REVIEW

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# Artificial intelligence-guided nutritional therapy in the ICU


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**Purpose of review**

Critical care nutrition remains a high-stakes and error-prone domain, particularly given the complex metabolic demands and heterogeneity of ICU populations. This review explores recent progress in integrating artificial intelligence with nutritional therapy in ICUs, highlighting its evolution and potential benefits in precision-guided support, along with current implementation challenges.

**Recent findings**

Widely used in adult and neonatal ICUs, parenteral nutrition faces persistent challenges including ordering errors, practice variability, and insufficient robust long-term outcome evidence. Recent advances in machine learning have demonstrated considerable potential in predicting nutrition-related complications (e.g. neonatal morbidities, cholestasis, feeding intolerances, and malnutrition), optimizing nutrient delivery through dynamic, real-time recommendations, and enhancing clinical decision-making with large language models (LLMs) that synthesize clinical guidelines and patient data into actionable insights. However, future studies must establish causal relationships between optimal parenteral nutrition and long-term outcomes while addressing confounding factors and ingredient heterogeneity.

**Summary**

Artificial intelligence-driven nutrition therapies have the potential to significantly improve the precision, safety, and personalization of ICU nutrition practices. Continued development and validation using standardized, comprehensive, longitudinal datasets, and validation in comparative clinical trials will be critical to realizing this transformative potential.



**Keywords**

artificial intelligence, causal inference, critical care nutrition, decision support systems, total parenteral nutrition


## INTRODUCTION

Nutritional therapy in ICUs is a critical component of patient recovery, influencing metabolic stabilization and long-term outcomes. Standard approaches such as enteral nutrition and parenteral nutrition form the foundation of care, tailored to the complex and individualized needs of critically ill patients. This review encompasses both neonatal and adult intensive care populations, with a greater representation of neonatal data and notable adult studies highlighted as appropriate. Unless stated in the title section, the patient population of relevant studies is clarified at the point of citation. Despite established practices, clinical implementation often varies due to institutional differences, anecdotal experience, and adopted guidelines [1]. Recent advances in machine learning may offer a pathway to precision-guided, standardized nutritional strategies [2▪].


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## KEY POINTS

- Artificial intelligence is improving critical care nutrition by transforming error-prone, guideline-based approaches into precision-guided, data-driven therapeutic strategies that can adapt to the complex metabolic demands and heterogeneity of ICU patient populations in real-time.
- Machine learning models demonstrate promising predictive accuracy for nutrition-related complications, successfully identifying high-risk patients for conditions including necrotizing enterocolitis, feeding intolerance, cholestasis, and parenteral nutrition ordering errors, enabling proactive interventions that improve patient safety and outcomes.
- Artificial intelligence-guided nutrition systems trained on large amount of represent breakthrough applications in nutritional optimization with high accuracy in replicating expert dosing decisions while also showing potential to reduce prescription errors and improve long-term gastrointestinal outcomes.
- Large language models emerge as powerful clinical decision-support tools that can rapidly synthesize unstructured medical data and guidelines into actionable recommendations, though implementation requires careful attention to hallucination risks and the integration of validation techniques.

## CURRENT NUTRITIONAL THERAPY IN THE ICU

### Parenteral nutrition patient populations

Parenteral nutrition provides intravenous nutritional support to patients unable to meet nutritional requirements via the gastrointestinal tract. When parenteral nutrition serves as the sole source of nutrients, it is termed total parenteral nutrition (TPN), whereas supplemental parenteral nutrition (sPN) complements enteral feeding to achieve full nutritional goals. Although exact ICU-specific data remain limited, it is estimated that 300 000–350 000 hospital patients annually receive parenteral nutrition in the United States [3]. Parenteral nutrition meets nutritional needs intravenously and is critical in both adult and neonatal populations, though their practices differ significantly [4]. Adults frequently receive parenteral nutrition due to major surgeries or chronic conditions [5]. In neonatal (NICU) and pediatric ICUs (PICU), approximately 70% of neonates in NICUs receive parenteral nutrition [6,7]. Unlike adults, neonates face unique challenges related to immature organ systems, fluid restrictions, and heightened metabolic stress [8–10,11▪]. These factors lead neonatal/pediatric parenteral nutrition vulnerable to both under-treatment and over-treatment, which demands high precision in formulation [12,13▪].

### Current challenges in nutritional therapy addressable by artificial intelligence

#### Safety/errors of parenteral nutrition ordering process

Errors in parenteral nutrition ordering and delivery pose significant safety risks to patient health [4,14,15], potentially causing metabolic complications or infections like hyperglycemia [4,16], electrolyte imbalances [4,16], and liver dysfunction [4,17▪]. The International Safety and Quality of Parenteral Nutrition Summit identified parenteral nutrition as among the most complex therapies, historically reporting error rates up to 22%, with 26% requiring clarification before digital tools were adopted [4,14]. Interventions such as standardized pediatric parenteral nutrition formulations, digital systems integrated with Electronic Health Records (EHRs), and barcode-assisted medication preparation have significantly reduced errors [4,18▪,19]. Despite these advancements, errors still occur from the data fragmentation across EHRs, which complicates effective clinical oversight and increases cognitive burdens on healthcare providers [20▪,21▪]. By incorporating features that enhance large-scale EHR integration and facilitate real-time risk prediction, artificial intelligence holds the potential to mitigate parenteral nutrition ordering errors [20▪,21▪]. A recent study highlighted this point by showcasing that artificial intelligence-driven predictive models accurately identified intravenous administration as having the highest likelihood of parenteral nutrition-related errors [22▪].

#### Variability across institutions and countries

Variability in parenteral nutrition practices across ICUs remains a persistent challenge, with significant implications for patient outcomes. Multiple regional guidelines exist, such as from the American Society for Parenteral and Enteral Nutrition (ASPEN), European Society for Clinical Nutrition and Metabolism (ESPEN), and Australian and New Zealand Society of Parenteral and Enteral Nutrition (AUSPEN), but their recommendation can vary on top of different healthcare infrastructure and available resources [15,23]. For example, ASPEN, used in the United States, emphasizes individualized nutritional formulations, especially for neonates [24], whereas AUSPEN emphasizes standardized recipes. ESPEN/ASPEN standards also often prove impractical in lower middle-income settings with limited formulations [15,24,25]. In contrast, AUSPEN's standardized parenteral nutrition formulations reduced prescription errors and improved adoption, but over-reliance can underdeliver key nutrients and impair growth [23,26–28]. The variability in parenteral nutrition practices leads to variations in safety and quality outcomes, underscoring the need for a more unified and adaptive approach to nutrition support [29■■].

### Lack of long-term outcome evidence

The long-range consequences of parenteral nutrition are still only partly known. A 2024 review found only seven randomized trials with a follow-up of greater than 1 year in PubMed; most of these trials were small and limited to the first few days in the ICU [30■]. In neonates, a systematic review found that aggressive early parenteral calories did not translate into consistently better neurodevelopment and explicitly called for long-term follow-up studies before firm guidance can be issued [31■]. Thus, robust longitudinal data on growth, functional independence, and quality of life are still missing. Because the available evidence is short-horizon, bedside decisions related to parenteral nutrition still rely on population averages and expert consensus [30■,32–34]. Collecting richer, long-term outcome data could enable artificial intelligence to address these issues in a data-driven approach [35,36].

## TRANSFORMATION OF ICU NUTRITIONAL CARE THROUGH ARTIFICIAL INTELLIGENCE

Artificial intelligence is increasingly adopted in critical care, due to the data-rich environment of ICUs [35]. Machine learning, the algorithm underpinning artificial intelligence, has already demonstrated value in several medical applications such as ventilator-weaning and mechanical-ventilation management tools [37] and global milk-omics models that forecast infant growth from multisite human-milk profiles [38]. Building on these successes, machine learning is now being explored for nutritional support. Machine learning models can monitor patient data, including lab measurements and EHRs [20■,21■,39■], to generate personalized nutritional recommendations that adjust to the patient's condition [2■,40]. In particular, machine learning effectively captures complex temporal patterns within dynamic clinical datasets, including nutritional intake, laboratory values, and vital signs [41■,42].

## Machine learning for predicting nutrition-related complications

### Neonatal morbidities and mortalities

Machine learning models have demonstrated robust predictive performance across significant neonatal morbidities, including bronchopulmonary dysplasia (BPD) [43,44■,45], necrotizing enterocolitis (NEC) [46■,47■], intraventricular hemorrhage (IVH) [48], and neonatal mortality [18■,49,50■,51]. These predictive models have proven especially beneficial in NICU settings by enabling early interventions and targeted nutritional strategies for vulnerable populations, such as very-low-birth-weight preterm infants. A single-center study based on historical patient data involving 3341 very-low-birth-weight preterm neonates in the NICU, with external validation data on 447 additional patients [52■], applied machine learning models to maternal and neonatal clinical data within 2 weeks after birth. The models accurately identified infants at higher risk of multiple morbidities, including mortality (78%), NEC (73%), and BPD (71%), demonstrating strong predictive performance that could qualify for future prospective or interventional validation.

### Early signs of neonatal jaundice

Identifying early signs of critical neonatal complications is also crucial. For example, neonatal jaundice, particularly prolonged or conjugated hyperbilirubinemia, often serves as an early clinical signal of cholestasis. Identifying neonatal jaundice promptly helps prevent severe outcomes like bilirubin encephalopathy and neurological complications. machine learning-driven causal inference research recently identified gut-derived bile acid metabolites as reliable biomarkers for early detection and risk assessment of neonatal jaundice [53■]. Given the persistent difficulty in timely detection of neonatal jaundice, especially in resource-limited regions, another retrospective study [51] analyzed neonatal data from 2008 to 2014 and applied multiple machine learning algorithms to predict mortality associated with neonatal jaundice and other critical neonatal conditions, achieving a predictive accuracy of 95.9%, outperforming conventional rule-based approaches. Notably, while it is more difficult to deploy these artificial intelligence models in low-resource or non-EHR settings, several studies in artificial intelligence for healthcare have shown it is feasible to do so through a combination of adaptations, such as constructing nonstandard EHR [54], point-of-care or device-centric artificial intelligence [55], minimal variable models [55], and cloud-assisted screening [55]. A single-center study using

 

85 neonatal data points with pathological jaundice, including 42 confirmed cases of biliary atresia, applied multiple machine learning algorithms to differentiate biliary atresia from other causes of neonatal cholestasis [56]. The models, using key biomarkers including elevated gamma-glutamyl transpeptidase (GGT), increased platelet counts, and alcoholic stools, achieved perfect diagnostic discrimination with 100% accuracy in the validation cohort of 25 patient data. While these studies are still a retrospective and hypothesis-driven, they highlight the potential of artificial intelligence to identify nutrition-related complications.

### Diarrhea and feeding intolerances

Beyond neonatal intensive care, machine learning has also shown substantial promise in predicting specific enteral nutrition-related complications such as diarrhea and feeding intolerance. The model trained on 756 adult ICU patients and tested on 227 test data [57▪] yielded an interpretable machine learning framework that predicts enteral nutrition-associated diarrhea, a direct complication of nutritional therapy, with an average accuracy of 75%. A retrospective study of 300 neurocritical care patients [58▪] also developed a predictive machine learning model using clinical variables such as age, mechanical ventilation, and serum albumin levels to accurately identify neurocritical patients at high risk of enteral nutrition-associated feeding intolerance, achieving over 90% predictive accuracy. Building on these findings, another recent retrospective machine learning study based on 487 adult ICU patients (tested on 97 data points) identified ICU patients at high risk for enteral nutrition-associated feeding intolerance with superior predictive performance (predictive accuracy >95%) [59]. It further enhanced predictive capabilities by integrating additional nutrition-specific variables, such as types of enteral nutrition solutions, delivery routes, and use of gastrointestinal stimulants, probiotics, and laxatives.

### Malnutrition

Machine learning approaches can identify patients at risk of malnutrition. A single-center benchmarking study involving 412 neonatal ICU patient data [60▪] systematically evaluated 22 machine learning algorithms to predict malnutrition risk and weight loss severity within the first 24 h of NICU admission. The advanced machine learning model XGBoost (Extreme Gradient Boosting), an algorithm that combines multiple decision trees to improve predictive accuracy, outperformed traditional screening tools such as the Neonatal Nutrition Screening Tool by 14%. While demonstrating strong predictive performance, this was a retrospective modeling study without prospective clinical validation or direct comparison with clinician assessment.

Expanding this predictive capability to adult ICU settings, a single-center prospective observational study involving 1006 adult ICU patients for model development and 300 adult patients for external validation [61▪▪] developed an machine learning model to identify patients at risk of malnutrition within the first 24 h of admission using comprehensive clinical and biochemical data, including serum albumin, electrolytes, and inflammatory markers. The model demonstrated strong predictive accuracy (87% in internal testing and 84% in external validation), which may lead to earlier detection for shorter mechanical ventilation duration and improved wound healing. Future prospective studies are needed to validate the clinical impact of early artificial intelligence-guided malnutrition screening.

Explainable artificial intelligence (XAI), which provides transparent, interpretable insights into model decisions, represents the next critical advancement, because it allows clinicians to understand and foster trust in predictions for nutrition-related complications [35,62,63]. The machine learning study of malnutrition prediction [61▪▪] uses SHAP (Shapley Additive exPlanations) analysis [64] to give clinical teams an immediate, interpretable 'why' behind machine learning predictions such as longer antibiotic duration due to increased risk of enteral nutrition-associated diarrhea and gastrointestinal intolerance [57▪], and for other applications including prealbumin levels [18▪,61▪▪], and cholesterol ratios [18▪].

## Artificial intelligence-guided models for nutrition delivery optimization in ICU

Recent advancements of artificial intelligence-guided applications extend toward precise nutrient delivery optimization. The latest study introduced TPN2.0 [2▪], a deep-learning model trained on a total of over 150 000+ neonatal ICU orders from multiple institutions. TPN2.0 demonstrated high accuracy from standardized formulas, closely reproducing expert-dosing decisions with near-perfect fidelity. This evidence-based work not only preserves personalization but also simplifies pharmacy compounding workflows. TPN2.0's 'physician-in-the-loop' system notably allows the model to adapt dynamically to individual physicians' preferences, thereby maintaining prescriptions closely aligned with each clinician's practice style. This synergy matters, as automating dose calculations and cross-checks reduces parenteral nutrition ordering errors in

NICUs. In blinded comparisons, neonatal nutrition specialists consistently rated these TPN2.0-supported formulas higher than routine clinician orders, underscoring the system's practical appeal for bedside teams. Future studies could perform prospective clinical implementation and randomized trials to validate these benefits. The retrospective study also showed improvement in long-term gastrointestinal outcomes, such as NEC and cholestasis, from a retrospective investigation. While determining true nutritional requirement is still under research, another recent single-center retrospective study involving 1210 neonatal ICU patient data [65■■] developed a machine-learning-based decision-support tool to automatically determine appropriate parenteral nutrition formulations based on what a multidisciplinary care team would have prescribed. The model was trained on 18 333 historical daily parenteral nutrition records collected over 17 years. By estimating the volume and macronutrients of the parenteral bag with an average correlation of 93%, very close to what expert clinicians would prescribe, this artificial intelligence-driven system has the potential to reduce clinician workload in NICUs. Future validations by randomized controlled trials remain necessary to evaluate whether model-suggested parenteral nutrition formulations can improve patient growth and clinical outcomes.

Parallel developments in adult ICUs reflect another trend that artificial intelligence-driven models can support timely clinical interventions. A 12-variable artificial intelligence-driven model embedded in the EHR identified enteral nutrition patients at high risk of diarrhea within 48 h of admission, potential to timely interventions such as electrolyte monitoring, probiotic administration, and feed-rate adjustments to prevent further complications [57■]. Artificial intelligence can also provide feasible solutions to careful caloric delivery and management in ICU aligned with evolving metabolic phases. A single-center observational modeling study involving 179 septic adult ICU patients, with external validation in 98 data points [66], developed deep learning models to estimate phase-specific energy targets: approximately 900 kcal/day in the early acute phase, 2300 kcal/day in the late acute phase, and 2000 kcal/day during rehabilitation. The models identified associations between energy delivery and mortality trends, and its potential to improve survival rates should next be evaluated in prospective studies.

### Large language models for clinical decision-making

Previous sections review deterministic machine learning for structured data; in healthcare, there is a large corpus of unstructured text data that machine learning can utilize. Within this context, large language models (LLMs) offer a potential solution. Compared with the earlier, deterministic machine learning predictive models that required fixed data entry, LLMs act as conversational 'co-pilots' that can read free-text notes and guidelines to deliver plain-language, data-agnostic recommendations clinicians can use [35,67■,68]. LLM-generated summaries are as complete and correct as physician-written notes yet 28 times faster [69], and can use medical notes to predict nutrition-related mortality risk more accurately than traditional tools while explaining the rationale in everyday language [70■,71,72]. In current deployments, they mostly perform three routine jobs: rapid triage; protocol navigation; and knowledge synthesis [73]. For example, ChatGPT builds sepsis knowledge graphs from multicenter data, linking biomarkers to complications and evidence-based therapies, thereby sharpening bedside decision-making [74■].

A key trade-off is that generative LLMs are not deterministic, that is, they can give off slightly different answers for the same inputs, but sometimes can go way off (aka hallucination), including inventing fake 'facts' and bias, or missing subtle numeric trends [71]. These stem from the model being trained to rather 'guess' than admit uncertainty [75■]. To mitigate these hallucinations, techniques such as chain-of-thought prompting and retrieval-augmented generation (RAG) that retrieve related information from curated corpus of data help reduce these errors [68,76■,77,78].

## CHALLENGES AND POTENTIAL OF MODELING COMPLEX NUTRITIONAL DATA

### Parenteral versus enteral confounding effects

Personalized nutrition strategies must address immediate metabolic needs and mitigate complications over prolonged ICU stays [79■]. However, clearly attributing outcomes to specific nutritional interventions remains challenging, given the complex interplay between enteral and parenteral nutrition. Patient outcomes vary significantly by delivery route due to confounding factors such as preexisting comorbidities, illness severity, and concurrent therapies [80,81,82■]. Additionally, ICU patients typically exhibit multiple simultaneous diseases and physiological disturbances, further complicating predictive analyses and obscuring the true impacts of nutritional strategies on clinical outcomes.

Causal inference methods, particularly those employing machine learning, offer promising frameworks for clarifying these relationships. Several studies have utilized these approaches to isolate nutritional effects from patient heterogeneity biases [83,84▪]. By employing counterfactual reasoning, these methods can estimate outcomes under alternative nutritional strategies, effectively separating true effects from confounding biases [84▪]. Although causal methodologies have shown potential in clinical and epidemiological contexts, their application in ICU nutritional therapy remains developing. Future research addressing methodological challenges is essential to validate these approaches and enhance precision and personalization in ICU nutritional management.

### Molecular heterogeneity

Ingredient heterogeneity in enteral and parenteral formulations further complicates nutritional therapy in the ICU, such as differing protein sources, carbohydrate compositions, or lipid emulsions (e.g. soybean oil-based versus fish oil-enriched preparations) [85]. Variations in macronutrient composition, calorie density, and bioactive components of the nutrition provided can result in different disease progression and recovery rates, which lead to diverse patient outcomes [86–88]. Recent literature suggests that leveraging artificial intelligence models to examine ingredient effects systematically can improve the precision of nutritional interventions [89▪]. Understanding the effects of nutritional profiles of various ingredients on biological processes may inform future efforts to customize care plans that align more closely with patients' nutritional needs, potentially improving recovery once validated in clinical settings [90–92].

Beyond heterogeneity in nutritional formulations, patient-specific molecular signatures critically influence therapeutic outcomes, where genomic, epigenetic, and metabolic profiles dictate individualized responses to intervention. Multiomics profiling can be considered to bridge this gap. In the NICU, metabolomics and lipidomics analyses have uncovered novel biomarkers linked to metabolic disorders and trajectory prediction [11▪]. Emerging evidence suggests that integrating EHR data with multiomics profiling using machine learning approaches can complimentarily improve predictive accuracy and expand biological discovery beyond what is possible with either modality alone, even in the context of limited sample sizes [21▪]. Furthermore, advanced multiomics causal inference approaches have delineated associations between gut microbiome dynamics, bile acid metabolism, and neonatal jaundice, which illustrate how molecular-level modeling can uncover actionable mechanisms in critical care nutrition [53▪]. Thus, future studies that incorporate omics-derived biomarkers into artificial intelligence-driven nutritional models could enable precision mapping between ingredient profiles (e.g. lipid emulsions, carbohydrate sources) and patient-specific metabolic responses, facilitating more context-aware ICU nutritional management with improved clinical relevance.

## CONCLUSION

Artificial intelligence has the potential to transform ICU nutrition from a fixed paradigm driven by guidelines to dynamic, data-based decisions. By leveraging machine learning models, multimodal EHR data streams, and LLMs, artificial intelligence can process complex data, flag safety errors, and accurately predict long-term recovery trajectories that were once hidden due to lack of follow-up. Early successes, such as TPN2.0 [2▪], have far surpassed the accuracy of most clinicians' decisions. With effective supervision by clinicians, artificial intelligence will bring great improvements to ICU nutritional therapy. However, the algorithm is only as powerful as its training data; global, standardized, longitudinal datasets are critical. Most of these retrospective studies demonstrate great potential but require future validation through adequately powered randomized controlled trials (RCTs) focused on patient-centered outcomes. Through rigorous validation in comparative clinical trials and fair implementation of machine learning models, artificial intelligence-guided nutritional therapy has the potential to provide safer, more personalized care and better outcomes for the most vulnerable patients.

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### Conflicts of interest

*D.P. is an associate of Takeoff41, Inc., a company developing AI solutions for clinical nutrition, T.P. and N.A. are co-founders of Takeoff41, Inc.*

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