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The Oral-Systemic Nexus in Artificial Nutrition: A Narrative Review of Periodontal Health, Biochemical Parameters, and Wound Healing Outcomes

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Abstract

Background: Patients dependent on enteral or parenteral nutrition (EN/PN) present a complex clinical paradox, receiving life-sustaining macronutrients while remaining at high risk for significant morbidity, particularly impaired wound healing. This vulnerability extends beyond caloric provision to a confluence of factors, including a high prevalence of oral and periodontal disease, dysregulation of critical nutrients (e.g., zinc), and a persistent systemic inflammatory state. **Aim:** This narrative review synthesizes current evidence (2015-2024) on the interplay between oral health status, key laboratory parameters (inflammatory markers, albumin, zinc), and wound healing in adult patients receiving EN/PN, with added emphasis on health informatics and nursing roles in integrated care. **Methods:** A comprehensive search of PubMed, Scopus, and CINAHL databases was conducted. Studies examining periodontal status, levels of CRP, albumin, zinc, and wound healing metrics in EN/PN populations were thematically analyzed, alongside literature on digital health tools and nursing-led interventions. **Results:** Evidence reveals a vicious cycle: poor oral hygiene and active periodontitis contribute to a systemic inflammatory burden (elevated CRP), which, combined with common hypoalbuminemia and zinc deficiency in EN/PN patients, critically impairs proliferative wound healing phases. Oral infection acts as a persistent reservoir of inflammation, exacerbating nutrient depletion and creating a non-permissive environment for tissue repair. Health informatics systems and structured nursing protocols can enhance monitoring, interdisciplinary communication, and patient-specific interventions. **Conclusion:** Effective wound management in this population necessitates a transdisciplinary approach. Routine oral health assessment and intervention must be integrated into standard nutritional care protocols, supported by health informatics tools and nursing-led coordination, alongside vigilant monitoring and repletion of zinc and protein, to mitigate inflammation and support healing.

Keywords: Enteral Nutrition; Parenteral Nutrition; Periodontal Diseases; Wound Healing; Inflammation; Zinc; Health Informatics; Nursing Care.

Introduction

Artificial nutrition support, encompassing enteral (EN) and parenteral (PN) nutrition, is a cornerstone of modern medical management for patients who cannot meet their metabolic requirements through voluntary oral intake (Shiraishi et al., 2020). While unequivocally life-preserving, this intervention does not inherently guarantee nutritional adequacy or positive health outcomes (Pironi et al., 2023). A significant and often under-addressed challenge in this population is the high incidence of impaired wound healing, ranging from non-healing surgical sites and pressure injuries to chronic fistulas. This compromised tissue repair exists despite the provision of calculated caloric and protein delivery, pointing to a multifactorial etiology beyond simple macronutrient supply (Stechmiller et al., 2019).

Emerging understanding frames this issue within a bidirectional oral-systemic nexus. Patients requiring EN/PN frequently possess underlying conditions (e.g., critical illness, head and neck cancer, neurological impairment) that predispose them to both

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poor oral hygiene and the development of periodontal diseases. Furthermore, the absence of oral feeding can reduce salivary flow and diminish the natural mechanical cleansing of oral surfaces, accelerating oral dysbiosis (Lee et al., 2021).

Concurrently, the metabolic stress of their primary illness, coupled with the limitations of formula-based nutrition, often leads to deficiencies in micronutrients like zinc and disruptions in protein metabolism, reflected by low serum albumin. Periodontal disease is now recognized as a chronic inflammatory condition capable of inducing low-grade systemic inflammation, measured by elevated C-reactive protein (CRP) (Werber et al., 2021). This review posits that in EN/PN patients, these elements converge: oral disease exacerbates systemic inflammation, which, synergistically with specific nutrient deficiencies, creates a profound barrier to effective wound healing. This narrative review aims to synthesize contemporary evidence linking periodontal health, key biochemical parameters (CRP, albumin, zinc), and wound healing outcomes in adults receiving artificial nutrition, thereby arguing for an integrated care model (Guo et al., 2023) supported by health informatics and nursing leadership.

Methodology

This narrative review was conducted to synthesize and critically appraise the contemporary literature exploring the interrelationships between oral health, key biochemical parameters, and wound healing in adult patients receiving enteral or parenteral nutrition. The methodology was designed to ensure a comprehensive and systematic search of relevant evidence published within a defined, recent timeframe, followed by a thematic analysis.

Search Strategy and Information Sources

A systematic electronic literature search was performed across three major databases: PubMed/MEDLINE, Scopus, and CINAHL (Cumulative Index to Nursing and Allied Health Literature). The search was restricted to articles published in English between January 2015 and December 2024 to capture the most current evidence and evolving clinical paradigms. The search strategy employed a combination of Medical Subject Headings (MeSH) terms and keywords related to the core concepts. Key search terms included: "Enteral Nutrition" OR "Parenteral Nutrition" OR "Artificial Nutrition" OR "Tube Feeding" AND "Periodontal Diseases" OR "Oral Health" OR "Gingivitis" OR "Periodontitis" AND "Wound Healing" OR "Tissue Repair" OR "Pressure Injury" OR "Surgical Wound" AND "Inflammation" OR "C-Reactive Protein" OR "CRP" OR "Cytokines" AND "Albumin" OR "Hypoalbuminemia" OR "Nutritional Status" AND "Zinc" OR "Trace Elements" OR "Micronutrients." Boolean operators (AND, OR) were used to combine concepts. The reference lists of relevant review articles and key primary studies were manually screened to identify additional pertinent publications not captured by the electronic search.

Eligibility Criteria and Study Selection

Studies were selected for inclusion based on predefined criteria. The population of interest was adults (≥18 years) receiving enteral or parenteral nutrition in any clinical setting (e.g., intensive care unit, long-term care, home care). Included studies needed to address at least two of the three core thematic domains: (1) oral/periodontal health status, (2) biochemical markers (specifically CRP, albumin, or zinc), and (3) wound healing processes or outcomes. All study designs were considered, including randomized controlled trials, cohort studies, case-control studies, cross-sectional analyses, and systematic reviews, to provide a broad synthesis of evidence. Exclusion criteria encompassed studies on pediatric populations, animal or in vitro studies, editorials, commentaries, and studies not available in full text or published outside the specified date range. After removal of duplicates, titles and abstracts were screened independently by the author for relevance. Full-text articles of potentially eligible studies were then retrieved and assessed against the inclusion criteria.

Data Extraction and Thematic Synthesis

A standardized, iterative approach was used for data extraction and synthesis. Key information was extracted from each included study, including author(s), publication year, study design, sample characteristics, primary and secondary outcomes related to the review's focus, and significant findings. Given the heterogeneous nature of the evidence (encompassing different study designs, patient subgroups, and outcome measures), a meta-analysis was not feasible. Instead, a narrative thematic synthesis was conducted. Extracted data were organized and analyzed to identify recurring themes, patterns of association, consensus in the literature, and gaps in knowledge. The synthesis was structured to address the central review question: How do oral health status and specific biochemical parameters interact to influence wound healing in the EN/PN population? The evidence was then integrated to construct the proposed pathophysiological model and clinical framework presented in this review.

Oral Health and Periodontal Status in the EN/PN Population

The oral cavity is often a neglected aspect of care in patients dependent on artificial nutrition, yet it is frequently a site of significant pathology. Studies consistently demonstrate a high prevalence of oral diseases in this group, including xerostomia, candidiasis, and notably, periodontitis (Patini, 2020). The etiology is multifactorial. Underlying conditions such as stroke, dementia, or head/neck cancer directly impair the patient's ability to perform oral care. Medication side effects, oxygen therapy, and mouth breathing contribute to xerostomia, reducing saliva's protective, buffering, and antimicrobial functions

(Meregildo-Rodriguez et al., 2022). In the context of EN, the lack of mastication further reduces salivary stimulation, while the oral intake of sugary or acidic medications can promote a cariogenic and dysbiotic biofilm (Dembowska et al., 2021).

Periodontal disease, characterized by the inflammation and destruction of the tooth-supporting tissues, is of particular systemic relevance. In bedbound or critically ill EN/PN patients, routine periodontal assessment is rarely performed, allowing inflammation to progress unchecked. The subgingival biofilm in periodontitis harbors gram-negative anaerobic pathogens and their virulence factors (e.g., lipopolysaccharide). These can readily translocate into the systemic circulation through ulcerated periodontal pockets, especially during routine activities like chewing or oral care in a compromised host (Santacroce et al., 2023). This bacteremia and the consequent host immune response drive a persistent systemic inflammatory state. Research in other medically compromised populations has firmly established periodontitis as a contributor to elevated serum CRP, interleukin-6 (IL-6), and other inflammatory mediators (Liccardo et al., 2020). It is therefore biologically plausible that in the EN/PN patient, a chronically infected oral cavity acts not as a passive bystander but as an active, persistent driver of systemic inflammation, directly competing with the metabolic resources required for distant wound repair (Salhi et al., 2023). Figure 1 represents the interrelationship between poor periodontal health and impaired wound healing in patients receiving enteral or parenteral nutrition (EN/PN).

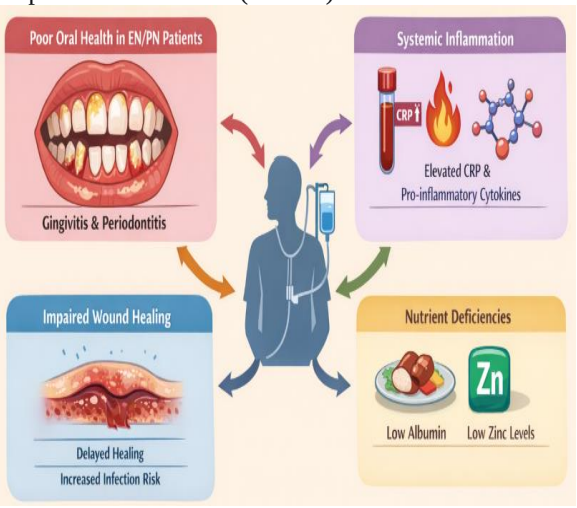

Figure 1: Periodontal Health, Systemic Inflammation, and Nutrient Deficiencies in Patients Receiving Artificial Nutrition

Key Biochemical Parameters

The systemic milieu of a patient receiving EN/PN is a critical determinant of healing capacity. Three interconnected laboratory parameters offer profound insight: inflammatory markers (primarily CRP), albumin, and zinc.

C-Reactive Protein (CRP) and Systemic Inflammation

CRP, an acute-phase protein synthesized by the liver in response to IL-6, is a robust nonspecific marker of inflammation. Elevated CRP levels are commonplace in patients requiring EN/PN due to their primary catabolic illnesses (e.g., sepsis, major surgery, trauma) (Chang et al., 2020). However, the contribution of oral infection is often an overlooked confounder. A chronic oral infection like periodontitis can maintain CRP elevations in a low-grade but persistent manner (Eickholz et al., 2022). This sustained inflammatory state is profoundly catabolic and anti-anabolic. Pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and IL-1β promote muscle proteolysis, directly antagonize anabolic hormones like insulin-like growth factor-1 (IGF-1), and disrupt the orderly sequence of wound healing by prolonging the inflammatory phase and inhibiting fibroblast proliferation and collagen synthesis (Aitcheson et al., 2021). Therefore, an elevated CRP in an EN/PN patient may signify not only the primary illness but also an unaddressed oral source, collectively impairing the wound environment.

Albumin and Protein-Energy Status

Serum albumin has traditionally been used as a marker of nutritional status and visceral protein stores. However, its interpretation is complex. While prolonged protein-energy malnutrition can lead to hypoalbuminemia, albumin is also a negative acute-phase reactant; its synthesis is suppressed, and its catabolism increased, during systemic inflammation (Soeters et al., 2019). Thus, in the inflamed EN/PN patient, low albumin often reflects the severity of the inflammatory response more accurately than pure dietary protein intake. Functionally, hypoalbuminemia contributes to wound healing impairment through mechanisms such as reduced oncotic pressure, leading to edema, which distances cells from nutrients and oxygen, and by its role as a carrier for essential molecules like zinc and fatty acids (Stechmiller et al., 2019). The combination of inflammation-driven hypoalbuminemia and increased capillary permeability creates a hostile microenvironment for tissue repair.

Zinc as The Critical Micronutrient for Repair

Zinc is a cofactor for over 300 enzymes involved in DNA synthesis, cell division, protein synthesis, and immune function—all processes central to wound healing (Diglio et al., 2020). Zinc deficiency is prevalent in EN/PN patients due to increased losses from wounds, gastrointestinal secretions, and urine during catabolic states, coupled with often-inadequate provision in standard formulas (Scheiermann et al., 2022). Deficiency manifests clinically with delayed wound healing, impaired lymphocyte function, and dermatitis. At the cellular level, zinc is crucial for the activity of matrix metalloproteinases required for extracellular matrix remodeling and for the

proliferation of fibroblasts and keratinocytes (Lin et al., 2017). Furthermore, zinc possesses antioxidant properties and can modulate the inflammatory response (Ozeki et al., 2020). Its deficiency, therefore, creates a perfect storm: impaired epithelialization and collagen deposition coupled with dysregulated inflammation. The relationship is bidirectional, as systemic inflammation can alter zinc homeostasis, sequestering it in the liver and reducing its circulating availability (Wessels et al., 2022). Figure 2 illustrates the bidirectional mechanisms linking periodontal disease, nutrient deficiencies, and impaired wound healing in patients dependent on artificial nutrition.

The Convergent Pathways

Wound healing is a finely orchestrated, sequential process comprising hemostasis, inflammation, proliferation, and remodeling. The EN/PN patient with poor oral health and aberrant biochemistry faces disruptions at multiple stages, as summarized in Table 1.

Table 1: Impact of Oral-Systemic Factors on Wound Healing Phases in EN/PN Patients

Wound Healing Phase	Primary Cellular Activities	Disrupting Factors in EN/PN Patients	Consequences
Inflammation	Hemostasis; neutrophil & macrophage recruitment; pathogen clearance.	Primed leukocytes from oral endotoxemia; persistently elevated TNF-α, IL-1β, CRP.	Exaggerated & prolonged inflammatory response; tissue damage via ROS/proteases; delayed progression.
Proliferation	Angiogenesis; fibroblast proliferation; collagen synthesis; re-epithelialization.	Zinc deficiency; hypoalbuminemia; ongoing catabolism from inflammation.	Impaired fibroblast/keratinocyte mitosis; flawed collagen synthesis; poor granulation tissue formation.
Remodeling	Collagen cross-linking; scar maturation.	Sustained MMP activity due to inflammation; continued nutrient insufficiency.	Weak, disorganized scar; high risk of wound breakdown and recurrence.

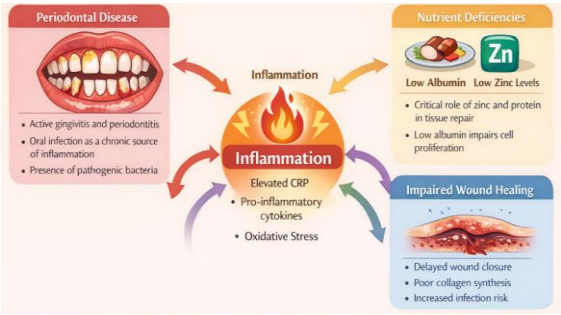

Figure 2: Mechanistic Pathways Linking Periodontal Disease, Systemic Inflammation, and Impaired Wound Healing in Artificial Nutrition

The presence of active periodontitis establishes a state of chronic low-grade endotoxemia. This primes and activates circulating neutrophils and monocytes, a phenomenon termed "inflammatory priming." When these primed leukocytes are recruited to a peripheral wound site, they can exhibit an exaggerated and prolonged inflammatory response, releasing large quantities of reactive oxygen species and proteolytic enzymes that cause collateral damage to healthy tissue and delay the transition to the proliferative phase (Hajishengallis & Chavakis, 2021). This persistent inflammation at the wound bed is fueled systemically by elevated CRP and pro-inflammatory cytokines, whose production is amplified by the oral bacterial challenge.

Concurrently, the resources for repair are scarce. Hypoalbuminemia, whether from inflammation or inadequate intake, compromises the structural building blocks for new tissue. More specifically, zinc deficiency directly cripples the proliferative phase. Keratinocytes and fibroblasts fail to multiply efficiently, collagen synthesis is flawed, and angiogenesis is impaired (Lin et al., 2017). The wound remains stuck in a state of chronic inflammation without progressing to reconstruction. This is exemplified in conditions like pressure injuries and non-healing surgical wounds, common in long-term EN/PN patients (Holzer-Geissler et al., 2022). Research indicates that wound fluid from non-healing wounds often shows elevated pro-inflammatory cytokines and matrix metalloproteinases, alongside decreased levels of growth factors and tissue inhibitors of metalloproteinases—a biochemical profile consistent with the combined impact of systemic inflammation and micronutrient deficiency (Nirenjen et al., 2023).

Thus, a vicious cycle is established: oral infection → systemic inflammation (↑CRP) → increased catabolism and nutrient dysregulation (↓albumin, ↓Zn) → impaired wound healing → prolonged hospitalization and increased metabolic demand → worsened oral neglect and nutritional status. Breaking this cycle requires a multifocal intervention strategy (Rowińska et al., 2021).

Integrated Management

The evidence underscores that managing wound healing in the EN/PN patient requires moving beyond siloed care. An integrated, transdisciplinary model is essential, involving clinicians, dietitians, wound care nurses, and dental professionals. A proposed framework for this integrated care is outlined in Table 2.

Table 2: Proposed Integrated Care Protocol for EN/PN Patients with/at Risk of Impaired Wound Healing

Domain	Assessment	Intervention	Frequency/Goal
Oral Health	Bedside oral exam (mucosa, plaque, gums); if possible, basic periodontal screening.	Mechanical plaque removal; mucosal moisturizing; antiseptic mouthrinse (per protocol); formal dental referral if periodontitis suspected.	**Daily** for basic care; **Weekly** structured assessment; **Once** upon EN/PN initiation for dental consult.
Biochemical Monitoring	Serum CRP, albumin, prealbumin, zinc.	Interpret CRP/albumin in concert; provide high-protein EN/PN (1.2-2.0 g/kg/day); supplement zinc if deficient or high losses (e.g., 20-40 mg/day elemental Zn).	**Weekly** for CRP/albumin in acute phase; **Bi-monthly** for zinc in stable long-term patients.
Wound Care	Standard staging/assessment; monitor exudate, granulation.	Advanced dressings; offloading; consider wound fluid biomarkers in research.	**Per wound care protocol.**
Interdisciplinary Communication	Shared electronic health record notes; team huddles.	Mandate oral health status in wound/nutrition notes; dietitian to flag inflammation/nutrient deficits; nurse to report oral findings.	**Continuous** and structured.

Health Informatics and Nursing Implications

The integration of health informatics and structured nursing care is pivotal in operationalizing the transdisciplinary model required for EN/PN patients with complex oral-systemic needs. Digital health tools, including electronic health records (EHRs), clinical decision support systems (CDSS), and mobile health applications, can streamline the monitoring of oral health, biochemical parameters, and wound progression (Wannheden et al., 2022). For instance, interoperable EHR modules can alert clinicians to abnormal CRP or zinc levels while flagging overdue oral assessments, thereby reducing oversight and fostering proactive intervention (Kelly et al., 2023).

Nursing staff, as frontline caregivers, play a central role in executing daily oral hygiene, assessing wound status, and recognizing early signs of infection or nutrient deficiency. Standardized nursing protocols—enhanced by digital checklists and telehealth platforms—can ensure consistency in oral care delivery and facilitate real-time documentation of oral mucosa condition, plaque index, and periodontal screening (Lei et al., 2023). Moreover, nurse-led education programs for patients and families on the importance of oral health in systemic healing can improve adherence and self-management in home EN/PN settings (Agustin et al., 2018).

Tele-dentistry and virtual interdisciplinary rounds further bridge gaps between dental, nutritional, and wound care specialists, especially in remote or resource-limited settings (da Costa et al., 2020). By leveraging health informatics, nurses can coordinate care more effectively, ensuring that oral health data is visible across the care continuum and that interventions are timely, personalized, and evidence-based.

Systematic Oral Health Assessment and Intervention

Oral care must be elevated from a basic hygiene task to a mandatory component of medical management, recognized for its systemic implications. Comprehensive protocols should encompass daily mechanical plaque removal using soft brushes or foam swabs, diligent moisturization of the oral mucosa, and the judicious use of antiseptic mouthwashes such as chlorhexidine, while remaining cognizant of its limitations, including potential taste alteration and mucosal irritation (Thomas et al., 2021). For long-term EN/PN patients, a formal dental evaluation to diagnose and treat periodontitis is a critical intervention, as untreated oral infection represents a controllable source of systemic inflammation. Evidence from analogous populations demonstrates the efficacy of such rigor; studies in critically ill and elderly cohorts have shown that structured oral care protocols can significantly reduce the incidence of ventilator-associated pneumonia and may modulate systemic inflammatory markers (Jun et al., 2021). However, the direct impact of periodontal therapy on distant wound healing outcomes, specifically in the EN/PN population, remains a pivotal and under-investigated area, meriting focused future research to quantify the benefits of oral infection control on tissue repair (Gershonovitch et al., 2020).

Targeted Biochemical Monitoring and Repletion

Concurrent with oral health management, nutritional support must be dynamically guided by

precise and reactive biochemical monitoring to create a permissive environment for healing. Serial monitoring of C-reactive protein (CRP) is essential to gauge the overall inflammatory burden. A persistently elevated CRP in the absence of an obvious clinical source should actively prompt investigation for occult infections, with oral and periodontal disease considered a prime etiology (Machado et al., 2021). The interpretation of serum albumin requires nuance; while low levels should trigger an evaluation of inflammatory status and the adequacy of protein delivery, it is primarily a marker of the inflammatory response rather than a direct nutritional endpoint (Soeters et al., 2019).

Protein provision should be optimized to meet elevated demands, typically ranging from 1.2 to 2.0 g/kg/day, guided by nitrogen balance studies where feasible to ensure anabolism (Cederholm et al., 2017). Micronutrient monitoring is equally critical, with zinc holding particular importance. Serum zinc levels should be assessed periodically, especially in patients with high-output fistulas or non-healing wounds. Repletion is crucial, with guidelines from the European Society for Clinical Nutrition and Metabolism (ESPEN) suggesting supplemental doses of up to 40 mg/day of elemental zinc in deficient patients with pressure injuries, acknowledging that higher doses may be required in cases of excessive gastrointestinal or wound losses (Elke et al., 2023; Wessels et al., 2017).

Fostering Collaborative Transdisciplinary Practice

The successful implementation of this integrated model is wholly dependent on the establishment of clear, structured communication channels that foster genuine transdisciplinary collaboration. This necessitates an expansion of traditional professional roles: the clinical dietitian must incorporate awareness of oral health's impact on systemic inflammation into nutritional assessments, while the wound care specialist should routinely inquire about oral health status and micronutrient levels, particularly zinc (Kim et al., 2021).

The nursing team's role in executing daily oral care and observing oral changes becomes a key source of clinical data. To operationalize this collaboration, institutional protocols must mandate a standardized oral health screening upon the initiation of EN/PN and at regular intervals thereafter, with clearly defined referral pathways to dental services (Qi et al., 2022). This shift from episodic, siloed interventions to a continuous, communicative care model is fundamental to disrupting the vicious cycle of oral infection, systemic inflammation, and impaired wound healing.

Conclusion

Patients receiving enteral or parenteral nutrition inhabit a precarious metabolic state where the provision of sustenance does not automatically confer healing. This review synthesizes evidence that places oral health, specifically periodontal status, at the center of a pathogenic triad alongside systemic inflammation and key nutrient deficiencies. The oral cavity, when diseased, serves as a constant reservoir of inflammation, exacerbating the catabolic state and diverting critical resources like zinc away from the complex task of tissue repair. The resultant biochemical milieu—characterized by elevated CRP, hypoalbuminemia, and zinc deficiency—creates a non-permissive environment for wound healing, leading to significant clinical morbidity.

To disrupt this vicious cycle, a paradigm shift is required. Care for the EN/PN patient must be inherently transdisciplinary, integrating rigorous oral health assessment and treatment into standard nutritional and wound management protocols. The adoption of health informatics tools and the empowerment of nursing professionals are essential to enable real-time monitoring, enhance interdisciplinary communication, and ensure consistent implementation of integrated care protocols. Future prospective studies are needed to directly quantify the impact of periodontal therapy on systemic inflammation and wound healing rates in this vulnerable population, as well as to evaluate the efficacy of digital health interventions and nursing-led models. Only by acknowledging and addressing this oral-systemic nexus—supported by technology and teamwork—can we optimize outcomes and fully realize the therapeutic potential of artificial nutrition support.

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