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Original article

Improving the safety and accuracy of pediatric parenteral nutrition prescribing using a real-time, patient-specific clinical decision support system: A within-subject comparative study

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ABSTRACT

Background/Objectives: Parenteral nutrition (PN) is a complex therapy in pediatric patients, requiring individualized calculations and strict adherence to therapeutic and pharmaceutical protocols. Manual PN prescribing is prone to variability, calculation errors and deviations from recommended stability and safety limits. Rather than com-paring final PN regimens administered to patients, this study evaluated the prescribing process itself by assessing the impact of a pediatric clinical decision support system on the accuracy, safety and consistency of PN prescribing through a within-subject com-parison of manual and clinical decision support system (CDSS)-assisted prescriptions for the same patients.

Methods: This was a single-center, within-subject, comparative observational study evaluating pediatric parenteral nutrition prescribing accuracy. For each of the 30 hospitalized pediatric patients, paired parenteral nutrition prescriptions were generated using two approaches: traditional manual clinician–pharmacist pre-scribing and CDSS-assisted prescribing. The two methods were compared in terms of nutrient dosing accuracy, adherence to

Abbreviations: PN, Parenteral Nutrition; CDSS, Clinical Decision Support System; ESPEN, European Society for Clinical Nutrition and Metabolism; ASPEN, American Society for Parenteral and Enteral Nutrition; GIR, Glucose Infusion Rate; WHO, World Health Organization.

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guideline-recommended ranges, physicochem-ical suitability, osmolarity limits, and stability-related alerts.
Results: CDSS-generated PN formulations showed significantly lower amino acid concentration, glucose con-centration and osmolarity than manual prescriptions ($P < 0.05$), with a slightly higher infusion rate. No differences were observed in glucose or lipid infusion rates. Manual prescriptions showed greater variability and included 16 clinically relevant deviations, such as excessive glucose concentrations, osmolarity violations, and electrolyte dis-crepancies. All deviations were automatically corrected by the CDSS. CDSS-assisted prescriptions also resulted in more consistent overfill adjustments and dosing values that remained within recommended limits.
Conclusions: The CDSS improved dosing precision, reduced prescribing variability and prevented formulation errors compared with manual PN prescribing, supporting its role as a clinical decision-support tool in pediatric parenteral nutrition practice. Further multicenter studies are needed to assess its clinical impact.

1. Introduction

Parenteral nutrition (PN) is a vital, often life-saving therapy for neonates, infants and children who are unable to meet their nutritional requirements through enteral feeding. However, it remains a complex intervention requiring precise, individualized calculations, particularly in pediatric patients with rapidly changing metabolic demands and narrow safety margins, which increase the risk of prescribing errors and complications [1–3].

The PN prescribing process is inherently complex, involving multiple steps such as indication assessment, precise nutrient calculations, formulation design and monitoring, each representing a potential source of error [2]. Variability in clinical experience and prescribing practices among healthcare professionals further contributes to PN-related medication errors, while serious incidents—including deaths—have been reported when stability and compatibility guidelines are not followed [4].

Safe and accurate prescribing is therefore a critical first step in PN therapy. However, in routine clinical practice, this process is challenged by the time required for complex calculations, the variability of patient-specific parameters, and the lack of integrated decision-support systems [2,5].

Guidelines for PN use have been developed by major scientific societies such as ESPEN and ASPEN [6,7]. While these guidelines support clinical decision-making, they cannot replace individualized clinical judgment, as highlighted by the Scottish Intercollegiate Guideline Network (SIGN) [8,9]. To date, however, no study has evaluated the impact of a structured, real-time clinical decision support system on individualized PN dosing that integrates therapeutic and pharmaceutical protocols, safety alerts and infusion overfill calculations.

Clinical decision support systems have shown promise in improving prescribing practices, with studies demonstrating reductions in prescribing errors, improved dosing precision and enhanced adherence to safety limits when integrated into computerized order entry systems [5,11,12]. Nevertheless, few systems are specifically designed for pediatric PN, and even fewer incorporate real-time individualized dosing algorithms, incompatibility alerts and infusion overfill calculations—features that are particularly important given the narrow safety margins in children [10].

To address these challenges, we implemented a pediatric PN-specific clinical decision support system (CDSS) in our hospital setting. The system integrates therapeutic and pharmaceutical

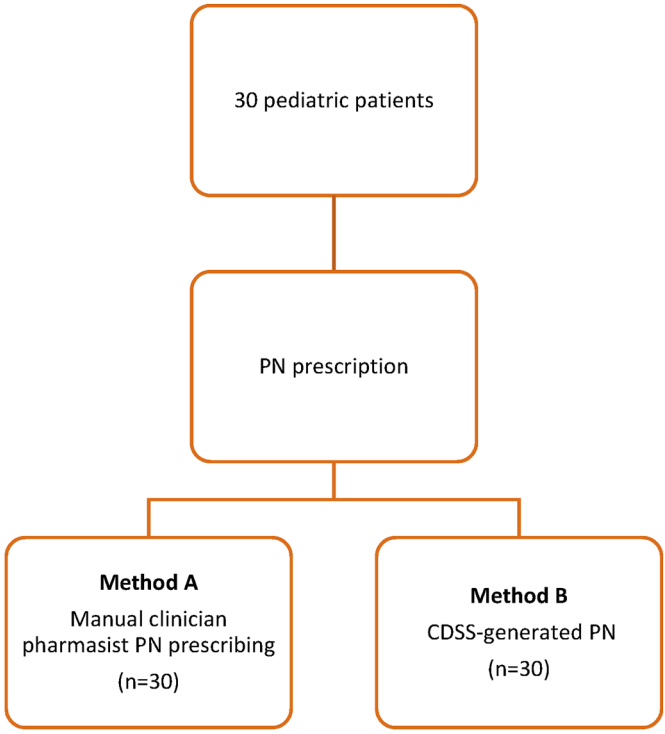

Figure 1. Schematic overview of the design of the study.

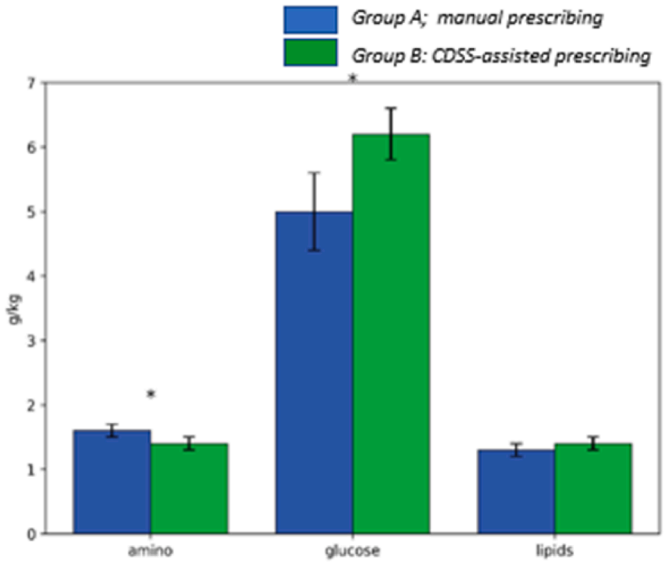

Figure 2. Differences in amino acid, glucose, and lipid dosing between manual clinician–pharmacist prescribing (Group A) and CDSS-assisted prescribing (Group B) regimens ($P < 0.05$ compared with manual prescribing).

protocols, patient-specific parameters, automated nutrient calculations, compatibility alerts and justification-based overrides.

Although both manual clinician–pharmacist prescribing and CDSS-assisted prescribing are validated approaches, this study focuses on a different aspect of parenteral nutrition prescribing. Rather than comparing the final PN regimens delivered to patients, the present study evaluates the prescribing process itself. By examining manual prescriptions prior to pharmacist correction and comparing them with CDSS-generated prescriptions for the same patients, differences in prescribing accuracy, stability and safety were assessed under identical clinical conditions.

This study was designed as a single-center, within-subject, comparative observational study. Paired PN prescriptions generated through routine manual clinician–pharmacist prescribing and CDSS-assisted prescribing were compared for the same hospitalized pediatric patients. The primary objective was to assess differences in dosing accuracy, adherence to guideline-recommended ranges and formulation safety, including stability- and compatibility-related deviations.

2. Materials and methods

2.1. Study design and setting

This study was designed as a single-center, within-subject, comparative observational study.

The study assessed adherence to guideline-based PN dosing and prescribing accuracy by comparing two prescribing approaches applied to the same pediatric patients:

(1) conventional clinician-manual PN prescribing (physician with pharmacist verification) and
(2) PN prescribing assisted by a clinical decision support system, with allowance for clinician-initiated adjustments.

This within-subject design enabled direct comparison of manual versus CDSS-assisted prescribing for the same patients, thereby minimizing inter-patient variability and isolating differences attributable to calculation methodology, embedded decision support and safety alerts. The present study focused on prescribing accuracy and physicochemical safety of PN formulations rather than patient-level clinical outcomes. Improved alignment with recommended nutrient ranges and automated safety checks support safer prescribing practices and represent key determinants of safe PN therapy.

All patients received the final parenteral nutrition regimen derived from routine manual clinician prescribing after mandatory pharmacist verification and correction, in accordance with standard clinical practice. CDSS-generated prescriptions were produced in parallel for comparative evaluation only and were not administered to patients.

Pharmacists were not blined to the study design, as prescriptions were reviewed and verified according to standard clinical procedures. However, CDSS-generated prescriptions were produced independently and were not accessible to pharmacists during routine verification of manual prescriptions, minimizing potential bias in pharmacist review.

2.2. Ethical approval

The study was approved by the Scientific and Ethical Committee of IASO Hospital (Approval No. 21–1118C). Parents or guardians provided informed consent for the use of children's clinical and personal data within the CDSS database.

2.3. Participants

Of thirty five eligible patients assessed during the study period, 30 met inclusion criteria and were enrolled. Eligibility criteria were age 3–17 years, requirement for PN during hospitalization and physician-prescribed PN support.

Patients receiving any enteral nutrition had their PN volumes adjusted accordingly. Exclusion criteria included instability, contraindications to PN, or missing essential clinical data.

Both prescribing approaches were applied to the same patients in a paired, non-randomized design, minimizing inter-patient variability.

The study included 30 pediatric patients (63.3% boys and 36.7% girls) with a mean age of 9.5 years (range: 3–17 years). For each patient, two PN prescriptions were generated (manual and CDSS-assisted), resulting in 30 paired comparisons between the two prescribing approaches. Regarding the route of parenteral nutrition administration, 11 patients (36.7%) received PN peripherally, while 19 patients (63.3%) received PN via central venous access.

2.4. Study procedures and methods

For each of the 30 enrolled pediatric patients, two parenteral nutrition prescribing pathways were generated, enabling a direct within-subject comparison under identical clinical conditions. The unit of analysis was the individual parenteral nutrition prescription, with each patient serving as their own control through paired manual and CDSS-assisted prescriptions. Prescribers generated CDSS-assisted prescriptions independently, without viewing the manual prescription.

- Method A – Manual clinician-pharmacist PN prescribing (Physician + Pharmacist): In routine practice, the attending physician prescribed PN manually according to ESPEN/ESPGHAN recommendations, incorporating individualized clinical judgment. Each prescription subsequently underwent mandatory pharmaceutical verification by a hospital pharmacist, who evaluated dosing accuracy, physicochemical compatibility, osmolarity constraints, and formulation stability prior to final approval.
- Method B –CDSS-generated PN: Using the same clinical dataset, a second PN regimen was produced through the CDSS. The system automatically calculated individualized nutritional requirements and constructed a complete PN formulation based on integrated therapeutic guidelines and pharmaceutical compatibility rules. The CDSS automatically generates a guideline-based prescription; clinicians may modify system-generated values when clinically indicated, with all overrides recorded within the system.

This within-subject, paired design enables precise evaluation of differences in dosing accuracy, guideline adherence, physicochemical suitability and formulation consistency between manual clinician–pharmacist prescribing and software-assisted automated PN generation (Fig. 1)

For each of the 30 enrolled pediatric patients, two parenteral nutrition prescriptions were generated under identical clinical conditions, enabling a direct within-subject comparison. The unit of analysis was the individual parenteral nutrition prescription, with each patient serving as their own control through paired prescriptions. For comparative purposes, the manual prescription analyzed in this study corresponded to the initial clinician-generated prescription prior to pharmacist correction, whereas the second prescription was generated using the CDSS. Prescribers generated CDSS-assisted prescriptions independently, without viewing the manual prescription.

2.5. Data collection

Demographic and clinical variables were extracted from medical records, including anthropometric measures, birth weight, underlying conditions, PN access, and concurrent treatments. Weight was determined with a calibrated electronic scale, with corrections applied in cases of obesity, malnutrition, or edema. Routine biochemical evaluations (electrolytes, glucose, triglycerides, albumin, urea, creatinine, and additional tests as clinically indicated) were performed to confirm clinical stability prior to PN initiation.

2.6. CDSS description and PN calculation framework

The CDSS integrates evidence-based ESPEN, ESPGHAN and pharmaceutical PN protocols in order to calculate individualized nutritional requirements derived from anthropometric measurements, underlying diseases, clinical conditions and medication profiles. For each patient, the system determines the complete spectrum of daily nutritional needs, including total energy, amino acids, carbohydrates, lipids, electrolytes, vitamins and trace elements. These values are generated through validated computational models that incorporate patient-specific physiological characteristics and guideline-based reference ranges.

To optimize dosing accuracy, the CDSS automatically applies adjusted body weight for obese children and corrected weight for patients with malnutrition, while defaulting to actual body weight in all other cases. The system also performs an overfill calculation to ensure that the full prescribed nutrient content is effectively delivered despite infusion set retention. Additional core capabilities include estimation of glucose infusion rate limits, automated osmolarity calculations, and recommendations regarding the suitability of peripheral versus central vascular access in order to minimize infusion-related complications.

The platform provides real-time alerts related to drug–nutrient incompatibilities, component stability concerns, and dosing deviations that may place the patient at risk of under- or over-nutrition. PN order templates have been standardized within the system to support clarity, reduce human error and facilitate consistent prescribing practices across clinicians. Furthermore, the CDSS offers predefined dosing options tailored to complex clinical conditions, including cases with multiple comorbidities (e.g., cardiac failure combined with ascites), for which calculations are automatically adapted based on established therapeutic and pharmaceutical protocols. Comprehensive documentation is generated for each case, encompassing the rationale for recommendations, selected dosing parameters and all adjustments made. Physicians are able to accept or override the proposed regimen; overrides require justification and are fully documented within the system.

2.7. Physician-prescribed regimens

In routine clinical practice, PN prescriptions were written by pediatricians according to current ESPEN and ESPGHAN recommendations, supplemented by individualized clinical judgment. Despite the availability of standardized protocols, notable variation existed among prescribers, reflecting differing interpretations of patient needs and clinical priorities. All physician-generated PN orders underwent a mandatory two-step review by a hospital pharmacist. This review involved assessment of macronutrient and micronutrient dosing accuracy, compatibility of prescribed components, expected physicochemical stability of the final formulation and appropriateness of the selected vascular access.

When discrepancies from accepted guidelines or compatibility concerns were identified, formulations were recalculated by the pharmacist and returned to the prescribing physician for revision and confirmation prior to compounding. This verification process was applied consistently across all 30 PN prescriptions in Method B, ensuring safety and adherence to established pharmaceutical standards.

2.8. Technical specifications of the CDSS

The CDSS was developed using a client–server architecture implemented in C# on the Microsoft.NET Framework 4.8, using Visual Studio 2019 and SQL Server 2019. The system incorporates an extensive library of age-specific PN protocols applicable to neonates, infants, children, adolescents and adults. An internal database of commercially available PN components enables the CDSS to assist clinicians in selecting appropriate solutions according to the prescriber's input, facilitating the construction of complete PN formulations aligned with the clinician's specified requirements.

The PN order form is fully codified and includes demographic data, clinical conditions and comorbidity-specific modifiers. Physicians retain the ability to modify protocol-derived parameters when clinically required. The CDSS also compares ready-to-use PN solutions with patient-specific

nutrient requirements, facilitating accurate matching between commercial products and individualized needs. Advanced computational modules determine calcium-to-phosphate ratios, osmolarity, non-protein kcal/g nitrogen, glucose infusion rates and lipid infusion rates.

Additional functionalities include generation of printable PN order forms and compounding labels, compatibility with automated compounding devices (ACDs), and export of anonymized datasets for auditing or research purposes. The system also allows recording of biochemical data, medication information and growth metrics, including WHO-based growth curves. The updated version used in this study has been validated by a multidisciplinary informatics–pharmacy team and is currently deployed in four maternity and pediatric units in Greece. Usability and functionality of the CDSS with integrated computerized provider order entry (CPOE) were assessed through a structured questionnaire completed by eleven physicians [13].

2.9. Outcome measures

The primary study outcome was prescribing accuracy, defined as adherence of prescribed nutrient doses and formulation parameters to guideline-recommended ranges and predefined safety and stability limits, when comparing clinician-generated parenteral nutrition formulations (Method A) with CDSS-assisted formulations (Method B).

Secondary outcomes included:

- the number and type of clinically relevant dosing, osmolarity or stability deviations identified in manual prescriptions
- variability of prescribed nutrient concentrations and infusion parameters between prescribing methods
- differences in physicochemical formulation characteristics (e.g., osmolarity, glucose and amino acid concentrations)
- consistency of overfill adjustments applied during prescription generation.

This outcome framework enables a robust within-subject evaluation of prescribing precision, safety, and consistency between traditional manual clinician–pharmacist parenteral nutrition formulation and CDSS-assisted parenteral nutrition generation with physician- or pharmacist-initiated adjustments.

2.10. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics, version 23.0. Continuous variables were assessed for normality using the Kolmogorov–Smirnov test and are presented as means with standard deviations. For within-subject comparisons between manual clinician-generated PN prescriptions (Method A) and CDSS-generated prescriptions (Method B), paired t-tests were applied for normally distributed variables. Categorical variables were analyzed using Fisher's exact test. Statistical significance was defined as a two-tailed P-value < 0.05. Given the within-subject paired design and the observed moderate to large differences in parameters, a sample size of 30 paired prescriptions was considered sufficient to detect clinically meaningful differences.

3. Results

CDSS-generated parenteral nutrition formulations demonstrated significant differences compared with manually prescribed formulations across several key parameters.

As shown in Table 1, CDSS-generated PN formulations demonstrated significantly lower amino acid concentration, glucose concentration and osmolarity compared with manual prescriptions (all $P < 0.05$). Infusion rate was also slightly but significantly higher in the CDSS group ($P = 0.012$). In contrast, no significant differences were observed for glucose infusion rate (GIR) or lipid infusion rate ($P = 0.586$ and $P = 0.602$, respectively).

Table 1
Descriptive characteristics of parenteral nutrition formulations comparing manual clinician–pharmacist prescribing (Group A) and CDSS-assisted prescribing (Group B) (n = 30)

Parameter	GROUP A - Manual (mean± standard deviation)	GROUP B - CDSS (mean± standard deviation)	*P-value*
Amino acid concentration (%)	3.4 ± 1.1	2.8 ± 0.6	**0.001**
Glucose concentration (%)	12.9 ± 2.9	12.3 ± 2.4	**0.013**
Osmolarity (mOsm/L)	1220.6 ± 228.0	1120.0 ± 184.2	**<0.001**
Infusion rate (ml/h)	57.2 ± 25.7	59.0 ± 25.5	**0.012**
Glucose Infusion Rate (mg/kg/min)	4.3 ± 1.4	4.3 ± 1.4	0.586
Lipid infusion rate (g/kg/h)	0.06 ± 0.03	0.06 ± 0.02	0.602

Beyond the significant differences in macronutrient concentrations, several stability-related findings distinguished manual from CDSS-assisted prescriptions. Manual PN formulations exhibited greater variability in key physicochemical parameters, reflected by their higher standard deviations in amino acid concentration (SD 1.1 vs 0.6), glucose concentration (SD 2.9 vs 2.4) and osmolarity (SD 228.0 vs 184.2), indicating lower consistency in manual formulations. All identified deviations in manual prescriptions were corrected by pharmacists prior to compounding.

Correspondingly, during pharmacist verification, manual prescriptions generated multiple stability alerts, including six instances of excessive glucose concentration, three alerts related to elevated osmolarity, five deviations in glucose dose per kg, and two alerts for sodium dosing. In contrast, the CDSS automatically applied embedded stability rules and corrected all sixteen of these deviations in real time, preventing threshold violations before final order generation.

The system additionally incorporated a standardized overfill adjustment, typically corresponding to an approximate 20 mL increase in the final infused volume (this may vary depending on the infusion set used, and the exact volume can be entered by the user as needed). This overfill volume is calculated proportionally across all component solutions according to their contribution to the final mixture. It is not intended to be infused to the patient but to remain in the bag, preventing the infusion set from emptying completely and avoiding air entrainment into the intravenous line.

Paired comparisons between manual (Group A) and CDSS-generated prescriptions (Group B) showed several significant differences in nutrient doses (Table 2). CDSS prescriptions resulted in higher fluid provision (50.5 ± 3.0 vs. 47.4 ± 3.1 ml/kg, $P < 0.001$) and lower amino acid dosing (1.4 ± 0.1 vs. 1.6 ± 0.1 g/kg, $P = 0.040$). Glucose dosing was also significantly higher in CDSS formulations (6.2 ± 0.4 vs. 5.0 ± 0.6 g/kg, $P = 0.037$). No statistically significant differences were observed between manual and CDSS prescriptions for lipids, sodium, calcium, magnesium, trace elements, or fat-soluble

Table 2
Comparison of nutrient doses (per kg) between manual clinician–pharmacist prescribing (Group A) and CDSS-assisted prescribing (Group B) for the same patients (paired analysis, n = 30)

All patients (n=30)	GROUP A - Manual (mean± standard deviation)	GROUP B - CDSS (mean± standard deviation)	*P-value*
Fluids (ml/kg)	47.4 ± 3.1	50.5 ± 3.0	**<0.001**
Amino acids (g/kg)	1.6 ± 0.1	1.4 ± 0.1	**0.040**
Lipids (g/kg)	1.3 ± 0.1	1.4 ± 0.1	0.646
Glucose (g/kg)	5.0 ± 0.6	6.2 ± 0.4	**0.037**
Sodium - Na (meq/kg)	2.9 ± 0.3	2.6 ± 0.2	0.210
Potassium -K (meq/kg)	1.6 ± 0.1	1.6 ± 0.1	
Calcium - Ca (meq/kg)	0.5 ± 0.0	0.5 ± 0.0	0.272
Phosphate -PHO_4 (mmol/kg)	0.4 ± 0.0	0.4 ± 0.0	
Magnesium Mg (meq/kg)	0.4 ± 0.0	0.4 ± 0.0	0.326
Trace elements (ml/kg)	0.3 ± 0.0	0.2 ± 0.0	0.125
Water-soluble vitamins (ml/kg)	0.4 ± 0.0	0.4 ± 0.0	**0.020**
Fat-soluble vitamins (ml/kg)	0.4 ± 0.0	0.4 ± 0.0	0.326

vitamins (all $P \geq 0.05$). For potassium and phosphate, all paired values were identical, and therefore no statistical comparison was applicable (Table 3) (Fig. 2).

The overfill step resulted in a similar average change in nutrient volumes in both the manual and CDSS methods, with no statistically significant differences. However, the CDSS applied this adjustment much more consistently, showing uniformly low variability across all components (SD $\approx$ 0.9%), while the manual method displayed much larger fluctuations, including high variability in some nutrients. This indicates that, although the mean effect of overfill was comparable, the CDSS distributed it more accurately and reliably due to its substantially lower variability (Table 3).

Mapping manually prescribed PN regimens onto the CDSS stability matrix, which incorporates predefined concentration ranges for all major components (e.g., glucose 50–155 g/L, lipid 20–60 g/L, sodium 0–150 mmol/L, calcium and magnesium 0–10 mmol/L, trace elements 0–10 mL/L, water-soluble vitamins 0–10 mL and fat-soluble vitamins 0–20 mL/L), identified a total of 50 parameter values outside protocol limits. These deviations comprised 13 values for total nitrogen, 7 for glucose concentration, 5 for lipid concentration, 2 for sodium, 1 for calcium, 1 for magnesium, 4 for trace elements, 16 for water-soluble vitamins and 1 for fat-soluble vitamins. In routine practice, such deviations must be detected and corrected manually by the pharmacist and prescribing physician, leaving some room for human error. In contrast, CDSS-generated regimens are automatically checked against the same stability matrix during order construction, and any out-of-range values are adjusted by the system before finalization, ensuring that the approved PN formulations remain fully compliant with predefined physicochemical and dosing limits.

4. Discussion

This study evaluated the impact of an integrated clinical decision support system (CDSS) on the accuracy, safety and consistency of pediatric parenteral nutrition (PN) prescribing.

Clinical decision support systems (CDSS) have been shown to reduce prescribing errors and improve adherence to guideline-based dosing, particularly in pediatric settings where dosing complexity is high [14,15]. Previous systematic reviews have demonstrated that CDSS-supported prescribing can improve physician performance and medication safety, although the impact on clinical outcomes remains uncertain. In this context, the present study extends existing evidence by focusing on real-time, patient-specific parenteral nutrition prescribing with integrated stability and compatibility checks.

By directly comparing handwritten, clinician-generated regimens with CDSS-assisted formulations for the same patients, we demonstrated that the automated, guideline-based approach significantly improved nutrient accuracy, minimized deviations from recommended ranges, and prevented the generation of unsafe or unstable PN solutions. These results reinforce the role of digital decision-

Table 3
Variability of overfill-induced proportional volume changes between manual clinician–pharmacist prescribing (Group A) and CDSS-assisted prescribing (Group B)

	Manual (Group A) Mean %	Manual (Group A) Standard deviation %	CDSS (Group B) Mean %	CDSS (Group B) Standard deviation %	*P*-value (paired t-test)
Glucose 10% (ml)	1.92	1.03	1.72	0.84	0.167
Vamin 18 EF (ml)	5.27	1.76	1.80	0.91	0.297
Glucose 50% (ml)	1.97	1.12	1.80	0.91	0.089
SMOFlipid 200mg (ml)	1.96	1.12	1.80	0.91	0.096
Potassium Chloride (ml)	1.96	1.12	1.80	0.91	0.100
Calcium Gluconate (ml)	1.55	2.52	1.80	0.90	0.532
Glycophos (ml)	1.95	1.14	1.78	0.91	0.112
Magnesium Sulfate-MgSO4 25% (ml)	1.98	1.20	1.78	0.89	0.098
Peditrace (ml)	1.97	1.22	1.85	0.91	0.297
Soluvit ® (ml)	1.96	1.13	1.79	0.90	0.091
Vitalipid Infant ® (ml)	1.96	1.13	1.79	0.90	0.095

support tools in enhancing the standardization and overall quality of PN prescribing, a process that remains highly complex and multidisciplinary [12].

An important finding of this study is the reduced variability and improved consistency associated with CDSS-assisted parenteral nutrition prescribing. Similar reductions in dosing variability have been reported in pediatric settings using clinical decision support systems for complex, weight-based medication prescribing, highlighting the broader role of CDSS in standardizing high-risk pediatric therapies [16]. Manual PN prescribing relies on multiple manual calculations and individual clinical judgment, which may introduce variability even when prescriptions are subsequently reviewed by pharmacists. In pediatric patients, where safety margins are narrow, such variability may increase the risk of unintended deviations from recommended dosing and physicochemical limits. By embedding guideline-based dosing ranges and pharmaceutical stability constraints directly into the prescribing process, the CDSS supports more standardized and predictable PN formulations, while still allowing clinician-initiated adjustments when clinically indicated. This approach may reduce cognitive burden during prescribing and shift multidisciplinary efforts from error correction toward optimization of individualized nutritional support [17].

In our study, statistically significant differences were observed between manual and CDSS-generated prescriptions for amino acid concentration, glucose concentration, osmolarity and infusion rate, while no significant differences were found for glucose infusion rate (GIR) or lipid infusion rate. Although the absolute differences in nutrient quantities between manual and CDSS-assisted prescriptions were relatively small, the main advantage of CDSS-supported prescribing lies in improved standardisation, reduced variability between prescriptions, and automated detection of deviations from recommended nutrient ranges or physicochemical stability constraints. These findings further support the ability of the CDSS to improve dosing accuracy without altering lipid or GIR delivery.

Manual PN prescriptions exhibited considerable variability and multiple deviations in both macronutrient and micronutrient components, particularly in amino acids, glucose and electrolytes. This finding is consistent with earlier studies showing inconsistent adherence to PN guidelines and frequent underestimation of pediatric energy and protein needs in routine practice [3,18,19]. In our sample, manual regimens often provided lower amino acid and glucose doses than CDSS-generated formulations. Similar improvements in nutrient adequacy have been observed in neonatal and pediatric settings where computerized PN systems and standardized electronic protocols were implemented [20].

Accurate estimation of energy requirements is fundamental in pediatric PN, as even modest nutrient deficits may impair recovery, growth and long-term development [5,6,21]. CDSS-generated regimens in our study delivered slightly higher caloric provision—still within recommended limits—reflecting improved alignment with guideline-based estimates of energy requirements. Lipid dosing remained within safe and comparable ranges across both methods, consistent with the lack of a statistically significant difference between manual and CDSS regimens [5,22].

While the average impact of overfill was similar between methods, the CDSS applied it in a far more steady and predictable way. This consistency reduces the small, unintended nutrient shifts that can occur with manual adjustments, making the automated approach a more reliable option for maintaining the intended PN composition.

Safety and physicochemical stability are critical considerations in PN compounding, especially regarding calcium–phosphate solubility, osmolarity, and glucose concentration—parameters influenced by pH, amino acid composition, dextrose concentration and mixing order [23,24]. When handwritten prescriptions were mapped to the CDSS stability matrix, multiple compatibility failures emerged, including calcium–phosphate incompatibilities, excessive osmolarity and unsafe glucose concentrations. Importantly, 20% of manually prepared peripheral PN regimens surpassed the recommended 12.5% glucose limit, increasing the risk of phlebitis, extravasation and catheter-related complications. In contrast, CDSS-generated orders complied with all compatibility and route-specific constraints, demonstrating the system's ability to prevent unsafe formulations upstream in the prescribing process.

Beyond physicochemical safety, our findings highlight the inherent variability of clinician-dependent PN prescribing. Deviations in vitamins, trace elements, electrolytes and macronutrients

have been widely reported and are often attributed to differences in experience, interpretive judgment and manual calculation methods [25–27]. Standardized electronic prescribing mitigates this variability by embedding guideline-based reference ranges and automated safety rules directly into the ordering process. Previous studies have shown that such systems reduce prescribing errors, enhance uniformity across clinicians and institutions, and decrease calculation workload—by up to 60% for complex PN orders [7,15,25,27,28].

Our results reinforce these advantages: CDSS-generated PN orders were complete, balanced and free of components outside recommended limits. By reducing the cognitive burden of dose calculations and eliminating transcription steps—one of the most common sources of PN errors [10,29]—the CDSS facilitated safer and more efficient prescribing workflows.

Equally important is the value of upstream decision support before PN compounding. PN is a high-risk therapy that requires a detailed two-step clinical and pharmaceutical review to ensure dosing accuracy, compatibility and suitability for vascular access [26]. In our study, pharmacist verification identified multiple clinically relevant issues in manual prescriptions, while no CDSS-generated regimen required reformulation In manual prescribing workflows, pharmacist verification represents a critical safety step prior to PN preparation. CDSS-assisted prescribing complements this process by introducing automated checks at the point of prescription generation, enabling potential incompatibilities or deviations from recommended ranges to be identified before the prescription reaches the pharmacy. This aligns with evidence showing that compounding errors persist even with automated devices (22% error rate when partially automated and 37% when fully manual), underscoring the importance of electronic order-entry systems with embedded CDSS features [30].

Finally, this study expands upon prior algorithm-based approaches for PN prescribing. Algorithms such as PNMatch have demonstrated high concordance with clinician-selected multi-chamber bag regimens and have contributed to reduced prescribing variability in adults. However, their functionality is restricted to the selection of commercially available PN products and does not include individualized nutrient calculation, real-time physicochemical stability safeguards or automated detection of deviations outside protocol limits [31]. In contrast, the CDSS evaluated here directly computes individualized pediatric nutrient requirements, incorporates therapeutic and pharmaceutical protocols, and enforces glucose infusion limits, osmolarity thresholds, electrolyte compatibility rules and overfill correction. Thus, our findings extend existing evidence by showing that advanced CDSS platforms can improve both dosing precision and safety in individualized pediatric PN prescribing, beyond product-matching algorithms alone.

This study has several limitations. Although it demonstrates improvements in prescribing accuracy, safety and consistency, these process-level outcomes do not directly translate into clinical outcomes, as the analysis was not designed to assess downstream endpoints such as growth, metabolic complications or length of hospital stay. The sample size was modest ($n = 30$) and the study was conducted in a single-center setting, which may limit generalizability. In addition, the study population included pediatric patients aged 3–17 years and did not include premature neonates, who represent a large proportion of patients receiving parenteral nutrition. Neonatal PN prescribing follows distinct nutritional protocols; therefore, evaluation of CDSS performance in neonatal populations warrants dedicated investigation. Although neonatal patients were not included in the present study due to distinct clinical considerations, recent evidence from a randomized controlled trial supports the effectiveness of CDSS-assisted parenteral nutrition in preterm neonates, demonstrating improved growth outcomes [32].

The lack of blining of prescribers and pharmacists represents a potential source of performance bias, which should be considered when interpreting the observed differences between manual and CDSS-assisted prescriptions. While the CDSS supports safer and more standardized prescribing, clinical judgment and human oversight remain essential to address patient-specific conditions not fully captured by guideline-based algorithms. Sex-specific analyses were not performed due to the limited sample size. Future multicenter studies should include larger and more diverse pediatric populations and evaluate cost implications and workflow efficiency to support institutional decision-making.

5. Conclusions

Although clinical assessment by physicians remains irreplaceable, parenteral nutrition (PN) prescribing is a multidisciplinary and complex process that can benefit from structured decision-support tools. In this study, the clinical decision support system (CDSS) improved adherence to guideline-based dosing by integrating patient-specific parameters, body-weight adjustments and predefined therapeutic options derived from its internal database. The system demonstrated good usability, and its algorithm—based on therapeutic and pharmaceutical protocols—enhanced the consistency of nutrient delivery while reducing calculation errors and formulation instability. Given the wide variation among existing PN guidelines, standardized algorithm-supported prescribing may contribute to safer and more reliable PN formulation, particularly for this high-risk therapy. Future multicenter studies are needed to evaluate whether these improvements in prescribing accuracy translate into measurable clinical outcomes, such as growth, metabolic complications and length of hospital stay, in pediatric populations.

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Author contributions

Conceptualization, A.C.K.; methodology, S.K and A.C.K.; validation, S.K., C.K. and A.C.K..; formal analysis, S.K..; investigation, C.K.; writing—original draft preparation, S.K..; writing—review and editing, S.K., C.K. and A.C.K..; supervision, A.C.K. All authors have read and agreed to the published version of the manuscript.

Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of IASO HOSPITAL (Approval No. 21-1118-C).

Data availability statement

Data are unavailable due to privacy or ethical restriction.

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Declaration of competing interest

The authors declare no conflicts of interest.

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