotes nutritional adequacy while maintaining rigorous food safety standards. This shift reflects a broader movement toward individualized nutrition care that prioritizes both clinical outcomes and quality of life.

2.9 Comparative Synthesis

Table 1: traditional neutropenic diet vs. modern food safety framework

Parameter	Traditional Neutropenic Diet (ND)	Evidence-Based Food Safety
Core Philosophy	Total dietary sterility / Low-microbial load via systemic exclusion.	Mitigation of pathogenic risk via strict hygiene and temperature control.
Fresh Produce	Strictly prohibited (raw fruits, salads, raw vegetables).	Permitted if washed thoroughly under running potable water.
Dairy & Meats	Avoidance of unpasteurized dairy; soft cheeses; cold cuts.	Pasteurized dairy permitted; meats cooked thoroughly to safe internal temperatures ($>75^{\circ}\text{C}$).

Parameter	Traditional Neutropenic Diet (ND)	Evidence-Based Food Safety
Microbiome Impact	Induces dysbiosis, thins mucus layer, elevates translocation risk.	Preserves microbial diversity and maintains intestinal barrier integrity.
Nutritional Quality	Low in dietary fiber, raw antioxidants, and vital micronutrients.	Nutrient-dense, antioxidant-rich, high-fiber, supports caloric adequacy.
Psychological Burden	High; drives food anxiety and worsens treatment anorexia.	Low; encourages meal enjoyment and improves Quality of Life (QoL).

2.10 Research Gap

Although substantial evidence suggests that neutropenic diets do not reduce infection risk, considerable variation remains in clinical practice worldwide. Many healthcare institutions continue to prescribe restrictive diets due to historical precedent and concerns regarding patient safety. Furthermore, limited research has evaluated long-term nutritional outcomes, microbiome alterations, patient adherence, and cost-effectiveness associated with dietary liberalization. Additional multicenter studies are required to establish standardized evidence-based nutritional guidelines for neutropenic oncology patients.

3. Conclusion and Future Recommendations

3.1 Conclusion

The neutropenic diet has been a long-standing component of supportive cancer care, developed with the intention of reducing exposure to foodborne microorganisms in immunocompromised patients. However, current evidence does not support its routine use as an effective strategy for preventing infections. Findings from randomized controlled trials, systematic reviews, and meta-analyses consistently demonstrate that neutropenic diets do not significantly reduce the incidence of febrile neutropenia, bacteremia, fungemia, or mortality when compared with liberalized diets that follow standard food safety precautions.

In addition to the lack of demonstrated clinical benefit, restrictive dietary practices may adversely affect nutritional status and patient well-being. Limiting fresh fruits, vegetables, and other nutrient-dense foods can reduce dietary variety and may contribute to inadequate intake of essential nutrients and dietary fiber. Emerging evidence also suggests that excessive dietary restriction may negatively influence gut microbiome diversity and intestinal health. Furthermore, strict food restrictions can increase anxiety around eating, reduce meal enjoyment, and negatively affect quality of life during an already challenging period of treatment.

The collective findings of recent research support a shift from restrictive neutropenic diets toward evidence-based food safety practices. Major organizations such as ESPEN and ASCO now emphasize safe food handling, preparation, and storage rather than the routine exclusion of specific food groups. A liberalized, nutrient-rich dietary approach combined with appropriate food hygiene measures appears to offer a more balanced strategy for supporting both safety and nutritional adequacy in oncology patients.

3.2 Future Recommendations

Based on the current body of evidence, several recommendations can be made to improve clinical practice, institutional policies, and future research related to nutritional management in neutropenic oncology patients. In clinical settings, healthcare institutions should reconsider the routine use of neutropenic diets and instead adopt evidence-based food safety guidelines as the primary approach to infection prevention. Oncology

dietitians should provide individualized nutrition care plans that ensure adequate intake of energy, protein, vitamins, minerals, and dietary fiber while maintaining appropriate food safety practices. Additionally, patient and caregiver education should focus on practical food safety measures, including proper hand hygiene, safe food storage, prevention of cross-contamination, and the use of appropriate cooking temperatures during food preparation.

At the institutional level, hospitals and cancer centers should review and update existing nutrition protocols to align with current recommendations from organizations such as ESPEN and ASCO. The development of standardized educational resources can help provide clear, consistent, and evidence-based guidance regarding safe food practices for immunocompromised patients. Furthermore, stronger interdisciplinary collaboration among oncologists, dietitians, nurses, and infection-control professionals is essential to ensure the effective implementation of patient-centered nutrition care and food safety education across healthcare settings.

Future research should focus on generating stronger evidence regarding the long-term impact of liberalized dietary approaches in neutropenic patients. Large multicenter prospective studies are needed to evaluate outcomes such as nutritional status, treatment tolerance, hospitalization rates, quality of life, and healthcare costs. Additional investigations should explore the relationship between dietary patterns, gut microbiome composition, and infection risk to better understand the biological implications of dietary restrictions. Future studies should also incorporate validated quality-of-life assessment tools to examine the psychological and social effects of dietary interventions during cancer treatment. Moreover, research involving diverse patient populations, cancer types, and healthcare settings will be important for developing universally applicable and evidence-based nutritional guidelines for individuals experiencing treatment-related neutropenia.

Declarations

Generative AI Disclosure

We used the AI tool Gemini to generate structural revisions, polish formatting, verify citation consistency, and apply the required author guidelines to the initial literature draft for our manuscript.

Conflicts of Interest

The authors declare no financial or personal conflicts of interest regarding the publication of this review paper.

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