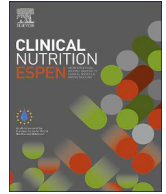




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Narrative Review

Malnutrition, sarcopenia and nutrition therapy for patients with diabetes - A general framework and focus on hospital care

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SUMMARY

Background & aims: The prevalence of diabetes is increasing globally and is particularly high among hospitalized patients, presenting challenges for inpatient care. While traditional inpatient management emphasizes glycemic control, medication adjustments, and comorbidity management, malnutrition and muscle loss remain underrecognized factors that significantly influence clinical outcomes. This review aims to highlight the role of malnutrition and muscle dysfunction in hospitalized patients with diabetes and to evaluate the potential of medical nutrition therapy (MNT), particularly diabetes-specific nutrition formulas (DSNFs), to improve patient outcomes.

Methods: This narrative review is based on the proceedings of a joint session between the Diabetes Nutrition Study Group (DNSG) and the European Society for Clinical Nutrition and Metabolism (ESPEN). Relevant literature was synthesized to explore the prevalence, pathophysiology, and clinical impact of malnutrition and muscle loss in diabetes, as well as the clinical applications of MNT and DSNFs in hospital and intensive care settings.

Results: Malnutrition is prevalent among hospitalized patients with diabetes yet frequently goes undiagnosed, contributing to delayed recovery, increased complications, and functional decline. Muscle mass and function are now recognized as key determinants of metabolic regulation and recovery. Recent advances in diagnostic frameworks, including those developed by the Global Leadership Initiative on Malnutrition (GLIM), offer practical tools for the early identification of malnutrition and sarcopenia. Evidence supports the use of MNT, particularly DSNFs, as a strategy to support glycemic control, preserve muscle mass, and reduce complications in both general hospital and ICU settings.

Conclusions: Malnutrition and muscle dysfunction are important but often overlooked components of inpatient diabetes care. Early identification using validated screening tools, coupled with timely

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implementation of MNT, including DSNFs, offers a promising strategy to improve metabolic management and clinical outcomes in hospitalized and critically ill patients with diabetes.

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1. Introduction

Diabetes is a chronic metabolic disease affecting more than half a billion people worldwide [1], with a prevalence increasing significantly among hospitalized patients [2]. Hospitalized patients with diabetes face unique challenges that complicate their care, including an increased risk of hypoglycemia and hyperglycemia due to disrupted metabolic regulation [3]. Older patients with diabetes often present with multiple comorbidities, such as hypertension, ischemic heart disease, chronic kidney disease, and cognitive impairment, contributing to higher hospitalization rates compared with individuals without diabetes [4].

Malnutrition is a significant, yet underrecognized complication in hospitalized patients with diabetes, leading to longer hospital stays and poorer clinical outcomes [5]. Patients with critical illness in the intensive care unit (ICU) are particularly vulnerable facing increased risks of severe malnutrition and stress-induced hyperglycemia, both of which are associated with increased morbidity and mortality [6]. Given these challenges, evidence-based medical nutrition therapy (MNT) is essential in addressing the complex nutritional needs of hospitalized patients with diabetes.

This narrative review, based on the proceedings of a dedicated joint session between the Diabetes Nutrition Study Group (DNSG) and the European Society for Clinical Nutrition and Metabolism (ESPEN) at the 2024 DNSG meeting in Uppsala, Sweden, explores the evolving role of nutrition in the management of hospitalized patients with diabetes. It begins by examining the prevalence, drivers, and consequences of malnutrition in this population, with a particular focus on the emerging significance of muscle mass and function in diabetes outcomes. The review then synthesizes current evidence on inpatient MNT, including the application of diabetes-specific nutrition formulas (DSNFs) in both general ward and ICU settings. Finally, it highlights ongoing challenges in implementation, and outlines future directions for research and clinical practice to optimize nutrition care for hospitalized patients with diabetes.

2. Malnutrition in diabetes: prevalence, drivers and impact

Malnutrition has emerged as a significant yet underrecognized complication in individuals with diabetes, especially those requiring hospitalization. While traditionally associated with underweight individuals, malnutrition may also present in patients living with overweight or obesity, particularly when low skeletal mass is present. The Global Leadership Initiative on Malnutrition (GLIM) criteria recognize low muscle mass, alongside weight loss and low BMI, as a key phenotypic criterion for diagnosing malnutrition, regardless of body size or fat content [7]. This is particularly relevant for patients with type 2 diabetes (T2D), in whom visceral and ectopic fat accumulation can coexist with significant muscle wasting.

2.1. Prevalence of malnutrition in diabetes

The true prevalence of malnutrition in individuals with diabetes remains difficult to quantify due to variability in diagnostic criteria and limited routine screening. However, available data

suggest a substantial burden, particularly in hospitalized [5] and older adult populations [8,9]. A recent systematic review and meta-analysis of 46 studies involving over 18,000 adult patients reported an overall malnutrition prevalence of 33 %, with an additional 44 % identified as being at risk of malnutrition [10].

2.2. Diabetes as a potential driver of malnutrition

The pathophysiology of diabetes may directly contribute to malnutrition. In type 1 diabetes (T1D), absent endogenous insulin impairs muscle protein synthesis and promotes protein degradation [11]. In T2D, insulin resistance is the primary metabolic derangement, and research has suggested that skeletal muscle of patients with T2D has reduced anabolic capacity compared to those without T2D [12]. In fact, people with undiagnosed T2D show greater impairment of lean muscle mass, suggesting that these changes occur early in the course of the disease [13]. As T2D progresses, chronic hyperglycemia drives oxidative stress, systemic inflammation, and further enhances insulin resistance, all directly impairing muscle protein anabolism [14,15]. These derangements also negatively impact muscle mitochondrial function and ATP production, leading to a cascade of metabolic disturbances that reduce the ability to preserve muscle mass and may cause functional impairments. A recent meta-analysis confirmed that diabetes accelerates the loss of muscle mass and strength through mechanisms such as insulin resistance, elevated levels of inflammatory cytokines, and alterations in endocrine function [16]. This effect is particularly pronounced in patients with a longer duration of diabetes (>6 years) and poor glycemic control (HbA1c >8 %), both of which are associated with significantly reduced muscle quality [17].

2.3. Aging and comorbidities as drivers of malnutrition in diabetes

Older age is a shared risk factor for both diabetes and malnutrition, and contributes significantly to the progressive loss of skeletal muscle. Demographic shifts, particularly the growth in older adult populations, are driving a projected increase in the prevalence of T2D over the next three decades [18]. This trend is further exacerbated by lifestyle changes, such as increased sedentary behavior, which heighten oxidative stress, systemic inflammation, and T2D risk [19]. Several studies have demonstrated the inability to preserve muscle mass in older patients with T2D, regardless of body weight or body mass index [13,20]. Comorbid conditions are highly prevalent among patients with T2D, and even more in older patients, including traditional cardiovascular and renal complications of diabetes, metabolic syndrome, and many others such as dementia, Parkinson's disease, cancers and osteoarthritis [21]. For example, incidence of malnutrition has been reported to gradually increase with the progression of chronic kidney disease [22]. Hospitalization represents a distinct setting where malnutrition becomes highly prevalent among patients with T2D, with rates reported between 60 % and 80 % [23,24]. Stress-induced hyperglycemia due to inflammation, and enhanced insulin resistance during most acute illnesses accelerates catabolic processes, leading to muscle as well as fat loss. These interconnected challenges emphasize the urgent need for

strategies to mitigate the impact of T2D in aging populations, including its negative impact on skeletal muscle and malnutrition, in both the outpatient and hospital settings.

2.4. Obesity as a driver of malnutrition in diabetes

In addition to diabetes- and aging-induced metabolic derangements that favor skeletal muscle loss and malnutrition onset, it is important to point out that obesity with excess total, abdominal and ectopic tissue fat is extremely common in T2D and may contribute to muscle loss and malnutrition. Even before the onset of diabetes, obesity-associated adipose tissue derangements may independently induce systemic inflammation, insulin resistance, and favor ectopic muscle fat accumulation [25], thereby enhancing tissue protein catabolism and mitochondrial dysfunction, with impaired muscle mass and quality. Physical inactivity is also common in patients with obesity as well as T2D, contributing to loss of skeletal muscle mass and function, with reduced protein anabolism, mitochondrial dysfunction [26] and muscle oxidative stress [27], further promoting a vicious cycle of metabolic dysregulation and muscle loss.

2.5. Impact of malnutrition in diabetes

Malnutrition has a broadly negative clinical impact, including in individuals with diabetes. Among hospitalized patients with T2D, malnutrition often results in prolonged stays, higher complication rates, and higher mortality [23,24], despite often being underdiagnosed. Beyond clinical outcomes, malnutrition imposes a substantial economic burden on healthcare systems, with annual expenditures for patients with malnutrition exceeding those without malnutrition [28].

3. The role of muscle mass and function in diabetes

3.1. Sarcopenic obesity

Sarcopenic obesity is defined as the coexistence of excess adiposity with low muscle mass and/or poor muscle function, which together exacerbate metabolic dysfunction and physical disability [29,30]. As the main glucose-utilizing tissue in the body, skeletal muscle is essential for maintaining metabolic health, and muscle loss may worsen insulin resistance, glucose disposal, metabolic syndrome features and particularly hyperglycemia [31]. Loss of muscle mass and function in persons with obesity also directly impairs physical fitness, exacerbating cardiac and respiratory complications with increased morbidity [31]. As demonstrated in a recent meta-analysis, sarcopenic obesity is a significant predictor of all-cause mortality in various clinical settings, including older people and hospitalized patients [32].

3.2. Sarcopenic diabetes

Sarcopenia is defined as a progressive and generalized skeletal muscle disorder characterized by loss of muscle mass, strength, and/or function [33,34]. Although traditionally viewed as an aging-related condition, sarcopenia is now increasingly recognized in individuals with diabetes—where chronic hyperglycemia, inflammation, and insulin resistance accelerate muscle degradation [35]. The emerging concept of sarcopenic diabetes refers to sarcopenia occurring in individuals with T2D, typically at an earlier age and with greater severity than in those without diabetes [36]. Despite its growing relevance, sarcopenic diabetes remains underdiagnosed, in part due to limited consensus on diagnostic criteria and inconsistent application of screening tools.

3.3. Diagnostic frameworks to identify sarcopenia in diabetes

Several diagnostic frameworks are now available to identify sarcopenia in the context of diabetes. The GLIM recognizes low muscle mass as a key phenotypic criterion for diagnosing malnutrition, particularly when paired with inflammation or disease burden as an etiologic factor [7]. In cases where muscle function is also impaired, these findings may also indicate sarcopenia. The European Working Group on Sarcopenia in Older People (EWG-SOP2) provides another widely adopted approach, emphasizing low muscle strength as the primary indicator, with confirmation by reduced muscle mass or quality, and poor physical performance signaling severe sarcopenia [34]. Among various assessment methods, handgrip strength may be practical and predictive, with thresholds of <27 kg in men and <16 kg in women indicating reduced muscle strength [34]. Muscle quantity and quality may be assessed through modalities such as bioelectrical impedance analysis (BIA), dual-energy X-ray absorptiometry (DXA), and cross-sectional imaging [37]. Computed tomography (CT) and ultrasound imaging also offer accurate quantification of muscle cross-sectional area and quality, and may be particularly valuable in hospitalized or critically ill patients [38,39].

3.4. Diabetes, frailty and disability – the role of malnutrition and sarcopenia

Diabetes and frailty are highly prevalent in older adults, with evidence suggesting that T2D may exacerbate the progression of frailty leading to poorer outcomes. Meta-analyses have revealed that frailty affects ~15 % of patients with T2D [40], and is consistently associated with increased mortality, hospital admissions, and disability rates [40,41]. One study found that patients with frailty had a 7-month shorter survival with diabetes compared to those without diabetes [42]. The combination of diabetes and frailty increased the risk of complications by 2.62 times compared to patients with T2D without frailty [43]. Additionally, T2D has been shown to reduce disability-free years in both men and women, further emphasizing its impact on quality of life and functional independence [44].

The mechanisms linking diabetes and frailty are multifactorial and rooted in lifestyle-related factors such as smoking, sedentary behavior, obesity, and hypertension, which may all drive inflammation and insulin resistance via elevated cytokine levels including tumor necrosis factor- α (TNF- α), interleukin 1 (IL-1), and interleukin 6 (IL-6) as well as additional protein-catabolic hormonal changes [45]. This persistent inflammatory state further contributes to enhance metabolic derangements, thereby increasing the risk of chronic conditions such as cardiovascular disease, cognitive dysfunction, and frailty. Sarcopenia and malnutrition may directly contribute to frailty by reducing muscle mass and function, alongside associated metabolic alterations. Successful aging, as observed in those who are 100 years or older, is associated with higher peripheral insulin sensitivity, which reduces inflammation, mitochondrial dysfunction, and adipocyte activity, thereby potentially promoting longevity [46].

Interestingly, risk factors for diabetes, sarcopenia and frailty substantially overlap, supporting a potential synergistic relationship between these conditions [47]. Indeed sarcopenic obesity directly contributes to disability and frailty, particularly but not limited to older adults [48,49]. Patients with diabetes and functional impairments are at elevated risk of mobility disability, instrumental activities of daily living (ADL) disability, and total ADL disability [50]. Independently of the presence of peripheral neuropathy, patients with diabetes often exhibit reduced gait speed and impaired balance, increasing their risk of falls [51].

These findings underscore the importance of early assessment of muscle health and timely implementation of comprehensive management strategies, including nutritional ones.

Disability in patients with T2D notably extends beyond functional impairments and encompasses accelerated cognitive decline and reduced overall survival. Dementia onset occurs approximately two years earlier in patients with diabetes compared to those without, and the progression of both functional and cognitive decline is faster, particularly in those diagnosed at a younger age or with a disease duration exceeding 15 years [52]. Magnetic resonance imaging (MRI) studies have demonstrated that sarcopenia features, which are more prevalent in frail compared to pre-frail individuals, were associated with reductions in grey matter volumes involved in motor control [42]. These findings further underscore the broader impacts of diabetes and complex interactions between metabolic derangements, muscle changes, disability and quality of life.

3.5. Available strategies to address muscle-related alterations in diabetes

Non-pharmacological strategies play a critical role in managing diabetes, particularly in older adults, to minimize the risks associated with both hypo- and hyperglycemia which can exacerbate geriatric syndromes, including nutritional muscle derangements, as well as falls, functional disability, cognitive impairment and depression [53]. Particularly in older adults, effective treatment strategies should adhere to five principles: avoid hypoglycemia, use treatments that reduce body weight with particular regard to overweight and obesity, avoid long half-life oral antidiabetic drugs to minimize hypoglycemia risk, assess treatments for beneficial effects on α and β cells, and lastly, leverage drug combinations for synergistic benefits [54]. Management goals include achieving good metabolic control, dietary interventions including higher protein intake and promoting physical exercise [55]. All of these approaches have potential to improve skeletal muscle mass and function.

In persons living with malnutrition or sarcopenia in the community, whether associated with older age or at earlier age due to T2D and comorbidities, attention to preserve muscle mass and function should be included among primary treatment goals. Malnutrition and sarcopenia, being highly prevalent and affecting over 50 % of older adults with diabetes, require early screening, particularly in patients with poor glycemic control, prolonged disease duration, and sedentary lifestyles. In patients at risk or affected by malnutrition, when dietary optimization is not able to reach nutritional requirements, medical nutrition with oral nutritional supplements as well as enteral or parenteral approaches should be considered.

Exercise is an effective therapy for improving glycemic control and mitigating frailty, also representing the strongest stimulator of muscle protein anabolism and part of multimodal treatment for malnutrition and sarcopenia. Tailored physical activity programs, adapted to the patient's specific conditions, are essential [56–58]. Evidence supports that physical exercise improves physical condition, though adherence remains a challenge, with attrition rates of ~40 % for aerobic exercises and ~50 % for elastic band exercises [59]. Despite these challenges, frailty conditions improve significantly following exercise programmes, with frailty prevalence reduced from 34 % to 25 % and further improvements in physical function and health outcomes [59]. In another study, a unique multi-modal intervention approach combined individualized, progressive resistance exercise programs (16 weeks), structured diabetes and nutritional education (7 sessions), and an investigator-supported training for optimal diabetes care [60].

After 12 months, this approach yielded significant benefits, including higher physical performance and cost savings of €400 per patient per year [56]. This evidence underscores the importance of combining exercise, education, and personalized care to optimize outcomes for patients with T2D.

4. Medical nutrition therapy in hospitalized patients with diabetes

4.1. Dysglycemia-based chronic disease

The dysglycemia-based chronic disease (DBCD) model offers a unique framework to understand and address diabetes [61]. It encompasses four stages of progression: risk factors, where insulin resistance drives disease development; pre-disease (i.e., prediabetes), marked by early β -cell dysfunction and mild hyperglycemia; disease (i.e., T2D), where diagnostic hyperglycemia thresholds are met; and micro-/macrovascular complications. Unlike traditional definitions that consider prediabetes in isolation, the DBCD model integrates prediabetes within a continuum, highlighting the interconnected pathophysiological roles of primary drivers (genetics, behavior, and environment) and secondary/metabolic drivers (abnormal adiposity, inflammation, insulin resistance, β -cell dysfunction, and vascular biology) as well as impacts of non-biological factors such as structural and social determinants of health. This approach has identified broader populations at risk [62], creating preventative care opportunities for early/sustainable intervention and tailored strategies such as inpatient MNT.

4.2. Role of inpatient medical nutrition therapy

Building on the DBCD model, inpatient MNT serves as a component of lifestyle medicine to manage and prevent chronic disease using non-pharmacological strategies. Although consultations for prediabetes are underutilized in hospitals, systematic reviews and meta-analyses show that structured MNT, delivered with dietitian involvement, can improve glycemic outcomes, anthropometrics, blood pressure, and most lipid levels in adults with this early DBCD stage [63]. For patients with T2D, MNT focuses on individualized meal plans, emphasizing reduced carbohydrate intake, low-glycemic index (GI) foods, limited free sugars, and healthy fats to improve glycemic control and cardiovascular health [64].

Medical nutrition therapy is also important in the management of gestational diabetes mellitus, with the primary goals of maintaining euglycemia, preventing excessive gestational weight gain, and reducing adverse pregnancy outcomes such as pre-eclampsia and macrosomia. Key strategies include a balanced macronutrient composition, reducing total carbohydrate intake, emphasizing low GI foods, and ensuring adequate protein and healthy fat intake [65]. Mediterranean diet-based MNT and use of high-complex dietary fiber have been shown to have a beneficial role in GDM management [66,67].

In hospitalized patients with T2D, inpatient MNT is often hindered by significant logistical and systemic challenges [68]. A major issue is the lack of synchronization between meals, carbohydrate intake, blood glucose monitoring, and insulin administration. A study comparing the effect of a flexible prandial insulin dosing, which adjusts mealtime insulin based on carbohydrate intake, to fixed dosing with predetermined insulin amounts, found that both strategies achieved similar glycemic control in hospitalized patients with T2D [69]. However, another pilot study conducted a few years later in two surgical units at a tertiary care teaching hospital found that flexible prandial insulin dosing

improved mean glucose levels at one of the units but not the other [70]. Additionally, the flexible dosing strategy was associated with enhanced physician and nursing satisfaction and confidence in insulin dosing accuracy when compared to fixed dosing [70]. These findings highlight that while both strategies can achieve adequate glycemic control, flexible prandial insulin dosing may offer additional benefits in enhancing healthcare professional satisfaction and confidence in hospital mealtime insulin dosing, emphasizing the need for synchronized MNT and insulin administration in hospitalized patients with T2D.

4.3. Challenges in implementing MNT

One of the most significant challenges in inpatient MNT is synchronizing meals, carbohydrate intake, and insulin administration. Hospital-wide protocols and infrastructure improvements, such as ensuring snack availability, avoiding insulin stacking, and incorporating nutrition education materials on meal trays, are needed to address these systemic issues. Additionally, tactical challenges include meal timing around procedures and delays in food delivery, and these must be resolved at the administrative level.

The evidence base presented for inpatient MNT is limited, with most recommendations extrapolated from outpatient studies. While studies on interventions such as, flexible insulin dosing have shown mixed results, research has highlighted the need for systematic reviews, meta-analyses, and adequately powered randomized controlled trials to establish evidence-based guidelines. Such studies should include active comparator groups representing best-practice standards in the hospital and comprehensive MNT interventions, rather than isolated nutritional components.

4.4. Inpatient medical nutrition therapy for malnutrition and sarcopenia

Malnutrition screening should be performed in all hospitalized patients at all ages, including those with obesity and diabetes. Malnutrition risk and overt malnutrition are reported to affect approximately one third of hospitalized patients, and they may worsen during hospital stay. Validated screening tools include Nutritional Risk Screening (NRS), and other tools are available with potential specific applicability in different patient groups [71]. Patients with established risk should undergo diagnostic assessment, with the recent GLIM criteria representing the global consensus-based simplified diagnostic approach that includes assessment of skeletal muscle mass or validated surrogates [7]. Once malnutrition is diagnosed, full nutritional assessment should be performed, including skeletal muscle function, which can allow for diagnosis of sarcopenia when muscle strength is reduced [34]. In the presence of malnutrition and/or sarcopenia, medical nutrition should include oral nutritional supplements, enteral or parenteral nutrition as applicable to reach evidence-based nutritional requirements, with monitoring of nutritional state during hospitalization. Special care should be given to optimization of metabolic and glycemic control, to avoid glycemic variability during nutritional treatment.

5. Diabetes-specific nutrition formulas: evidence and application

DSNFs are specialized oral or enteral nutritional supplements designed to support glycemic control and nutritional adequacy in patients with pre-diabetes and diabetes. Compared to standard

formulas, DSNFs typically contain a lower carbohydrate content, often replacing rapidly digestible carbohydrates with slowly digestible starches. They are enriched with monounsaturated fatty acids (MUFA) to enhance lipid profiles and glycemic stability, and contain higher levels of soluble and insoluble fiber to promote satiety, delay gastric emptying, and blunt postprandial glucose excursions. These formulas are also designed with a low glycemic index (GI) profile, collectively aiming to reduce hyperglycemia, lower insulin requirements, and improve metabolic control [72]. Table 1 highlights the composition of standard formulas and diabetes-specific nutrition formulas commonly used in hospitalized patients in the USA.

Clinical evidence supports the use of DSNFs across a range of settings. In the acute setting, there are demonstrable benefits of DSNFs on postprandial glucose response when compared with standard nutrition formulas [73–75]. Several meta-analyses have shown that long-term use of DSNFs significantly improve glycemic control by lowering postprandial glucose, fasting blood glucose, glucose variability, and HbA1c compared to standard formulas, without adverse effects on lipid profiles [76–78]. Additionally, these meta-analyses demonstrated reduced insulin requirements and fewer complications, with DSNFs containing high monounsaturated fat content also improving HDL cholesterol [76–78]. Importantly, these benefits were achieved without increased gastrointestinal side effects, supporting the safety and efficacy of DSNFs in long-term management of diabetes [72].

The transcultural Diabetes Nutrition Algorithm (tDNA), developed in 2010, serves as a practical framework to guide the implementation of medical nutrition therapy, including the use of DSNFs, in individuals with prediabetes and T2D across diverse cultural and geographic settings [79]. As one structured approach to DSNF application, the tDNA provides evidence-informed recommendations tailored to patient characteristics such as body weight, glycemic control, and comorbidities. For example, individuals with T2D who are overweight or obese are advised to consume 2–3 DSNFs per day as meal or snack replacements within a calorie-restricted diet, while those with uncontrolled diabetes (HbA1c >7 %) are recommended 1–2 DSNFs daily as part of a low glycemic index meal plan. Although these recommendations are grounded in available evidence, specific dosing regimens have not been validated through randomized clinical trials and are based on expert consensus. Therefore, successful adaptation and implementation of DSNFs via the tDNA or similar frameworks requires careful consideration of local cultural, socioeconomic, and healthcare system factors.

6. Special considerations in the intensive care unit settings

Patients in the ICU face significant metabolic and nutritional challenges, including a high risk of malnutrition and hyperglycemia, both of which are associated with increased morbidity and mortality [6]. Adequate nutrition is crucial for recovery, with early enteral nutrition (EN) a preferred modality, with parenteral nutrition (PN) reserved for patients with varying degrees of enteral intolerance. Case finding for malnutrition in the ICU using nutritional screening and GLIM criteria are essential, along with close monitoring and individualized nutritional strategies to adapt to patients' needs [80]. Hyperglycemia affects 22 %–46 % of hospitalized patients receiving EN or PN, and is often exacerbated by factors such as advanced age, preexisting diabetes, and infections [81]. To address these challenges, DSNFs can be utilized to optimize glycemic control, offering a promising approach to improving clinical outcomes in the ICU.

Table 1

Composition of standard formulas and diabetes-specific nutrition formulas commonly used in hospitalized patients in the USA.

Formula	Calories (kcal/mL)	Carbohydrate (g/L)	Fat (g/L)	Protein (g/L)	Manufacturer
Standard formulas					
Jevity® 1.0 Cal	1.0	155	35	44	Abbott nutrition
Nutren® 1.0	1.0	127	38	40	Nestle nutrition
Osmolite® 1.2 Cal	1.2	158	39	55	Abbott nutrition
Jevity® 1.2	1.2	169	39	56	Nestle nutrition
Fibersource® HN	1.2	160	39	53	Nestle nutrition
Isosource® 1.5 Cal	1.5	170	65	68	Nestle nutrition
Jevity® 1.5	1.5	216	50	64	Nestle nutrition
Diabetes-specific nutrition formulas					
Glucerna® 1.0 Cal	1.0	96	54	42	Abbott nutrition
Nutren® Glytrol®	1.0	100	48	45	Nestle nutrition
Glucerna® 1.2 Cal	1.2	115	60	60	Abbott nutrition
Diabetisource® AC	1.2	100	59	60	Nestle nutrition
Glucerna® 1.5 Cal	1.5	133	75	82	Abbott nutrition

6.1. Clinical guidelines

Numerous guidelines, including those from the American Diabetes Association (ADA), the American Society for Parenteral and Enteral Nutrition (ASPEN), and the ESPEN, emphasize the critical role of MNT in managing diabetes, particularly in ICU settings [82–84]. The latest ESPEN guidelines recommend initiating MNT for all ICU admissions, especially those staying for more than 48 h, focusing on early EN or PN, individualized energy and protein targets, and close monitoring of metabolic needs [85]. Hyperglycemia, a frequent complication in the ICU, arises from factors such as stress-induced glucose intolerance, pre-existing diabetes, metabolic syndrome, or glucocorticoid therapy [86,87]. Insulin remains the cornerstone of hyperglycemia management in the hospital, but it is associated with increased mortality [88–90], highlighting the need for alternative strategies, such as DSNFs to reduce insulin dependency while maintaining glycemic control.

6.2. Clinical guidelines and studies

Numerous studies and guidelines have evaluated the efficacy of DSNFs in managing hyperglycemia under these conditions, with growing evidence supporting their benefits. When high in MUFAs, DSNFs have demonstrated improved glucose control and reduced metabolic risk factors compared to standard formulas, particularly in patients with diabetes or stress-induced hyperglycemia [78]. While early ASPEN guidelines in 2013 did not recommend DSNFs for EN in patients with hyperglycemia [91], the 2023 ESPEN guidelines recognized their potential to improve glucose profiles and suggested limits on carbohydrate (5 mg/kg/min) intake in patients with critical illness [92]. Low-carbohydrate DSNFs have been shown to be associated with lower mean glucose levels, reduced glycemic variability, and decreased insulin use compared to standard formulas [93,94]. Furthermore, recent practice guidelines for the ICU emphasize the importance of formulations with low GI/GL carbohydrates and optimal protein for the nutritional management of dysglycemia [95].

6.3. Protein in diabetes-specific nutrition formulas and muscle mass loss in the intensive care unit

Patients in the ICU often experience substantial loss of muscle mass and strength, with recovery remaining a significant challenge post-discharge [96]. Indeed malnutrition and sarcopenia may ensue during and following ICU stays also in patients with no

pre-existing nutritional derangements. The degree of muscle mass loss is closely tied to the severity of illness [97,98], so protein intake is an important component of nutritional therapy. Notably, DSNFs not only address glycemic control but also provide higher protein content, which is essential for preserving muscle mass. Studies have shown that high-protein DSNFs (5.7g/100kcal/100 ml) reduce insulin requirements, glycemic variability, and the incidence of hypoglycemic events in patients with mechanical ventilation and hyperglycemia ICU when compared with high-protein standard EN formulas [99]. By combining higher protein intake with lower carbohydrate content, these specialized formulas help mitigate muscle loss while improving glycemic outcomes, making them an important component in the management patients in the ICU with diabetes.

6.4. Parenteral nutrition in the intensive care unit

In the ICU, when EN feeding fails to meet nutritional targets, PN should be considered, despite an increased risk of hyperglycemia [100]. Unlike EN feeding, there are no diabetes-specific parenteral formulas available, making glycemic control heavily reliant on individualized insulin regimens adjusted to the volume and composition of PN. Effective management of PN-induced hyperglycemia requires a multidisciplinary approach, involving diabetes specialists, dietitians, and pharmacists, along with the integration of technology such as CGMs. These devices enable real-time monitoring of glucose fluctuations and allow timely adjustments to insulin therapy. Recommendations for managing PN-related hyperglycemia in the ICU emphasize frequent glucose monitoring, tailored insulin regimens, and collaborative team-based care to optimize outcomes [101].

6.5. Economic impact of diabetes-specific nutrition formulas

In addition to the nutritional benefits, DSNFs may offer significant economic advantages, particularly in resource-constrained healthcare settings. A key study comparing DSNFs with standard formulas demonstrated lower mortality rates, a reduced ICU length of stay, decreased insulin requirements at admission and discharge, and an overall reduction in total ICU costs [102]. These findings highlight the potential for DSNFs to not only improve clinical outcomes but also alleviate financial burdens associated with critical care for patients with diabetes. As the global population requiring diabetes management continues to grow, these results underscore the importance of DSNFs in ICU settings while calling for further research to solidify the evidence base for their economic and clinical impacts.

7. Challenges and future directions

Despite the high prevalence of malnutrition, sarcopenia, and frailty among people with diabetes, especially those who are older or hospitalized, clinical awareness remains low. Without broader recognition among clinicians and policymakers, these complications continue to be underdiagnosed and undertreated, leaving patients at increased risk of adverse outcomes. Historically, the absence of consensus definitions and standardized diagnostic algorithms has further contributed to inconsistent clinical practice. The 2019 GLIM criteria marked an important step forward, providing practical diagnostic tools based on phenotypic and etiologic criteria—particularly relevant for patients with diabetes [7,103]. Similarly, efforts by the ESPEN and the European Association for the Study of Obesity (EASO) have introduced a validated algorithm for diagnosing sarcopenic obesity, incorporating screening, diagnosis, and staging to standardize care across diverse populations [30,104].

While MNT and DSNFs hold considerable promise in optimizing metabolic and nutritional outcomes in hospitalized patients with diabetes, several practical, clinical, and evidence-related challenges must be addressed to support their effective implementation. Screening remains inconsistently performed across hospital settings despite the growing burden of malnutrition and sarcopenia in diabetes [105,106]. Other barriers include inadequate dietitian staffing in many institutions, delayed consultations, limited nurse involvement, dependence on physician sign-off for dietitian recommendations, and lack of feeding assistance for many patients in the hospital [107]. These issues lead to under-recognition of at-risk patients and delays in initiating timely nutritional interventions.

Although DSNFs have demonstrated benefits in glycemic control, most supporting studies are small, of short duration, or conducted under tightly controlled conditions, limiting generalizability to routine inpatient care. Outcomes are often limited to glycemic parameters, with less focus on functional recovery, complication rates, or long-term metabolic health. Furthermore, evidence remains scarce for specific subgroups, including those with type 1 diabetes, advanced renal impairment, or those requiring parental nutrition, emphasizing the need for well-powered, multicenter trials evaluating clinically meaningful endpoints.

Cost and accessibility represent additional limitations. DSNFs are generally more expensive than standard formulas due to their specialized formulations, raising concerns about cost-effectiveness and equitable access, particularly in publicly funded or resource-constrained healthcare systems. Their availability may be restricted by hospital formularies, limited insurance coverage, and clinician hesitancy due to unfamiliarity or perceived limited benefit. While some analyses suggest DSNFs may reduce downstream costs by minimizing complications and insulin needs [102], these findings require confirmation in real-world settings.

In patients with critical illness, diabetes further complicates nutrition care, as stress hyperglycemia driven by metabolic disruption is linked to increased infection risk, longer hospital stays, and higher mortality [6]. DSNFs have demonstrated utility in this context by improving glycemic stability, reducing insulin requirements, and potentially improving outcomes in the ICU setting [99]. However, further research is required to refine indications and protocols in this high-risk group.

Taken together, these challenges underscore the need for integrated models of care that combine early screening, individualized MNT, and appropriate use of DSNFs within a multidisciplinary framework. Skeletal muscle is emerging as a central target in diabetes-related complications, linking nutrition directly to

outcomes such as physical function, cognition, and survival. Future clinical practice should prioritize early identification of nutritional risk, validated use of DSNFs, and adoption of innovative tools such as AI-assisted decision support and culturally adapted nutrition algorithms to close existing care gaps and improve the quality of diabetes care in hospitalized patients.

Author contributions

JCN drafted the manuscript. JIM, RB, FJT-S, CD, AR, CWCK, LC and JLS reviewed the manuscript for important intellectual content. All authors reviewed and approved the final manuscript.

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JIM received honoraria for lectures from Abbot Nutrition and Merck, and serves on the Advisory Boards of Abbott Nutrition and Twin Health.

FJT-S has participated in conferences and medical advisory organised by Abbot, AMGEN, UCB and Italfarmaco.

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RB and CD have no conflicts of interest to declare.

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