

Perspective

Therapeutic Carbohydrate Reduction for Lipedema: Guidelines for a Patient-Centered, Holistic Approach

Carrie Reedy ¹, Siobhan Huggins ², Leslyn Keith ^{2,*}

1. Carrie Reedy Functional Nutrition, Australia; E-Mail: carriereedyfn@gmail.com

2. Lipedema Project, Research Division of Lipedema Simplified, LLC, USA; E-Mails: siobhan.e.huggins@gmail.com; leslyn@lipedemaproject.org

* **Correspondence:** Leslyn Keith; E-Mail: leslyn@lipedemaproject.org

Academic Editor: Magdy Elnashar

Special Issue: [Nutrition, Carbohydrate Intake and Health](#)

Recent Progress in Nutrition

2025, volume 5, issue 3

doi:10.21926/rpn.2503019

Received: May 31, 2025

Accepted: August 28, 2025

Published: September 03, 2025

Abstract

Lipedema is a chronic, often misdiagnosed disease characterized by painful, disproportionate fat accumulation in the extremities. Commonly mistaken for obesity or lymphedema, lipedema primarily affects women and has long been thought to be resistant to dietary intervention, a belief originating from its initial description by Allen and Hines at the Mayo Clinic in 1940. However, emerging research challenges this notion, revealing that individuals with lipedema often respond positively to therapeutic carbohydrate (CHO) reduction, particularly ketogenic diets (KD). Effective management of lipedema requires a comprehensive, holistic approach. Nutritional strategies should not only target symptom relief but also support overall health by considering physical comorbidities, mental and emotional well-being, and individual cultural and social factors. In this paper, we present an updated perspective on CHO-reduced dietary interventions for lipedema and propose a patient-centered framework to personalize nutrition plans for sustained success and improved quality of life.



© 2025 by the author. This is an open access article distributed under the conditions of the [Creative Commons by Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium or format, provided the original work is correctly cited.

Keywords

Lipedema; obesity; inflammation; nutrition; ketogenic diet; lymphatic; holistic

1. Introduction

Lipedema is a poorly understood disorder that primarily affects females [1]. It is characterized by excessive and disproportionate fat accumulation, usually in the lower body, along with pain or heightened sensitivity and other distinctive skin and tissue changes in the affected areas [2]. In more severe presentations, individuals may experience significant pain, poor mobility, and a severely reduced quality of life [3]. One of the most distinguishing features of lipedema is its resistance to traditional weight-loss measures, such as low-calorie dieting and exercise [4].

Due to the similarities between lipedema and obesity, individuals with lipedema often face accusations of noncompliance when traditional weight-loss measures, such as low-calorie, low-fat diets and rigorous exercise, fail to produce results. Even bariatric surgery has been reported to lead to weight loss primarily in the upper body, which can further accentuate body disproportion and may be the first time that lipedema is recognized in an individual [5, 6]. Further, the repeated failure to lose weight combined with a lack of understanding among healthcare professionals and exposure to anti-fat bias in daily life can result in eating disorders, despair, and hopelessness [7, 8].

As clinicians, we are coming to understand that lipedema is more than pathophysiology and physical symptoms, and also includes mental health and quality of life issues. For this reason, we are compelled to adopt a more holistic attitude to ensure comprehensive care [9, 10]. Many clinicians include dietary intervention as part of a holistic and comprehensive care plan. We suggest that dietary intervention by itself also needs to be holistic and patient-centered. Therefore, we propose a comprehensive, holistic approach to nutritional intervention that addresses the physical, psychological, emotional, and social needs of individuals with lipedema to support more effective and sustainable outcomes.

2. Therapeutic CHO Reduction

Low-CHO diets are safe and effective for promoting health and wellness and treating and/or managing many chronic diseases, including lipedema [11-13]. They also lend themselves well to personalization using a holistic approach. A list of example foods is provided in the supplementary material to illustrate the variety of options that patients can adapt to their preferences. (Carbohydrate-Reduced Eating Recommendations). One paper states emphatically that the optimal formulation of a therapeutic CHO reduction diet requires tailoring to an individual's medical history, comorbidities, and health status [14].

Table 1 offers recommendations for macronutrient distribution, including CHO, fat, and protein, specifically for managing lipedema symptoms. Therapeutic CHO reduction can include a wide spectrum of CHO consumption. In their consensus document, the Scientific Forum on Nutrition, Wellness, and Lower-Carbohydrate Diets defined lower-CHO diets as less than 130 grams of daily CHO, with ketogenic levels not to exceed 50 grams per day [15]. Fat intake may also have a large range, dependent upon individual energy needs, preferences, and comorbidities. A minimum of 30

grams of essential fatty acids is required for body functions, such as cell growth, providing energy, wound healing, and hormone production. Intake levels may vary daily and can be more than 150 grams per day for some individuals. Typically, as the level of CHO consumption decreases, intake of fat will increase to meet energy needs and support satiety. Protein levels should be adequate but not consistently excessive, with a recommended range of at least 1.2-1.5 grams per kilogram of ideal body weight. Although some patients will consume much more protein, meeting this minimum requirement will prevent loss of lean body mass, yet preclude proteins from being utilized as an energy source [16]. In our clinical experience, some patients benefit from spreading protein intake throughout the day to help with digestive and metabolic issues.

Table 1 Daily macronutrient distribution when employing a CHO-reduced eating pattern for lipedema. CHO levels can be decreased below 50 g per day to promote ketosis, or up to 130 g per day for a moderate CHO approach. As CHO is lowered, fat proportionally increases above the 30 g minimum to provide energy and support satiety and adequate caloric intake. Protein levels indicate a minimum intake using calculated ideal body weight and can be increased according to preference and specific needs of the patient.

Macronutrient	Target
CHO	<50 g and up to 130 g
Fat	30 g minimum
Protein	1.2-1.5 g/kg ideal body weight minimum

3. Effectiveness of Therapeutic CHO Reduction for Lipedema

Recent clinical trials have begun to challenge the long-standing belief that lipedema symptoms are resistant to all forms of weight-loss diets. Scientific findings and anecdotal reports from the lipedema community increasingly suggest that CHO-reduced diets can facilitate successful weight loss and limb volume reduction, even in individuals who previously struggled with other dietary approaches. The benefits are now so widely recognized that KDs have been incorporated into the official lipedema diagnosis and treatment guidelines in both the United States and Germany [17, 18].

Notably, research now demonstrates that varying degrees of CHO restriction can significantly improve a wide range of lipedema symptoms, including reductions in total body weight, total and visceral fat, pain, edema, and improvements in quality of life [19-25]. When comparing different dietary approaches, clinical studies consistently show that more intensive CHO restriction is associated with greater symptom relief [4, 20, 26]. In particular, participants frequently report a marked reduction in pain, often independent of weight loss, with more substantial CHO restriction [4, 25].

The mechanisms behind the benefits of therapeutic CHO reduction in lipedema are likely multifactorial. For instance, improvements in edema and fluid retention may result from lowered glucose intake, normalized insulin levels, increased ketone production, or their combined effects. Elevated insulin promotes sodium and fluid retention [27], so reducing CHO intake, and thus insulin, can help relieve swelling, tightness, and heaviness for patients with lipedema.

Additional mechanisms may involve broader metabolic, energetic, and biochemical changes triggered by CHO reduction and ketone production. A scoping review of 64 studies on KDs for

neurological and pain-related diseases found improved mitochondrial function and decreased oxidative stress as key contributors to positive outcomes [28]. Specifically, in studies involving patients with lipedema, CHO-restricted diets have been associated with improvements in metabolic profile [26, 29] and lower levels of inflammatory markers [24], which may contribute to lipedema symptom relief.

4. Holistic Approach to Therapeutic CHO Reduction for Lipedema

A patient-centered, holistic approach to care emphasizes the importance of treating the whole person, rather than focusing solely on symptoms or a specific diagnosis. The holistic model acknowledges that health and well-being are shaped by a dynamic interplay of physical, psychological, emotional, and social factors. The goal of a holistic approach is to promote overall wellness, prevent illness, and support healing by addressing the interconnected nature of these dimensions. Figure 1 shows how the holistic approach can be applied to nutritional care for lipedema specifically.

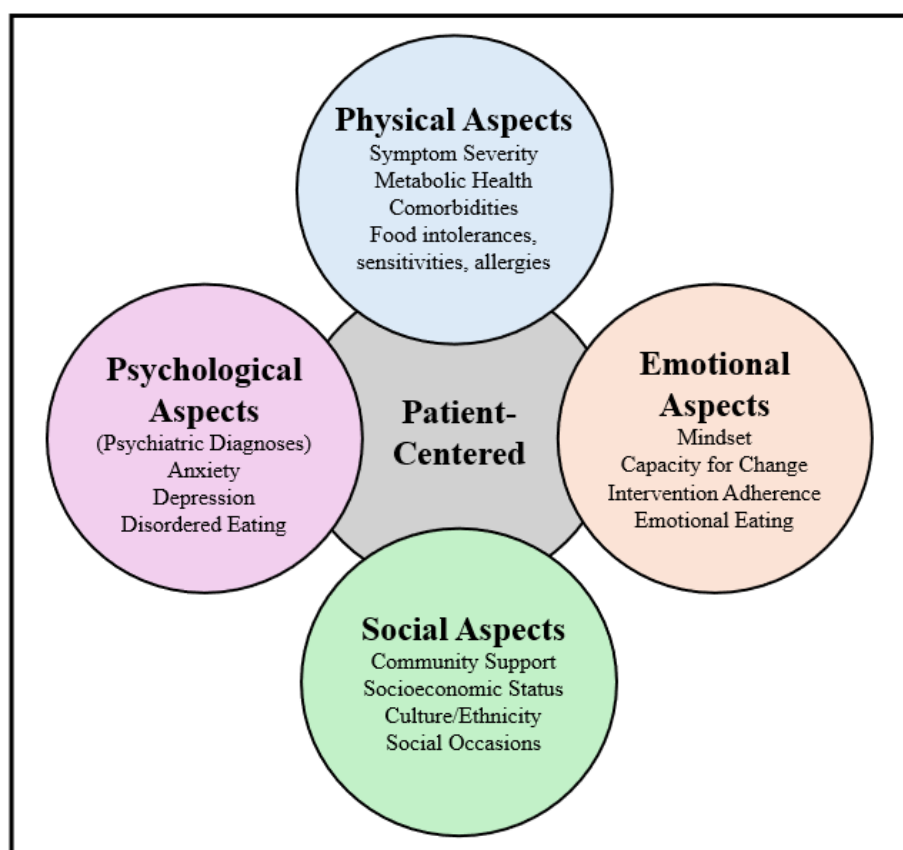


Figure 1 A Patient-centered, holistic approach to therapeutic CHO reduction for lipedema. The patient is represented in the center, as their preferences, goals, and concerns always help guide care. Four domains are also considered for holistic nutritional care. The physical domain encompasses considerations relating to their physical health, including both lipedema and other comorbidities. The emotional domain includes their emotional experience, including readiness to adopt change and ability to sustain nutritional intervention. The social domain includes the influence of their surrounding community, such as family, friends, peers, and the larger culture.

Finally, the psychological domain includes any psychiatric diagnoses and the potential impact on their ease in adopting nutritional therapy.

In this paper, we present general and specific dietary guidelines that have proven effective in managing lipedema symptoms, along with strategies for tailoring these guidelines through a patient-centered, holistic lens. We begin by outlining approaches for determining appropriate levels of CHO reduction based on an individual's unique physical, psychological, emotional, and social needs. We then explore additional considerations, including the role of ketosis, the impacts of ultra-processed foods, calorie restriction, and the long-term sustainability of a KD. Finally, we offer practical tools and tips for monitoring progress and evaluating the effectiveness of dietary interventions over time.

5. Physical Aspect

The physical aspect of nutritional holistic care includes lipedema symptom severity, metabolic health, comorbidities, and intolerances/sensitivities/allergies to certain foods. Concerns about potential nutrient deficiencies associated with lipedema and with a KD are highlighted. Each of these features and issues can prompt not only a particular level of CHO reduction but also certain food choices.

5.1 Severity of Lipedema Symptoms

Physical symptoms commonly associated with lipedema include disproportionate and excess fat accumulation in the extremities, pain/heightened sensitivity in the affected fat tissue, tissue alterations (such as fibrosis and nodular fat), non-pitting edema, easy bruising in affected areas, and limited or no response to typical weight loss measures [2]. The earliest reports of lipedema from the Mayo Clinic included descriptions of symmetrical and excessive subcutaneous fat in the lower body in affected females [1, 30]. Recent research into lipedema adipose pathophysiology has shown both adipocyte hypertrophy and hyperplasia, altered extracellular matrix, hypoxia, and inflammation in lipedema-affected adipose tissue [31-33]. Similar to excessive adipose deposition, pain and heightened sensitivity are hallmark symptoms of lipedema that can severely negatively impact mobility, quality of life, and mental health [34, 35]. Distinct tissue alterations, such as fibrosis and nodular fat, in lipedema adipose tissue, as well as evidence of dilated blood vessels and microangiopathy that can lead to non-pitting edema and easy bruising, have been identified [7, 33, 36]. Lastly, while the presence of edema is controversial, altered lymphatic functioning has been identified even in early stages, including increased pumping frequency and anomalous lymphatic structures [37]. If these changes are validated in follow-up studies, this may shed light on the subjective experience of swelling and non-pitting edema seen in patients with lipedema.

The severity of the physical symptoms of lipedema can be depicted pictorially in stages from mild to severe, as seen in Figure 2. Although staging is useful for monitoring a patient over time, there are several challenges with staging. One is that there are no distinct demarcations between stages to allow objective statements about which stage a patient is in. Secondly, staging is largely morphological and not always associated with symptom severity or the duration of the disease [2]. For example, a patient may present as being in stage 1 with mild skin dimpling, nodular

subcutaneous fat on her legs, and ankle cuffing, but also complain of severe pain and tenderness to touch.

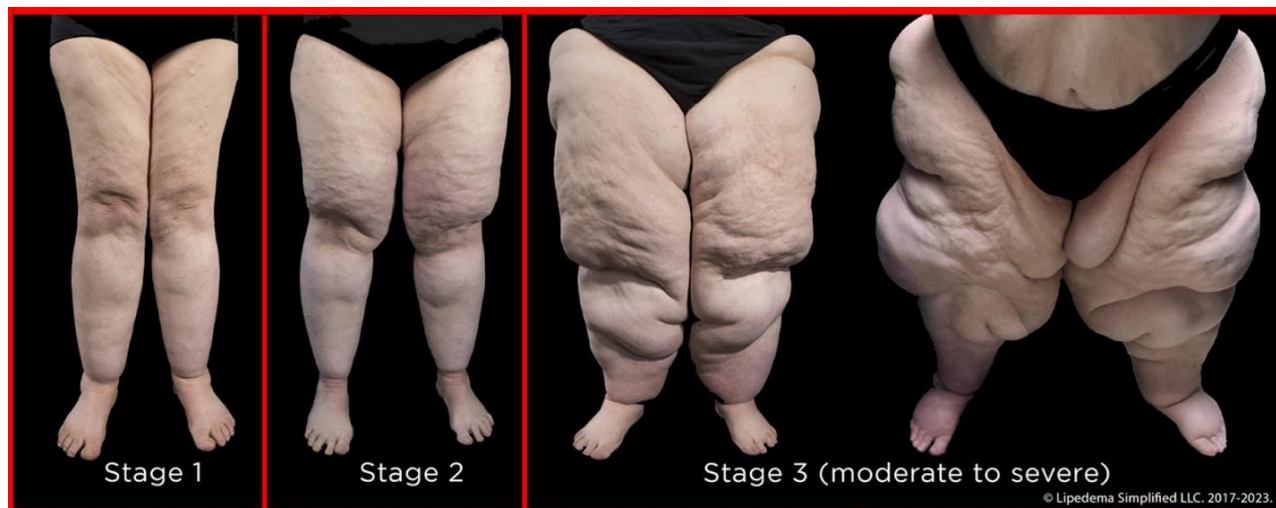


Figure 2 Stages of lipedema, demonstrating the visual presentation in the lower body and potential progression of the disease. Stage 1 presents with minimal skin and tissue changes and symmetrical disproportion in the extremities (shown here in the lower body), which ends abruptly at the ankle, if calf involvement is present. Stage 2 includes a mattress-like appearance to the skin and further tissue accumulation. Stage 3 includes both moderate and severe presentations, with severe tissue accumulation. In severe presentations of Stage 3, the disproportion may become asymmetrical, with large skin/tissue extensions resulting in protruding folds of adipose tissue called “lobules”, as well as potential involvement of the feet if lymphedema has also developed. Images courtesy of Lipedema Simplified LLC. Used with permission.

Patients can present with a wide range of symptom severity, which can influence their priorities in how they are managed. Patients who are experiencing symptoms on the more severe end of the spectrum feel a greater sense of urgency for swift and effective treatment. Due to the potential influence of decreased CHO intake and increased ketone exposure on the physical symptoms of lipedema, therapeutic CHO reduction may be an optimal option [38]. A patient with severe pain and heightened sensitivity to body areas affected by lipedema, for example, may be motivated to rapidly reduce her CHO intake to ketogenic levels to realize maximal pain relief as quickly as possible. In contrast, a patient with mild intermittent pain may choose to only modestly reduce her CHO intake, or she may opt for a gradual approach due to a less urgent need for pain relief. See Figure 3 to understand the wide range of CHO reduction, from a low-CHO omnivorous diet to a zero-CHO animal-sourced diet, that can be tailored to the patient’s needs.

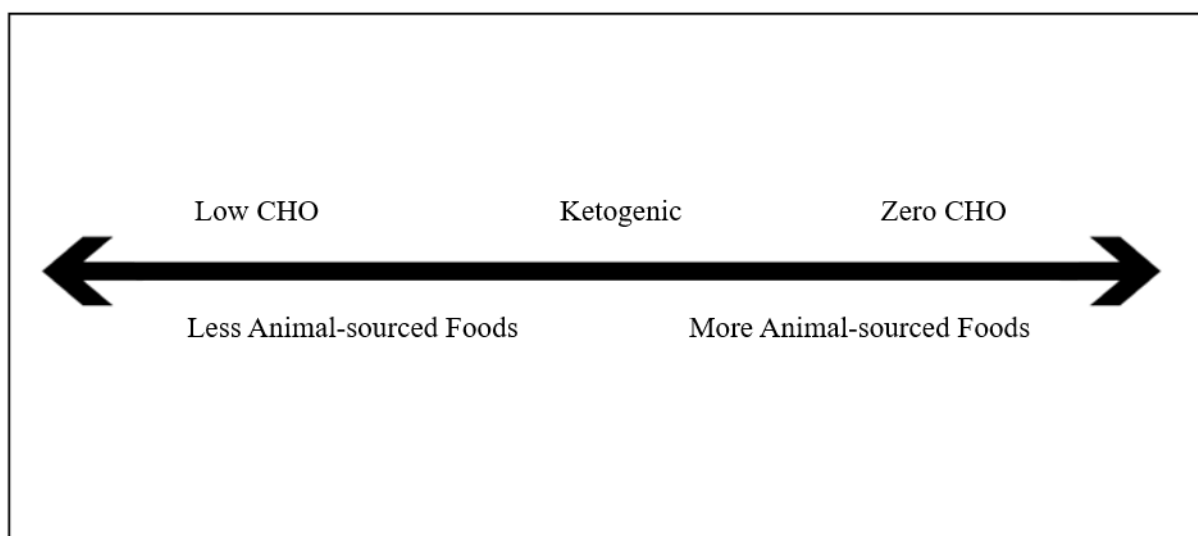


Figure 3 Spectrum of therapeutic CHO reduction diets, ranging from a low CHO eating pattern that tends toward a vegetarian ketogenic diet and uses very little animal-sourced foods, to a zero CHO diet that is almost exclusively animal-sourced.

All patient symptoms should be documented and monitored to evaluate the response to a nutritional intervention, regardless of the etiology of each symptom. For instance, the presence of edema in lipedema has been recently challenged as a valid characteristic of lipedema, with proponents of this view suggesting that lipedema would be more accurately named lipalgia, or a disorder of painful fat [39]. It is noteworthy, however, that an overwhelming majority of patients with lipedema have one or more comorbidities [10], many of which may cause edema. Essentially, then, patients with lipedema are likely to have edema and will benefit from a dietary intervention known to reduce water retention regardless of whether the edema experienced is from lipedema itself or due to a comorbidity. CHO reduction has been used to reduce edema in several populations and may act through multiple mechanisms to control swelling experienced by patients with lipedema [38]. Suggestions for specific tests and assessments for monitoring patient progress will be discussed later in this paper.

5.2 Metabolic Health

Metabolic health refers to the optimal functioning of processes that regulate energy production and utilization in the body, encompassing factors like blood sugar levels, lipid metabolism, insulin sensitivity, blood pressure, and body fat distribution. Maintaining good metabolic health is crucial for overall well-being and the prevention of chronic diseases.

More research is needed on the metabolic health status of patients with lipedema. Some reports indicate that there is a low prevalence of diabetes and dyslipidemia in lipedema, despite a Body Mass Index (BMI) greater than 30 kg/m² [10]. In support of this, a recent comparison between lipedema and controls found better glycemic control with lower HbA1c in lipedema [40]. However, this study also showed that, along with higher inflammatory and oxidative stress markers, higher insulin levels were noted in the study group with lipedema, potentially indicating impaired insulin sensitivity despite a lack of elevated HbA1c. Additionally, repeated weight loss and regain, common among patients with lipedema, is known to contribute to metabolic dysfunction [41].

It is increasingly being recognized that the hormonal milieu has a large impact on adipose tissue metabolism, especially insulin levels and insulin resistance within the tissue. Although a full discussion is beyond the scope of this paper, Friedman et al. [42] provide an in-depth review, underscoring another pathway by which CHO reduction may support lipedema management through its effects on insulin and metabolic health. This is especially pertinent given research showing tissue regrowth after lipedema reduction surgery in over 50% of cases in some populations, pointing to the role of underlying biochemical disorders in driving lipedema tissue growth [43].

It remains unclear how common impaired insulin sensitivity is among individuals with lipedema. However, findings from an Italian cohort showed that Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), fasting insulin, and C-reactive protein (CRP) levels increased with advancing lipedema stage. Additionally, higher HOMA-IR was associated with lipedema tissue in the upper arms [44]. These findings confirmed an earlier paper that asserted an association between increased insulin resistance with worsening obesity in patients with lipedema [45]. While further research is needed to confirm these findings, they suggest that individuals with lipedema may be at risk of developing insulin resistance, even in the absence of diabetes. If substantiated, this could indicate that insulin resistance, or related factors, may have a role in the progression of lipedema.

These insights position insulin resistance as a potential treatment target in lipedema, independent of diabetes status. Notably, elevated HOMA-IR has been linked to increased inflammation, reduced health-related quality of life, poorer general health markers, and higher all-cause mortality in non-diabetic adults [46-49]. While patients with lipedema are often described as metabolically healthier than the general population, this comparison is limited, as only 6.8% of U.S. adults meet criteria for optimal cardiometabolic health [50]. Thus, early signs of metabolic dysfunction in lipedema should not be overlooked, as a significant subset of patients may still face meaningful metabolic challenges. Because obesity in lipedema is linked to poorer metabolic health, its role as a comorbidity will be addressed in a later section.

Substantial research shows the positive impact of therapeutic CHO reduction on metabolic health [51-53]. If an unhealthy metabolism is confirmed by lab tests, introducing a lowered intake of CHO will be a valid option and can improve the patient's overall health. Should insulin resistance be a factor, limiting CHO intake to ketogenic levels (less than 50 grams/day) may be the appropriate intervention. If there is no evidence of insulin resistance via pathology testing, experimenting with less CHO restriction (50-100 grams/day) may be the appropriate initial step to help support weight loss efforts, yet allow for less drastic dietary changes. However, even if insulin resistance is not present, a KD may still provide unique benefits in terms of symptom relief compared to simple CHO reduction [20]. As such, taking both symptom severity and metabolic health into account when working with the patient can help guide recommendations. It is also important to note here that a patient who is taking medication to manage type 2 diabetes or hypertension will need to be carefully monitored as a CHO-reduced diet is implemented to adjust dosage or completely deprescribe medication as needed.

5.3 Comorbidities

When designing patient-centered dietary interventions for lipedema, it is important to address comorbidities that can influence inflammation, fat distribution, and metabolic regulation. Targeted CHO-reduced protocols may improve symptoms and overall well-being. Notable comorbidities to

lipedema in recent studies reported obesity (37.6%), allergies (36.8%), hypothyroidism (31.1%), sleep disorders (25.5%), depression (25.5%), and chronic venous disease (86.2%) [10, 54]. Rates of metabolic disorders like diabetes, dyslipidemia, and hypertension are generally lower than in BMI-matched populations, though some studies report a higher hypertension prevalence (24.5-31%) [10, 55]. Nutrient deficiencies, particularly selenium and vitamin D, are also noted [56-58]. This section addresses obesity, chronic venous disease, food allergies and intolerances, sleep disturbances, hypothyroidism, and nutrient deficiencies. Mental health concerns are discussed in the Psychological Aspect section. Autoimmunity and gastrointestinal issues are also briefly considered due to a high prevalence in our clinical experience.

5.3.1 Obesity

With the percentage of those experiencing obesity along with lipedema reported to be 37-50% [59], the clinician must recognize and support weight loss strategies with effective dietary approaches. Differential diagnosis of lipedema, lymphedema, and obesity becomes important but also challenging due to overlapping symptoms. BMI is unreliable in lipedema because excess lower-body fat can inflate values; instead, a waist-to-height ratio (WHtR) above 0.5 is a more accurate indicator of comorbid abdominal obesity [60].

Addressing obesity when present is an important aspect of lipedema care, not only because obesity increases the risk of a variety of comorbidities, but also because adipocytes can become hypertrophic in obesity, which induces inflammation [61]. Inflammation in adipose tissue may, in turn, induce local insulin resistance in the tissue, which may also partially explain the link between obesity and chronic low-grade inflammation. Lipedema has been widely recognized as a chronic inflammatory disease, and the presence of obesity-induced inflammation may exacerbate some of the symptoms of lipedema.

Because of its demonstrated effectiveness in reducing both obesity [62, 63] and lipedema fat [13, 24] in multiple clinical trials, a CHO-reduced diet may be the optimal eating plan for treating both diseases. Additionally, reducing obesity, particularly through CHO-reduced diets, has been shown to lower systemic inflammatory markers [62], potentially easing other symptoms of lipedema. Although the mechanisms are still to be elucidated, by reducing areas of non-lipedema adiposity, it may be possible to prevent further development of lipedema tissue and perhaps obesity-related conditions [29]. Certainly, attempting an eating regimen that minimizes ultra-processed, refined, and sugar-laden foods can help improve metabolic health (as discussed above), which may have a positive impact on adiposity.

5.3.2 Chronic Venous Disease

Along with obesity, chronic venous disease (CVD) is one of the most noted comorbidities of lipedema in the literature, suggesting that a referral to rule out vascular disease and complications may be wise. In a study of 707 women with lipedema along with 216 controls, those with lipedema were almost 12 times as likely to have varicose veins [64], the most common manifestation of CVD [65]. Most recently, a study of 360 women with lipedema found that CVD co-occurred with lipedema in almost 72% of participants [44]. Additionally, it was found that patients with obesity, lipedema, and/or lymphedema have an elevated risk of venous thromboembolism, a complication of chronic venous disease that should be ruled out if symptoms are observed [66]. Diagnosis and treatment

may be complicated further by the overlap in lipedema and venous disease symptoms, such as leg heaviness and swelling, and the ability of each disease to exacerbate the other [67].

Along with a vascular workup to determine the specific nature and severity of a patient's venous disease, dietary intervention in the form of CHO reduction may help relieve some of the associated symptoms. Although there have been some conflicting results, the majority of clinical trials in a meta-analysis of 27 randomized controlled trials showed improved cardiovascular health with low-CHO and KDs, with greater reduction in CHO intake associated with more improvements [53]. Therefore, the severity of the patient's venous disease can influence a clinician's recommendations on the amount of CHO reduction.

5.3.3 Sleep Disorders

Sleep disorders, including sleep apnea, insomnia, and other forms of disrupted sleep, affect approximately 25% of individuals with lipedema, according to one study [55]. Sleep disruption in this population may result from several factors, including restless legs, lipedema-associated pain and discomfort, or blood sugar dysregulation.

In one study, nearly 53% of participants with lipedema reported physical complaints such as restless legs and cramps, which can interfere with sleep [68]. These symptoms may be alleviated through dietary changes and/or supplementation with micronutrients such as vitamin B6 (pyridoxine), magnesium, and iron [69]. Some studies also highlight the benefits of polyphenol-rich, CHO-reduced foods, such as berries, nuts and seeds, and extra virgin olive oil, in managing restless legs [70].

Managing lipedema-related pain that disturbs sleep can be complex. While the exact cause of pain in lipedema is unknown, chronic inflammation in affected adipose tissue is a suspected contributor [35]. Encouragingly, recent clinical trials and case reports consistently show that noninflammatory, CHO-reduced diets significantly reduce the severity and frequency of lipedema-related pain [21, 23, 25].

Poor sleep increases daytime hunger and the tendency toward emotional eating of high-CHO 'comfort' foods, which may worsen lipedema symptoms [71, 72]. Additionally, insomnia during menopause has been linked to increased insulin resistance [73]. Improving sleep through targeted interventions, such as therapeutic CHO reduction, can enhance adherence to dietary changes and improve overall quality of life [50].

5.3.4 Hypothyroidism and Other Endocrine Disorders

Endocrine dysregulation appears to play a role in the pathophysiology and comorbid profile of lipedema [74]. Hormonal imbalances can influence adipose tissue distribution, inflammation, and fluid retention, all of which are characteristic features of lipedema. For instance, high stress levels leading to altered cortisol rhythms, or overt conditions such as Cushing's syndrome, may contribute to weight gain and impaired metabolic regulation through disrupted hunger signaling and appetite dysregulation, which may impact lipedema development and progression [75]. Polycystic ovary syndrome, marked by androgen excess, insulin resistance, and ovarian dysfunction, is occasionally reported in individuals with lipedema and may further exacerbate abnormal fat accumulation and systemic inflammation [10]. Additionally, many individuals with lipedema exhibit signs of sex hormone imbalance, further implicating endocrine dysfunction in symptom expression [76]. Thyroid

disorders, particularly hypothyroidism and Hashimoto’s thyroiditis, are also common and may contribute to symptoms such as fatigue, fluid retention, and resistance to fat loss [10, 77]. If a comorbid endocrine disorder is present and affects fat metabolism or weight regulation, it should be identified and addressed as part of a comprehensive treatment approach. However, research into endocrine associations remains limited, and findings are often mixed. The interplay between hormonal factors underscores the need for further investigation into endocrine dysregulation as both a comorbidity and a potential driver of lipedema.

Lowered thyroid functioning specifically has been found in 27%-36% of women with lipedema in various studies [17, 44, 78]. When compared to a 1-2% prevalence in the general population, even with a greater incidence in females [79], altered thyroid function poses a significant comorbidity for patients with lipedema. Significantly, Patton et al. [44] found that Hashimoto’s thyroiditis was the leading cause of those diagnosed with hypothyroidism in their study. Clinically, it is important to discover the specific nature and cause of altered thyroid function to determine how best to proceed. Low thyroid states can stem from low levels of thyroid supportive nutrients, chronic undernutrition, or an autoimmune condition such as Hashimoto’s thyroiditis.

Nutrient deficiencies that can lead to hypothyroidism include iodine, selenium, iron, vitamin D, and tyrosine [80]. Assessing for and then incorporating more of the required nutrients into the diet, preferably from both plant and animal sources, may be sufficient and can be easily accomplished while still reducing CHO consumption. See Table 2 for a list of nutrients and foods that can support thyroid function.

Table 2 Nutrients and foods that support thyroid functioning. On the left, nutrients that support thyroid functioning are listed, followed by low CHO dietary sources on the right.

Thyroid Function Support	
Nutrient	Food
Iodine*	seaweed, fish, eggs, dairy
Selenium	Brazil nuts, tuna, turkey, eggs, sunflower seeds
Iron	red meat, poultry
Zinc	oysters, beef, dark chicken meat, and pumpkin seeds
Tyrosine	chicken, turkey, eggs, fish, dairy, almonds, avocado

* May be contraindicated in autoimmune conditions such as Hashimoto’s thyroiditis.

Another potential contributor to reduced thyroid function is Famine Response Hypothyroidism, a physiological adaptation characterized by decreased thyroid hormone activity in response to chronic undernutrition. This condition may be particularly relevant for women with lipedema, many of whom have a history of repeated low-calorie dieting. The body’s famine response leads to a reduction in the conversion of the inactive thyroid hormone thyroxine (T4) to the biologically active triiodothyronine (T3), resulting in a lowered metabolic rate aimed at conserving energy [81]. Notably, participants in the Biggest Loser weight loss competition exhibited persistent thyroid dysfunction as many as six years after the program concluded [82], highlighting the long-term effects of extreme caloric restriction. To mitigate this adaptive response, ensuring sufficient nutrient intake, particularly adequate protein, is critical for supporting healthy thyroid function and metabolic recovery.

For other patients, the issue is one of autoimmunity impacting the function of the thyroid gland, such as Hashimoto’s thyroiditis. Testing for thyroid autoantibodies will help identify this potential cause, allowing for appropriate intervention and medical monitoring. Once an autoimmune diagnosis is confirmed, it is beneficial to address the factors that contribute to the development of autoimmunity, such as impaired intestinal permeability, alterations in the microbiome, and heightened immune response to viral and bacterial exposures [83]. Further discussion of autoimmune conditions is discussed in the next section.

The potential beneficial impacts of CHO reduction on thyroid function have been investigated of late and can influence the dietary choices of patients who have this comorbidity [84]. Therefore, patients can be encouraged to incorporate low-CHO foods that support thyroid function, while reducing, though not necessarily eliminating, the intake of goitrogenic foods that may impair thyroid hormone synthesis. See Table 3 below for a listing of foods with goitrogenic properties. It should be noted that preparation techniques such as soaking, sprouting, fermenting, and cooking can significantly reduce the goitrogenic activity of certain foods by deactivating compounds that interfere with iodine uptake. However, some goitrogenic foods, particularly legumes, also contain antinutrients such as lectins and phytates, which can inhibit the absorption of the key minerals discussed above that are essential for optimal thyroid function [85]. Therefore, both food choices and preparation methods should be considered when guiding dietary strategies for individuals with thyroid concerns.

Table 3 Nutrients and foods with goitrogenic or other properties that may interfere with thyroid function. On the left, nutrients with goitrogenic properties are listed, followed by lower CHO dietary sources on the right.

Thyroid Function Interference	
Nutrient	Food
Glucosinolates	Cruciferous vegetables* (broccoli, cauliflower, cabbage, kale, and Brussels sprouts)
Isoflavones	Soy and soy products (tofu, edamame, soy sauce, soy milk, miso, tempeh, natto)
Phytates	Legumes (chickpeas, lentils, soybeans, peanuts) and nuts (pistachios, almonds)

* The level of goitrogens can be reduced with certain preparation methods.

5.3.5 Autoimmunity

The development of autoimmunity is a complex process influenced by a combination of genetic, environmental, and immune system factors [86]. Previously, it was believed that autoimmunity developed when the immune system mistakenly targets and attacks the body’s own tissues, leading to inflammation, tissue damage, and dysfunction. Newer theories have suggested a variety of physiological and immunological insults can lead to the development of autoimmune conditions, such a loss of immune tolerance and dysregulation of the T-regulatory system, as well as pathological modification of the affected tissue and resulting autoimmune reaction [87, 88]. There is also speculation that the microbiome, impaired intestinal permeability, along with various viral and epigenetic insults, can impact the development of autoimmunity [83, 89].

Dietary interventions can play a significant role in managing autoimmune diseases by reducing inflammation and supporting immune function [90]. Nutrients such as vitamin D, zinc, and selenium are critical for maintaining a balanced immune system, and deficiencies in these may exacerbate

autoimmune activity [91-93]. Certain studies also indicate a potential link between gluten consumption and the surge in non-celiac autoimmune and inflammatory conditions [94]. Additionally, in a comparison of 40 patients with Hashimoto's thyroiditis utilizing a CHO-restricted diet versus a normal diet for 6 months, a reduction in thyroid water content and antibody levels was noted only in the low-CHO group [95]. Therefore, a therapeutically CHO-reduced diet, which is usually gluten-free, can be of potential benefit to those with autoimmune disorders. See below as we discuss allergies and food sensitivities.

5.3.6 Irritable Bowel Syndrome

The prevalence of gastrointestinal (GI) disorders, such as irritable bowel syndrome (IBS), associated with lipedema has ranged from 3.1-32.9%, with increased incidence seen in more advanced stages [10, 44, 54]. From a clinical perspective, GI issues are seen quite commonly in patients with lipedema (CR, clinical experience).

Assessing digestive symptoms before and during dietary intervention is, therefore, imperative. Should there be an exacerbation of symptoms of diarrhea, assessing whether fat malabsorption could be playing a role can be helpful. If so, consider lowering dietary fat intake. Should there be an exacerbation of constipation, consider introducing additional magnesium and prokinetics to see if they help.

Although comprehensive management of IBS is beyond the scope of this paper, the clinician should be aware that common comorbidities of lipedema, such as hypothyroidism, can slow digestion and exacerbate IBS. Similarly, side effects of some medications popular with patients with lipedema, such as pain medication and GLP-1 agonists, can also slow down digestion.

Several studies have shown a favorable impact on IBS symptoms with various levels of CHO restriction. In a review of studies that examined the impact of restricted CHO intake on gut microbiota, the authors found mixed implications. They suggested the use of probiotics to maintain a balanced, healthy gut microbiome [96]. More recently, a case series report of 10 patients with IBS reported a favorable impact on symptoms with a Carnivore diet (completely animal-sourced and very low CHO intake), suggesting that CHO reduction is a promising intervention for IBS [97].

5.3.7 Allergies/Food Sensitivities

Food intolerances, allergies, and adverse food reactions may arise from both immunological and non-immunological mechanisms, with inflammation playing a central role [98]. Amato et al. [99] have proposed that certain foods may exacerbate lipedema symptoms not only through their impact on weight gain but also by promoting systemic inflammation. While a variety of testing methods exist to identify food sensitivities, these vary in reliability. The current gold standard remains a structured elimination diet to evaluate individual responses to suspected food triggers [100].

Evidence on food sensitivities in lipedema is limited and largely anecdotal, highlighting the need for rigorous research to determine the effects of eliminating or reducing specific dietary components and to clarify the mechanisms by which certain foods may influence symptoms. Clinically, many patients report improvements after reducing or removing potentially inflammatory foods, and some benefit from a structured elimination and reintroduction process to identify personal triggers [101]. Commonly reported problem foods include gluten, dairy, nightshade

vegetables, highly processed seed oils, artificial sweeteners, sugar substitutes, and high-histamine foods. When symptoms persist despite a CHO-reduced diet, or when flares occur after certain meals or dietary changes within a ketogenic framework, a temporary elimination protocol with systematic reintroduction and symptom monitoring may be appropriate.

5.3.8 Nutrient Deficiencies in Lipedema

While more extensive research is needed to investigate the full scope of potential nutrient deficiencies in patients with lipedema, initial research highlights two potential nutrients of concern: vitamin D and selenium. As discussed above, both vitamin D and selenium deficiency are associated with autoimmune disorders [91, 93], which can be a comorbidity of lipedema.

The samples in two studies showed that a vast majority of participants (77-84.6%) with lipedema were below the normal level for vitamin D, and that this was inversely associated with BMI [44, 57]. Vitamin D insufficiency is fairly common in the general population [102] and is associated with overweight and obesity [103, 104], but preliminary data seem to show that this nutrient deficit may more often occur when lipedema is present [57]. If a vitamin D deficiency is identified, vitamin D-rich foods that align with a CHO-reduced diet, such as wild-caught salmon, egg yolks, red meat, and beef liver, can be encouraged. In addition to promoting healthy sun exposure, vitamin D supplementation is often necessary and can be an effective strategy to restore and maintain optimal levels.

Selenium deficiency has also been identified as a potential nutrient of concern in patients with lipedema. In a study comparing individuals with lipedema, lymphedema, and lipo-lymphedema, selenium deficiency was present in 41.9% of individuals with lipedema and 53% with lipo-lymphedema [56]. In contrast with individuals with lymphedema, selenium levels did not significantly differ by BMI in either group, suggesting that this finding was not due to the presence of overweight or obesity. Further study is required to evaluate if selenium deficiency is common in lipedema and, if so, to identify its cause. Regardless, monitoring of selenium may be warranted in patients with lipedema to identify any existing deficiency. Increasing intake of selenium-rich foods, such as Brazil nuts, seafood, meat, poultry, and organ meats, can be added if indicated to improve selenium levels.

6. Emotional Aspect

Components of the emotional aspect of nutritional holistic care can influence the process of making and sustaining changes in a chosen eating plan. Women with lipedema may have been affected by healthcare disparities such as delayed diagnosis, limited or no access to optimal treatments, and anti-fat bias from healthcare professionals [3]. Acknowledging the emotional aspects can be pivotal for the individual trying to make lasting dietary changes. Issues addressed here are mindset, capacity for making change, adhering to an eating plan, and emotional eating.

6.1 Mindset

Before making any dietary change to manage lipedema symptoms, it is important to recognize whether a person is someone who prefers quick, dramatic changes (fast approach) or someone who

thrives with gradual, small adjustments (slow approach), as this can help tailor a dietary transformation to suit individual personalities and lifestyles.

If a patient with lipedema is a ‘diver’, they might prefer jumping in with both feet, committing to an entirely new dietary approach all at once. This approach would suit someone who finds motivation in bold, all-in changes and who can handle the intensity of a sudden shift. Alternatively, if a patient is a ‘toe dipper,’ taking a more gradual, step-by-step approach might be more effective. Small, incremental changes allow for adjustments without feeling overwhelmed and can help build sustainable habits over time.

The key is choosing an approach that can be maintained. A ‘diver’ might thrive in the short term but could struggle with long-term consistency, while a ‘toe dipper’ might take longer to see results but is more likely to sustain change in the long run. Both mindsets are legitimate strategies for implementing change and will generally require some level of support. Additionally, the clinician needs to understand that there is a range of mindsets between ‘diver’ and ‘toe dipper’, and patients may change where they are on the spectrum over time (see Figure 4). Tailoring interventions and support to a patient’s current mindset will be the most effective strategy.

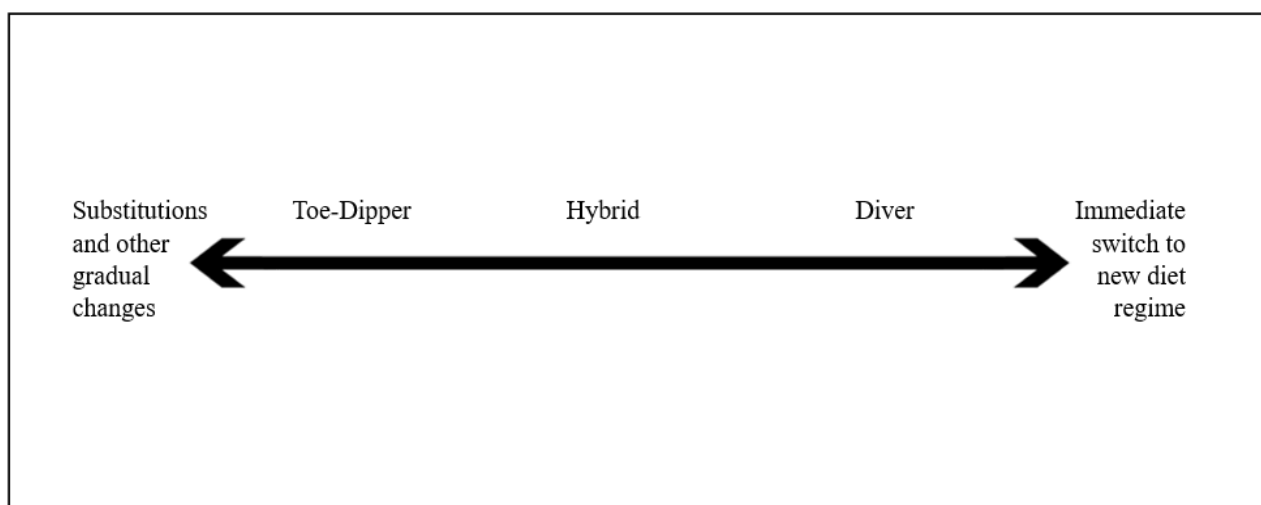


Figure 4 The range of mindsets toward making dietary changes. On the left, the “Toe-Dipper” represents patients who are best supported with gradual change due to a low capacity for abrupt change. On the far right, the “Diver” represents patients who are most comfortable immediately adopting strict definitions and guidelines when making dietary changes.

6.2 Capacity for Change

The capacity for change is another important factor to consider when recommending dietary change. The Transtheoretical Model (TTM) is a framework for understanding how people intentionally change behavior. Key concepts of TTM are developing self-efficacy and confidence in one’s ability to change, learning through relapse, and continually reevaluating reasons for making changes [105].

The Stages of Change include Precontemplation, Contemplation, Preparation, Action, and Maintenance [105]. In the Precontemplation stage, individuals are not ready to change their eating pattern within six months, either by resisting changing altogether or considering making changes,

but might be sometime in the distant future. The goal during this stage is to raise awareness and provide information about lipedema and CHO restriction. In the Contemplation stage, individuals are thinking about changing how they eat within the next six months and are seeking information to weigh the pros and cons of attempting a dietary change. During Preparation, individuals are committed and may have already attempted a diet change before, making this stage ideal for providing support and goal-setting that is tailored to their unique situation. In the Action stage, individuals have made changes within the past six months but face a high risk of relapse. Ongoing support is crucial. In the Maintenance stage, individuals have sustained changes for at least six months, and have a lower relapse risk, but continuous reinforcement is still important. It is important to remember that progress does not always occur linearly, and a patient may go back and forth between stages. Understanding the stages of change and where a person may be in their dietary intervention journey helps the clinician to customize interventions while improving adherence and the prognosis for long-term success.

Setting appropriate goals along the way to making and sustaining dietary changes cannot be overstated. Many patients with lipedema have tried and failed weight loss diets previously and may be hesitant to trust that another change in their eating pattern will be successful. As part of the holistic approach, it is important to establish realistic expectations and an understanding of what is anticipated. The clinician is urged to work together with the patient to develop concrete, achievable goals that may focus on other measures of success besides or in addition to weight loss goals. For example, reduced pain, decreased body circumference measures, improved functional mobility, percent body fat, or fatigue can be gratifying and motivating goals.

6.3 Adherence to Interventions

When suggesting dietary changes for lipedema, adherence in the real world is influenced by an individual's ability to follow a treatment plan. A model put forth by Gretchen Rubin suggests that people have different 'tendencies' that impact their ability to adhere to a diet plan [106]. These tendencies are named Upholders, Questioners, Obligers, and Rebels.

Upholders are likely to meet both external and internal expectations, so they will generally adhere to dietary changes once they have committed to them. They are motivated by both personal goals and healthcare provider guidance. Questioners, conversely, require justification and explanations to accept expectations. They are likely to need strong evidence, data, and reasons for why dietary changes are necessary for lipedema. They may also want to modify the advice to fit their needs and preferences, which can make personalized plans more effective for them.

Obligers easily meet external expectations but struggle with internal ones. For them, adherence is best when there is accountability, such as regular check-ins or follow-ups. For patients with lipedema who are Obligers, reminders and external support will encourage them to stick to dietary changes. Rebels, on the other hand, resist both internal and external expectations. They may respond better when they feel they have ownership of the decisions and are given the freedom to choose their dietary approach.

Understanding these tendencies can help personalize interventions, improving a patient's capacity to adhere to dietary recommendations and achieve better outcomes. For further information on this topic, we recommend reading *The Four Tendencies* by Gretchen Rubin.

6.4 Emotional Eating

Emotional eating is an urge to consume food in response to emotional stress rather than physical hunger. The kind of food that is overeaten under stressful conditions tends to be highly palatable ‘comfort foods’, meaning that these foods trigger a temporary pleasure response [107]. While not classified as an eating disorder, the regular use of emotional eating as a coping strategy for negative emotions can potentially lead to issues like binge eating.

Research has shown that patients with lipedema may experience more challenges with emotional regulation than the general population [108]. This can lead to challenges when using comfort foods as a strategy for handling stressful life experiences. If it is suspected that a patient with lipedema is using a maladaptive behavior like emotional eating, the Dutch Eating Behavior Questionnaire (DEBQ) can be used [109]. Although not validated for the lipedema population, the DEBQ may still be a useful tool for identifying and monitoring dysfunctional eating behaviors [110].

It is important to offer alternative and effective coping strategies for the patient who has relied upon emotional eating. Abruptly removing even a maladaptive and largely ineffective strategy before adequately adopting another tactic will be problematic and likely cause the patient to refuse to change their behavior. Experimenting with non-food approaches to emotional regulation, such as mindfulness, breathing exercises, and pleasurable distraction (going for a walk or talking to a friend) can be attempted. It may also be helpful to remove high-CHO foods from the house to avoid temptation. Consider various levels of CHO reduction to see how this impacts appetite regulation. Although emotional eating is not driven by hunger, improved satiation can make alternative tactics easier to instigate.

7. Psychological Aspect

The psychological aspect of nutritional holistic care delves into mental health concerns and psychiatric diagnoses that may require medication, such as anxiety, depression, and disordered eating. The patient taking psychiatric medication will require monitoring by a specialist, preferably one in metabolic psychiatry, when changing their diet. Several studies have shown a need for lowering medication dosage or even deprescribing medication in response to lowering CHO intake, which requires a physician with experience making adjustments to medications [111-113].

7.1 Depression and Anxiety

While more research is needed to identify exact rates, several studies have identified significant levels of depression, anxiety, and related symptoms in individuals with lipedema [3, 10, 108, 114]. In some cases, rates of depression are as high as 43.6% compared to 18.5% in the control group [3]. In another study, impaired emotional regulation was noted in many patients with lipedema [108].

Depression and anxiety may partially be the result of living with a chronic, often disfiguring, disease like lipedema. Increased rates of health anxiety and depression have been noted in other chronic diseases like stroke, Alzheimer’s disease, and diabetes [115], and thus it may be no surprise that a similar phenomenon may be true in lipedema. However, this does not decrease the impact that these conditions can have on the quality of life of those with lipedema and comorbid depression or anxiety.

It is also important to recognize that if depression or anxiety is present in a patient who has lipedema, this may impact their ability or ease in adopting a nutrition-focused management protocol. For example, depression can come with low motivation or fatigue, which may impact the patient's readiness to cook for themselves. Anxiety may result in feelings of uneasiness or uncertainty, which may decrease confidence and increase hesitancy over trying a new dietary strategy to manage their symptoms. As such, identifying mental health issues in patients with lipedema may help individualize their care.

The results from several clinical trials and case reports demonstrate the effectiveness of therapeutic CHO reduction in the management of mental illness, particularly depression [111-113]. Adams et al. [111] reported that depressive symptoms in patients with diabetes using a KD improved in their 2-year study. Similarly, in a recent retrospective analysis of 31 patients with treatment-refractory mental illnesses (major depressive disorder, bipolar disorder, and schizoaffective disorder), the majority had significant improvement in their symptoms using a KD [112]. It is important to note that over half of the participants in this study required the dosage of their psychiatric medications to be lowered due to the positive effects of the diet and required careful monitoring, as mentioned above.

7.2 Disordered Eating

Eating disorders are classified as mental health conditions marked by maladaptive eating behaviors and distorted attitudes toward food and body image. Common characteristics of eating disorders include preoccupation with food, distorted body image, and obsessive thoughts or compulsive behaviors related to eating. Prominent examples of eating disorders include anorexia nervosa, bulimia, and binge eating disorder.

Several studies have noted the high frequency with which women with lipedema, particularly in the later stages, have an eating disorder diagnosis [8, 116, 117]. In a study of 100 patients diagnosed with lipedema, 74% had a history of eating disorders, 12% with periodic binge eating attacks, 8% with bulimia, and 16% with anorexia nervosa [117]. Fetzer & Fetzer [116] reported that 45% of 250 respondents claimed a diagnosis of an eating disorder. Clarke et al. [8] found that 16% of participants with self-reported lipedema had an eating disorder diagnosis. These figures are significantly higher than the 8.4% global prevalence among women [118].

The lack of awareness about lipedema, misdiagnosis of obesity, and a tendency for mainstream medicine to classify obesity as a character flaw can all contribute to the development of an eating disorder, especially in women with lipedema who often have fought a lifelong battle to lose weight [119]. An experienced metabolic health practitioner who is knowledgeable about lipedema may be an optimal member of the team to guide a patient with an eating disorder to adopt a therapeutically CHO-reduced diet.

Therapeutic CHO reduction has shown promise as an intervention with patients who have an eating disorder, despite concerns that a restrictive dieting pattern could trigger maladaptive eating behaviors [120]. In case series reports for both binge eating disorder [120] and anorexia nervosa [121], patients were not only able to achieve and sustain normalized weight but also decreased anxiety and improved overall mental well-being. In a study of youths with type 1 diabetes who had shown disordered eating behaviors, participating in a guided nutrition program did not cause any increase in maladaptive behaviors [122]. These reports suggest that therapeutic CHO reduction, if

applied holistically, may also be an effective intervention for patients with lipedema who have an eating disorder.

8. Social Aspect

The social aspect of nutritional holistic care refers to the social factors and relationships that influence a patient's health and well-being. This aspect encompasses a patient's interpersonal relationships, social support networks, living environment, socioeconomic status, and cultural background. These factors can significantly affect a person's ability to access appropriate treatment, adhere to an eating plan, and maintain overall health and quality of life. Additionally, social and cultural influences are frequently noted as barriers to making dietary changes for individuals with various chronic diseases, highlighting this as a potential focus in dietary adherence in lipedema management as well [123, 124].

In this section, we discuss the social impacts on nutrition and adhering to a chosen dietary plan, including the importance of community and social support systems, socioeconomic factors, cultural and ethnic influences, and managing food-centered social occasions. A clinician will need to acknowledge the potential impact of all of these concerns while helping the patient navigate these challenging issues and situations.

8.1 Importance of Community

A supportive network of family, friends, coworkers, and community groups is invaluable for a patient with a chronic illness. In a literature review by Elfhag Rössner [125], social support was one of the main factors associated with weight loss maintenance, a finding supported by a more recent meta-analysis performed by Lemstra et al. [126]. Additionally, Rotberg et al. [127] found that low-income Latinos with type 2 diabetes were able to achieve better glycemic control when part of a supportive community.

Women with lipedema face substantial social challenges, such as weight stigma and social isolation, making a supportive community all the more important for this population [128]. In an online survey by Clarke et al. [8] of over 1300 women with self-reported lipedema, almost 68% reported staying at home more, and just under 60% expressed feeling lonely. Younger women with lipedema have reported that social support through relationships or support groups had a significant impact on their ability to manage their symptoms [129]. Falck et al. [130] noted that women with lipedema had substantial limitations in their daily activities and social life due to their symptoms.

Women report a feeling of belonging and social connectedness when part of either online or in-person lipedema support groups [128, 129]. Women feel acknowledged, validated, and understood when part of a community of peers who are living with lipedema. Groups specific to lipedema and ketogenic or low-CHO diets can provide encouragement and motivation, share information and resources, and bolster confidence for the patient with lipedema adopting a CHO-reduced diet.

8.2 Socioeconomic Status

Socioeconomic status (SES) shapes health in a multitude of ways and may be one of the most powerful determinants of health [131]. Factors of SES include income, education level, employment

status, living conditions, and social standing, all of which can profoundly impact access to healthcare resources and optimal health outcomes [132].

While participants in a study by Dudek et al. [3] described their economic status to be average or good, self-management of lipedema symptoms still created a financial burden. It may be that symptoms of lipedema, particularly in its later stages, can limit the ability to work, and the resulting financial hardship reduces access to appropriate treatments, as reported in another study [133].

Ketogenic and reduced-CHO diets are often viewed as expensive ways to eat. A patient of lower SES and/or one who has a significant financial burden due to lipedema and other comorbidities may be hesitant to commit to an eating plan that is believed to increase grocery bills. Clinicians will need to counsel their patients on how to eat a CHO-reduced diet on a budget, such as purchasing meat and poultry that is on special, using coupons, and other cost-saving methods. A free guide (Low-Carb on Any Budget by Mark Cucuzzella, MD and Kristie Sullivan, MD) can be downloaded here: <https://oneofonebillion.org/library/lowcarbforanybudget>. More suggestions from low-CHO coach Brian Wiley can be found here: <https://toward.health/is-low-carb-eating-expensive/>.

8.3 Cultural and Ethnic Influences

Cultural beliefs, traditions, and language barriers can influence health behaviors and interactions with the healthcare system. Of concern here is how a patient with lipedema can be aided in her desire to reduce CHO consumption while still respecting her cultural values. This may be a challenge initially, but by working on this issue together, the practitioner and patient can build a personalized plan that is more likely to succeed.

One issue that may arise is the introduction of animal-sourced foods for a patient who has traditionally used a vegetarian diet for cultural, religious, or moral reasons. Additionally, there may be some anxiety due to a common misconception that low-CHO diets must be heavily animal-sourced eating plans. Perceptions and values can seem to be at odds with the motivation to modify the diet to improve health. While it is true that nutrient deficiencies and the inability to reduce CHO consumption enough to impact symptoms may preclude a strictly plant-sourced diet [134], patients can succeed on a broad spectrum of eating plans from less animal-sourced to entirely animal-sourced diets (see Figure 3). Including such foods as low-CHO dairy products, eggs, poultry, and fatty fish may be acceptable, as long as there are no other cultural or medical reasons for their avoidance.

Certain foods may be considered important or central to the patient's culture or ethnicity. For instance, a patient who identifies with a Hispanic culture may be accustomed to dishes that consistently include moderate to high-CHO ingredients such as corn, beans, and rice. Substitution of lower-CHO vegetables such as eggplant or cauliflower may smooth the way to reducing CHO intake. Other high-CHO foods may only be special to a certain holiday, such as particular breads used in a traditional Jewish celebration. Possible solutions may include going off-plan for this special event or finding ingredient or food substitutes to lower the CHO content. Lastly, it may be helpful to research traditional foods associated with a patient's culture or ethnicity. It may be that foods considered to be traditional have only been so for more recent history. Interested clinicians can consult resources on ancestral diets to learn more.

8.4 Managing Social Occasions

Managing food-centered social occasions can be challenging, particularly when newly transitioning to eating in a therapeutic CHO-reduced manner. Special occasions and celebrations are typically dominated by foods high in sugar and starch that are not on a low-CHO eating plan. Favorite food choices may be hard to resist when faced with peer pressure or feelings of embarrassment or deprivation when eating differently from others.

Several strategies can be employed to improve success in social occasions. For example, patients may find it helpful to prepare a ready reason for their dietary choices ahead of time, such as symptom management or following medical advice, and give a list of foods they will avoid. This allows friends and family to understand the dietary restrictions ahead of time, allowing them to be more supportive rather than sabotaging the patient's attempts to stay on plan. Role-playing conversations or situations that may arise during social occasions can give patients the confidence to navigate these challenges successfully.

Finding out before an event the types of food that will be served allows for the opportunity to bring a dish or snack that aligns with their current dietary choices, if appropriate. Alternatively, having a small meal before attending a social event can make it easier to avoid temptation and to stick to their eating plan. Additionally, clinicians can help their patients focus on the foods that are permitted and enjoyed on an eating plan rather than those that are to be avoided. This can mitigate feelings of deprivation when traditional holiday foods, for example, may need to be avoided.

9. Other Considerations for the Holistic Practitioner

For the clinician who wishes to incorporate therapeutic CHO reduction diets into the holistic care of lipedema, there are several other considerations, including the potential impacts of ketosis, impacts of ultra-processed foods, speculations regarding the necessity of caloric restriction, and concerns with the long-term use of a KD.

9.1 Impact of Ketosis

While a variety of trials have indicated that a KD is helpful for reducing lipedema symptoms, it is currently unclear whether the level of ketosis is important for symptom relief. In other disease states, there is some evidence that a deeper level of ketosis (higher level of blood ketone levels) may have a beneficial effect in certain circumstances, such as chronic kidney disease [135-137], heart failure [138, 139], and bipolar disorder [140].

Investigation into the dose-dependent effects of ketone bodies on disease states is still in the early stages, and larger trials are needed to verify initial findings. Additionally, just because some diseases may benefit from deeper ketosis, it does not mean that lipedema symptoms will respond this way. However, the effects of different levels of CHO restriction on symptoms of lipedema in several clinical trials show promise that deeper ketosis may be a significant factor in better reductions in pain and lower body fat [4, 20, 26].

Due to the lack of research on this topic concerning lipedema, a personalized approach is essential. Patients can actively track their ketone levels using a home monitor, such as a blood ketone monitor, to assess whether deeper ketosis alleviates pain, reduces swelling, or boosts energy.

This real-time feedback empowers them to refine their dietary strategy, potentially enhancing symptom management and overall well-being.

9.2 Impacts of Ultra-Processed Foods

Ultra-processed foods (UPFs) are industrial formulations typically made with little or no whole foods and containing ingredients not commonly used in home cooking, such as flavorings, colorings, emulsifiers, and other additives designed to enhance palatability and shelf life. Although research into the effects of UPFs is still in its infancy, emerging evidence has begun to point to areas of concern with excess consumption. Ingredients like industrial additives, for example, have been shown to contribute to increased intestinal permeability, which may contribute to chronic conditions like autoimmune diseases [94]. Some trials have also sought to directly investigate the impact of UPFs. In an *ad libitum* randomized controlled trial, a diet composed of UPFs resulted in increased food intake and weight gain [141]. While further study is needed, as the trial was only two weeks long and did not contain a washout period between the intervention and control diet, this does mimic what some see in clinical practice when patients consume a diet primarily composed of UPFs.

UPF consumption has surged globally, accounting for 58% of total caloric intake in the U.S., according to the NHANES dataset [142]. Given how common high UPF intake is, a practical starting point for lipedema patients may simply be to reduce or eliminate these foods to assess symptom improvement. While research on UPFs and lipedema is limited, clinically, many patients report symptom relief from focusing on unprocessed or minimally processed foods when adopting a therapeutically CHO-reduced diet.

9.3 Is Calorie Restriction Necessary If Using a KD for Lipedema?

Currently, evidence regarding *ad libitum* KDs for the management of weight in patients with lipedema is lacking. The current research is dominated by calorie-controlled studies, either eucaloric or calorically restricted. However, existing mechanistic data do suggest that CHO-reduced diets, including KDs, may have benefits resulting from proposed metabolic advantages, appetite-regulating effects, or both [42, 143]. The combination of these factors, as well as others potentially yet to be discovered, may result in calorie restriction being unnecessary for some patients with lipedema who are seeking weight loss.

Identifying whether caloric restriction is necessary for the day-to-day management of lipedema is an important question to answer for the benefit of the patient. If calorie restriction is not necessary to improve body composition and symptoms of lipedema, this removes a burden from the patient by simplifying their management plan by removing unneeded aspects of their individualized protocol. This may be especially beneficial if the patient has had experience with calorie-restricted protocols and, characteristic of lipedema, has found limited success and feelings of frustration or hopelessness as a result. Therefore, it is the opinion of the authors that *ad libitum* CHO-reduced diets should be investigated as a plausible, intuitive strategy for some patients with lipedema to achieve and maintain improved body composition.

9.4 Issues/Concerns with Long-Term Usage of a KD

Historically, there has been concern surrounding the application of a KD for long-term use. Typically, concerns focus on cardiovascular disease, fatty liver, kidney function, and the risk of nutrient deficiencies. Given that lipedema is a chronic disease with no known cure, any dietary intervention used to manage symptoms and prevent excess fat gain has the potential to be used long-term. As such, it is important to address these concerns given the availability of new evidence over recent years.

Long-term studies on the effects of low-CHO and KDs on patients with lipedema would be beneficial to help establish more concrete recommendations and contraindications. Currently, no such long-term trials exist. As discussed at the beginning of this paper, KDs can be personalized, such as by increasing or decreasing protein or fat intake to accommodate the patient's situation and unique response to the diet.

9.4.1 Cardiovascular Disease

Concerns have been raised about the potential cardiovascular risks of CHO-reduced and KDs, particularly due to their high-fat content and effects on lipid profiles. The literature reports variable impacts on cholesterol markers depending on factors such as population characteristics, BMI, and the degree of CHO restriction. Importantly, reintroducing CHO can often reverse elevations in LDL-cholesterol. While studying the effect of ketogenic metabolism on lipid levels remains under active investigation [144, 145], specific research in the lipedema population is limited.

In one study of 24 women with lipedema and 24 with obesity following a low-CHO diet for seven months, the lipedema group showed a mean 15% increase in LDL-cholesterol, though individual responses varied widely [29]. Both groups experienced reductions in triglycerides, increases in HDL-cholesterol, and improvements in glucose and insulin levels. Therefore, given the potential for elevated LDL in some patients with lipedema on a KD, careful monitoring is recommended, especially for those considering long-term dietary adherence for symptom relief. If LDL levels rise and intervention is needed, transitioning to a moderate low-CHO diet (100-150 g/day) often normalizes cholesterol levels [146]. For patients sensitive to even moderate CHO intake, pharmacologic options may be considered. Additional testing and functional testing, such as Carotid Intima-Media Thickness (CIMT) scans, Coronary Artery Calcium (CAC) scans, or CT-angiograms, can help assess cardiovascular risk over time.

9.4.2 Non-Alcoholic Fatty Liver Disease

Questions have also been posed regarding other possible effects of KDs due to their composition. High-fat diets have been linked to non-alcoholic fatty liver disease (NAFLD), and thus, concerns regarding a high-fat KD have also been raised. In a recent trial of a KD for lipedema, for example, additional hepatic protective nutraceuticals were part of the protocol used to pre-emptively address this issue [26]. However, despite such concerns, both trials using CHO restriction for treatment of NAFLD and post hoc analyses in populations using CHO restriction for other conditions have instead shown improvement in markers of liver function and health [147-149].

However, if the patient has a history of NAFLD or if there is a heightened risk due to comorbid conditions like obesity, routine monitoring of liver function can be performed to verify that the

patient remains in good health. Recommended liver function tests and other suggested labs are provided in Table 4.

Table 4 Suggested laboratory tests for assessing and monitoring patients with lipedema on long-term CHO-reduced diets. The left column lists key areas of focus, reflecting both lipedema-specific concerns and common considerations for prolonged KD use. The middle column outlines recommended tests, and the right column explains the rationale for monitoring in this context.

Concern	Lab Tests	Rationale
Liver Panel	ALT, AST, GGT	Evaluate liver function to monitor existing fatty liver and/or verify fatty liver does not develop on a higher fat CHO-reduced diet.
Kidney Panel	creatinine, BUN, eGFR	Evaluate kidney function to monitor existing kidney disease and/or verify kidney function does not deteriorate if a high-protein, CHO-reduced diet is used.
Heart Health	Total Cholesterol, HDLc, LDLc, Tg	Evaluate cardiovascular risk in combination with inflammation/oxidation markers. Additionally, to monitor changes in lipid profile due to the possible influence of a CHO-reduced diet on LDL in a subset of patients.
Thyroid Panel	TSH, T3, T4, rT3 T3/rT3 ratio Thyroid Antibodies	Evaluate thyroid function, to monitor existing disease, such as hypothyroidism or autoimmune thyroid disease, and/or to verify thyroid function does not deteriorate with a CHO-reduced diet.
Metabolic Health	Fasting glucose and insulin, HOMA-IR	Evaluate hyperinsulinemia and insulin resistance as a facet of metabolic health, to monitor existing disease, and help determine the level of CHO reduction best suited for the patient.
Nutrient Deficiencies	D, Selenium, carnitine, folate, electrolyte panel	Evaluate nutrient status, to monitor common nutrient deficiencies of concern for lipedema, inflammatory disorders, following KDs long term, and/or those that are common in the general population.
Inflammation/Oxidation	C-reactive protein (CRP), glyc-A, MPO	Evaluate inflammation level, both to assist in monitoring of other diseases and risk (cardiovascular, autoimmune), and to evaluate changes in response to a CHO-reduced diet.

9.4.3 Kidney Function

Concerns have been raised about the long-term use of CHO-restricted diets due to their typically high protein content, which may increase the burden on the kidneys by elevating the need to filter protein metabolism byproducts. This has prompted caution, especially for individuals with chronic kidney disease (CKD). However, recent research challenges these concerns. A one-year crossover study in healthy males found no adverse effects of high protein intake on kidney function [150]. Likewise, a recent meta-analysis associated higher protein intake, even from animal sources, with a reduced risk of CKD [151].

Regarding the use of CHO-reduced diets specifically, an analysis of individuals following a very low-CHO diet for type 2 diabetes management found that renal function, as measured by eGFR, was either maintained or improved over two years [135]. These findings were supported by an ad hoc clinical review of patients with normal renal function or mild CKD using similar CHO-restricted protocols in a clinical setting, which also showed no impairment, and in some cases, potential improvement in kidney function [152]. However, these initial findings have not addressed the effects of high-protein diets in individuals with severe CKD, so caution remains warranted in such cases.

If a patient with lipedema has a history of CKD or is at risk of CKD due to comorbidities like type 2 diabetes, then routine monitoring of renal function is advised. If a high protein diet is contraindicated for the patient or if kidney function worsens, adjusting to a moderate protein ketogenic approach may be warranted to personalize the approach to their situation.

9.4.4 Nutrient Deficiencies and KDs

Some concern has been raised regarding the risk of nutrient deficiencies when utilizing a KD. Much of this concern can be traced back to the use of Classical Ketogenic Diets (CKD) in the treatment of pediatric epilepsy. However, the reliance on CKD to make broad assumptions about CHO-reduced diets may not be appropriate, given the differences between CKDs and modern KDs used for diseases like lipedema.

CKDs are extremely high-fat diets with a 4:1 ratio of fat to protein and CHO combined [153]. It has been suggested in more recent reviews of these protocols that inadequate intake of animal-sourced protein may have contributed to the selenium and carnitine deficiency in these populations [154]. In contrast, protein restriction is not recommended for patients with lipedema. In fact, Dr Gabriele Faerber recommends specifically a 'protein-optimized' low CHO diet for her patients with lipedema [155]. Protein content should be 15-30% of total caloric intake, or at least 1.2-1.5 g/kg of ideal body weight as a minimum intake, regardless of caloric consumption. These recommendations are similar to those found in long-term KD studies [16].

A well-formulated KD for managing lipedema should ensure that sufficient protein and nutrient-rich whole foods are consumed to avoid nutrient deficiency. Given the lack of long-term studies on the use of whole food KDs in patients with lipedema, routine monitoring for carnitine and selenium deficiency, along with any other nutrients of concern, can be performed with patients who intend to utilize a KD long term to verify the well-being and long-term success of the patient.

10. Assessment and Evaluation

Clinically, we find that using a combination of screening tools enables both the patient and the clinician to determine the effectiveness of the interventions and can serve as an alert for adjustments to diet, when necessary. Routine and specialized monitoring can be accomplished in a clinical setting to ensure that the patient remains in good health and does not develop any nutrient deficiencies. A CHO-reduced dietary plan can and should be adjusted and adapted over time as the circumstances of the patient change or in the case of any comorbidities that may occur over their life. If necessary, a non-ketogenic CHO-reduced approach can be used if a KD is not well-tolerated or is not preferred. Here, we suggest methods of monitoring a patient with lipedema, including symptom tracking, lab tests, and other evaluation methods.

10.1 Symptom Tracking

While weight will be documented, overall weight loss must not be the only, or even the most important, anthropomorphic measure that is captured. Perhaps the most significant changes that a patient with lipedema will experience while following a CHO-reduced diet will be improved management of her symptoms associated with lipedema. Tracking lipedema symptoms, such as easy bruising, swelling, pain, and tissue quality, can be used to observe the effects of interventions and progress toward goals. In addition to assessing for lipedema symptoms, it is also helpful to document such things as energy level, mood, and patient satisfaction with the intervention. Although not meant to be an exhaustive list, Table 5 provides some examples of symptoms and issues to track and possible assessment tools.

Table 5 Suggested assessments/tools for tracking lipedema symptom response to dietary intervention. On the left, the specific focus of concern or symptom is listed. The recommended assessments that can be used to track changes over time are listed in the right-hand column.

Concern	Assessments
Excessive Body Fat	Body Composition Analysis (bioimpedance, ultrasound, DXA scan), Body Weight, Skinfold Calipers, WHtR
Pain/Heightened Sensitivity	Visual Analog Pain Scale, Semmes Weinstein Monofilament Test
Edema/Fibrosis	Kaposi-Stemmer Sign, Tonometer, Circumferential Measurements
Fatigue	Fatigue Severity Scale
Functional Mobility	Timed Up and Go Test, 6-Minute Walk Test
Quality of Life	RAND SF-36 (Short Form Health Survey), Lymphedema Life Impact Scale (LLIS), Obesity and Weight Loss Quality of Life (OWLQOL)

Pathology testing for nutrient levels, inflammation markers, and metabolic regulation can also provide a quantifiable way of determining the effectiveness and safety of dietary interventions. See Table 4 for suggested laboratory tests along with their rationale. Lastly, some practitioners and their

patients may wish to track ketone levels using breath, blood, or urine, as discussed previously, if it is desirable to measure the impact of ketosis.

10.2 Key Takeaways for Monitoring Safety and Effectiveness

Long-term use of KDs for lipedema management raises concerns about cardiovascular disease, NAFLD, kidney function, and nutrient deficiencies. Recent evidence suggests well-formulated KDs can be safe and effective with proper monitoring and personalization to the patient's needs and comorbidities. Baseline health assessments around these areas, followed by routine monitoring during annual checkups, are recommended to detect changes in symptoms (e.g., pain, edema, fatigue), laboratory markers (e.g., liver, kidney, lipid panels, nutrient levels), and functional measures (e.g., CIMT, CAC scans). If adverse effects occur, adjustments to the KD, such as moderating protein or CHO intake, or referrals to specialists familiar with KDs, may be warranted. While current research on properly formulated KDs is promising, long-term studies specific to lipedema are needed to establish definitive guidelines and identify any unique risks for this population.

11. Conclusion

Lipedema is a chronic disease that can impact all aspects of an individual's life, necessitating the concerted effort of clinicians to treat the whole person using a patient-centered, holistic approach. Although dietary interventions were once considered ineffective for managing lipedema, emerging evidence increasingly supports the therapeutic potential of CHO reduction in alleviating lipedema symptoms. Further, a growing body of evidence suggests that CHO-reduced diets can be adjusted to accommodate a patient's comorbidities and changes in life circumstances. A growing number of individuals with lipedema are now turning to informed healthcare providers for guidance in adopting personalized nutritional strategies.

To maximize adherence and long-term success, dietary modifications must be approached within the context of a holistic, patient-centered framework. This paper has outlined evidence-informed recommendations for implementing a CHO-reduced dietary plan, emphasizing the importance of tailoring interventions to the individual's physical, emotional, psychological, and social circumstances. Furthermore, we have provided practical strategies for monitoring outcomes to ensure both safety and efficacy. These insights aim to support clinicians in delivering comprehensive, responsive care that aligns with the complex needs of the lipedema population.

Author Contributions

All three authors contributed equally to the conception and drafting of the manuscript, critically revised it for important intellectual content, and reviewed and approved all versions of the article from initial submission to final publication. Specifically, LK initiated the project, developed an outline of content for the manuscript, and provided content related to lipedema diagnosis and therapy. CR provided and scrutinized content with respect to the application of evidence-based nutrition science to assess, diagnose, and manage dietary needs in order to support health, prevent disease, and optimize clinical outcomes. SH provided and scrutinized content regarding evidence-

based therapeutic CHO reduction, metabolism, and impacts on general health and on patients with lipedema.

Competing Interests

The authors have declared that no competing interests exist.

AI-Assisted Technologies Statement

Artificial intelligence (AI) tools were used solely for basic grammar correction and language refinement in the preparation of this manuscript. Specifically, OpenAI's ChatGPT was employed to improve the readability and linguistic clarity of the English text. All scientific content, data interpretation, and conclusions were developed independently by the author. The authors have thoroughly reviewed and edited the AI-assisted text to ensure its accuracy and accept full responsibility for the content of the manuscript.

Additional Materials

The following additional materials are uploaded to the page of this paper.

1. Carbohydrate-Reduced Eating Recommendations.

References

1. Allen EV, Hines EA. Lipedema of the legs: A syndrome characterized by fat legs and orthostatic edema. *Proc Staff Meet Mayo Clin.* 1940; 15: 184-187.
2. Keith L, Seo C, Wahi MM, Huggins S, Carmody M, Faerber G, et al. Proposed framework for research case definitions of lipedema. *Lymphat Res Biol.* 2024; 22: 93-105.
3. Dudek JE, Białaszek W, Gabriel M. Quality of life, its factors, and sociodemographic characteristics of Polish women with lipedema. *BMC Womens Health.* 2021; 21: 27.
4. Sørli V, De Soysa AK, Hyldmo AA, Retterstøl K, Martins C, Nymo S. Effect of a ketogenic diet on pain and quality of life in patients with lipedema: The LIPODIET pilot study. *Obes Sci Pract.* 2022; 8: 483-493.
5. Kaefer M, de Andrade SF, de Oliveira LE, Pasqualoto LB, Ciceri AC, Tioda IS, et al. Lipedema resistance after bariatric surgery. *Braz J Health Rev.* 2024; 7: e74998.
6. Cornely ME, Hasenberg T, Cornely OA, Ure C, Hettenhausen C, Schmidt J. Persistent lipedema pain in patients after bariatric surgery: A case series of 13 patients. *Surg Obes Relat Dis.* 2022; 18: 628-633.
7. Buso G, Depairon M, Tomson D, Raffoul W, Vettor R, Mazzolai L. Lipedema: A call to action! *Obesity.* 2019; 27: 1567-1576.
8. Clarke C, Kirby JN, Smidt T, Best T. Stages of lipoedema: Experiences of physical and mental health and health care. *Qual Life Res.* 2023; 32: 127-137.
9. Forner-Cordero I, Forner-Cordero A, Szolnoky G. Update in the management of lipedema. *Int Angiol.* 2021; 40: 345-357.
10. Ghods M, Georgiou I, Schmidt J, Kruppa P. Disease progression and comorbidities in lipedema patients: A 10-year retrospective analysis. *Dermatol Ther.* 2020; 33: e14534.

11. Ludwig DS. The ketogenic diet: Evidence for optimism but high-quality research needed. *J Nutr.* 2020; 150: 1354-1359.
12. Zhu H, Bi D, Zhang Y, Kong C, Du J, Wu X, et al. Ketogenic diet for human diseases: The underlying mechanisms and potential for clinical implementations. *Signal Transduct Target Ther.* 2022; 7: 11.
13. Verde L, Camajani E, Annunziata G, Sojat A, Marina LV, Colao A, et al. Ketogenic diet: A nutritional therapeutic tool for lipedema? *Curr Obes Rep.* 2023; 12: 529-543.
14. Calkins M, Buchanan L, Kalayjian T, Dikeman D, Cucuzzella M, Westman E. Carbohydrate reduction for metabolic disease is distinct from the ketogenic diet for epilepsy. *J Metab Health.* 2024; 7: 95.
15. Volek JS, Yancy Jr WS, Gower BA, Phinney SD, Slavin J, Koutnik AP, et al. Expert consensus on nutrition and lower-carbohydrate diets: An evidence-and equity-based approach to dietary guidance. *Front Nutr.* 2024; 11: 1376098.
16. Moriconi E, Camajani E, Fabbri A, Lenzi A, Caprio M. Very-low-calorie ketogenic diet as a safe and valuable tool for long-term glycemic management in patients with obesity and type 2 diabetes. *Nutrients.* 2021; 13: 758.
17. Herbst KL, Kahn LA, Iker E, Ehrlich C, Wright T, McHutchison L, et al. Standard of care for lipedema in the United States. *Phlebology.* 2021; 36: 779-796.
18. Faerber G, Cornely M, Daubert C, Erbacher G, Fink J, Hirsch T, et al. S2k guideline lipedema. *J Dtsch Dermatol Ges.* 2024; 22: 1303-1315.
19. Cannataro R, Michelini S, Ricolfi L, Caroleo MC, Gallelli L, De Sarro G, et al. Management of lipedema with ketogenic diet: 22-month follow-up. *Life.* 2021; 11: 1402.
20. Jeziorek M, Szuba A, Kujawa K, Regulska-Ilow B. The effect of a low-carbohydrate, high-fat diet versus moderate-carbohydrate and fat diet on body composition in patients with lipedema. *Diabetes Metab Syndr Obes.* 2022; 15: 2545-2561.
21. Sandnes FH. Effect of ketosis on pain and quality of life in women with lipedema. Tromsø, Norway: UiT The Arctic University of Norway; 2022.
22. Di Renzo L, Gualtieri P, Zomparelli S, De Santis GL, Seraceno S, Zuena C, et al. Modified mediterranean-ketogenic diet and carboxytherapy as personalized therapeutic strategies in lipedema: A pilot study. *Nutrients.* 2023; 15: 3654.
23. Pitotti G, Vincente S, Basciani S, Michelini S. Lipedema and nutrition: High fat ketogenic diet as treatment of choice. *J Gastroenterol Hepatol Rep.* 2024; 5: 1-9.
24. Amato AC, Amato JL, Benitti DA. The efficacy of ketogenic diets (low carbohydrate; high fat) as a potential nutritional intervention for lipedema: A systematic review and meta-analysis. *Nutrients.* 2024; 16: 3276.
25. Lundanes J, Sandnes F, Gjeilo KH, Hansson P, Salater S, Martins C, et al. Effect of a low-carbohydrate diet on pain and quality of life in female patients with lipedema: A randomized controlled trial. *Obesity.* 2024; 32: 1071-1082.
26. Apkhanova TV, Sergeev VN, Krukova MM, Vasilyeva VA, Kulchitskaya DB, Konchugova TV, et al. Influence of ketogenic diet and nutraceutical correction in the complex treatment of lower limbs lipedema. *Bull Rehabil Med.* 2021; 20: 26-36.
27. DiNicolantonio JJ, O'Keefe JH. Added sugars drive insulin resistance, hyperinsulinemia, hypertension, type 2 diabetes and coronary heart disease. *Mo Med.* 2022; 119: 519-523.

28. Field R, Field T, Pourkazemi F, Rooney K. Low-carbohydrate and ketogenic diets: A scoping review of neurological and inflammatory outcomes in human studies and their relevance to chronic pain. *Nutr Res Rev.* 2023; 36: 295-319.
29. Jeziorek M, Szuba A, Sowicz M, Adaszyńska A, Kujawa K, Chachaj A. The effect of a low-carbohydrate high-fat diet on laboratory parameters in women with lipedema in comparison to overweight/obese women. *Nutrients.* 2023; 15: 2619.
30. Wold LE, Hines JR EA, Allen EV. Lipedema of the legs: A syndrome characterized by fat legs and edema. *Ann Intern Med.* 1951; 34: 1243-1250.
31. Suga H, Araki J, Aoi N, Kato H, Higashino T, Yoshimura K. Adipose tissue remodeling in lipedema: Adipocyte death and concurrent regeneration. *J Cutan Pathol.* 2009; 36: 1293-1298.
32. Poojari A, Dev K, Rabiee A. Lipedema: Insights into morphology, pathophysiology, and challenges. *Biomedicines.* 2022; 10: 3081.
33. Kamamoto F, Baiocchi JM, Batista BN, Ribeiro RD, Modena DA, Gornati VC. Lipedema: Exploring pathophysiology and treatment strategies-state of the art. *J Vasc Bras.* 2024; 23: e20240025.
34. Aitzetmüller-Klietz ML, Busch L, Hamatschek M, Paul M, Schriek C, Wiebringhaus P, et al. Understanding the vicious circle of pain, physical activity, and mental health in lipedema patients-a response surface analysis. *J Clin Med.* 2023; 12: 5319.
35. Chakraborty A, Crescenzi R, Usman TA, Reyna AJ, Garza ME, Al-Ghadban S, et al. Indications of peripheral pain, dermal hypersensitivity, and neurogenic inflammation in patients with lipedema. *Int J Mol Sci.* 2022; 23: 10313.
36. Kruppa P, Gohlke S, Łapiński K, Garcia-Carrizo F, Soultoukis GA, Infanger M, et al. Lipedema stage affects adipocyte hypertrophy, subcutaneous adipose tissue inflammation and interstitial fibrosis. *Front Immunol.* 2023; 14: 1223264.
37. Rasmussen JC, Aldrich MB, Fife CE, Herbst KL, Sevic-Muraca EM. Lymphatic function and anatomy in early stages of lipedema. *Obesity.* 2022; 30: 1391-1400.
38. Keith L, Seo CA, Rowsemit C, Pfeffer M, Wahi M, Staggs M, et al. Ketogenic diet as a potential intervention for lipedema. *Med Hypotheses.* 2021; 146: 110435.
39. Bertsch T, Erbacher G, Corda D, Damstra RJ, Van Duinen K, Elwell R, et al. Lipoedema-myths and facts, Part 5. *Phlebologie.* 2020; 49: 31-50.
40. Nankam PA, Cornely M, Klötting N, Blüher M. Is subcutaneous adipose tissue expansion in people living with lipedema healthier and reflected by circulating parameters? *Front Endocrinol.* 2022; 13: 1000094.
41. Wang H, He W, Yang G, Zhu L, Liu X. The impact of weight cycling on health and obesity. *Metabolites.* 2024; 14: 344.
42. Friedman MI, Sørensen TI, Taubes G, Lund J, Ludwig DS. Trapped fat: Obesity pathogenesis as an intrinsic disorder in metabolic fuel partitioning. *Obes Rev.* 2024; 25: e13795.
43. Herbst KL, Hansen EA, Salinas LM, Wright TF, Larson EE, Schwartz JS. Survey outcomes of lipedema reduction surgery in the United States. *Plast Reconstr Surg Glob Open.* 2021; 9: e3553.
44. Patton L, Ricolfi L, Bortolon M, Gabriele G, Zolesio P, Cione E, et al. Observational study on a large Italian population with lipedema: Biochemical and hormonal profile, anatomical and clinical evaluation, self-reported history. *Int J Mol Sci.* 2024; 25: 1599.
45. Faerber G. Obesity and chronic inflammation in phlebological and lymphatic diseases. *Phlebologie.* 2018; 47: 55-65.

46. Chen J, Wildman RP, Hamm LL, Muntner P, Reynolds K, Whelton PK, et al. Association between inflammation and insulin resistance in US nondiabetic adults: Results from the third national health and nutrition examination survey. *Diabetes Care*. 2004; 27: 2960-2965.
47. Kazukauskienė N, Podlipskyte A, Varoneckas G, Mickuviene N. Health-related quality of life and insulin resistance over a 10-year follow-up. *Sci Rep*. 2021; 11: 24294.
48. Caporaso NE, Jones RR, Stolzenberg-Solomon RZ, Medgyesi DN, Kahle LL, Graubard BI. Insulin resistance in healthy US adults: Findings from the national health and nutrition examination survey (NHANES). *Cancer Epidemiol Biomarkers Prev*. 2020; 29: 157-168.
49. Zhang X, Li J, Zheng S, Luo Q, Zhou C, Wang C. Fasting insulin, insulin resistance, and risk of cardiovascular or all-cause mortality in non-diabetic adults: A meta-analysis. *Biosci Rep*. 2017; 37: BSR20170947.
50. O'Hearn M, Lauren BN, Wong JB, Kim DD, Mozaffarian D. Trends and disparities in cardiometabolic health among US adults, 1999-2018. *J Am Coll Cardiol*. 2022; 80: 138-151.
51. Partsalaki I, Karvela A, Spiliotis BE. Metabolic impact of a ketogenic diet compared to a hypocaloric diet in obese children and adolescents. *J Pediatr Endocrinol Metab*. 2012; 25: 697-704.
52. Volek JS, Clinthorne J, Yancy Jr WS. Applying a nutrition security lens to the dietary guidelines for Americans to address metabolic health. *Front Nutr*. 2023; 10: 1141859.
53. Wang Z, Chen T, Wu S, Dong X, Zhang M, Ma G. Impact of the ketogenic diet as a dietary approach on cardiovascular disease risk factors: A meta-analysis of randomized clinical trials. *Am J Clin Nutr*. 2024; 120: 294-309.
54. Luta X, Buso G, Porceddu E, Psychogiou R, Keller S, Mazzolai L. Clinical characteristics, comorbidities, and correlation with advanced lipedema stages: A retrospective study from a Swiss referral centre. *PLoS One*. 2025; 20: e0319099.
55. Chava Y, Hanne C. Lipedema fat and signs and symptoms of illness, increase with advancing stage. *Arch Med*. 2015; 7: 1-8.
56. Pfister C, Dawczynski H, Schingale FJ. Selenium deficiency in lymphedema and lipedema-A retrospective cross-sectional study from a specialized clinic. *Nutrients*. 2020; 12: 1211.
57. Al-Wardat M, Alwardat N, Lou De Santis G, Zomparelli S, Gualtieri P, Bigioni G, et al. The association between serum vitamin D and mood disorders in a cohort of lipedema patients. *Horm Mol Biol Clin Investig*. 2021; 42: 351-355.
58. Cannataro R, Cione E. Nutritional supplements and lipedema: Scientific and rational use. *Nutraceuticals*. 2022; 2: 270-277.
59. Czerwińska M, Ostrowska P, Hansdorfer-Korzon R. Lipoedema as a social problem. A scoping review. *Int J Environ Res Public Health*. 2021; 18: 10223.
60. Brenner E, Forner-Cordero I, Faerber G, Rapprich S, Cornely M. Body-mass-index vs. Taille-zu-Größe-Verhältnis bei Patientinnen mit Lipohyperplasia dolorosa (vulgo Lipödem). *J Dtsch Dermatol Ges*. 2023; 21: 1179-1187.
61. Wu H, Ballantyne CM. Metabolic inflammation and insulin resistance in obesity. *Circ Res*. 2020; 126: 1549-1564.
62. Yuan X, Wang J, Yang S, Gao M, Cao L, Li X, et al. Effect of the ketogenic diet on glycemic control, insulin resistance, and lipid metabolism in patients with T2DM: A systematic review and meta-analysis. *Nutr Diabetes*. 2020; 10: 38.

63. Choi YJ, Jeon SM, Shin S. Impact of a ketogenic diet on metabolic parameters in patients with obesity or overweight and with or without type 2 diabetes: A meta-analysis of randomized controlled trials. *Nutrients*. 2020; 12: 2005.
64. Aday AW, Donahue PM, Garza M, Crain VN, Patel NJ, Beasley JA, et al. National survey of patient symptoms and therapies among 707 women with a lipedema phenotype in the United States. *Vasc Med*. 2024; 29: 36-41.
65. Ortega MA, Fraile-Martínez O, García-Montero C, Álvarez-Mon MA, Chaowen C, Ruiz-Grande F, et al. Understanding chronic venous disease: A critical overview of its pathophysiology and medical management. *J Clin Med*. 2021; 10: 3239.
66. Khalid MU, Prasada S, Jennings C, Bartholomew JR, McCarthy M, Hornacek DA, et al. Venous thromboembolic outcomes in patients with lymphedema and lipedema: An analysis from the national inpatient sample. *Vasc Med*. 2024; 29: 42-47.
67. Wright T. Lipedema: A devastating disease too often overlooked [Internet]. Virginia Beach, VA: Vein Magazine; 2019. Available from: https://drthomaswright.com/wp-content/uploads/2019/04/vein_v12i1_lipedema_comp3.pdf.
68. Romeijn JR, de Rooij MJ, Janssen L, Martens H. Exploration of patient characteristics and quality of life in patients with lipoedema using a survey. *Dermatol Ther*. 2018; 8: 303-311.
69. González-Parejo P, Martín-Núñez J, Cabrera-Martos I, Valenza MC. Effects of dietary supplementation in patients with restless legs syndrome: A systematic review. *Nutrients*. 2024; 16: 2315.
70. Xu XM, Ruan JH, Tao T, Xiang SL, Meng RL, Chen X. Role of vitamins in the pathogenesis and treatment of restless leg syndrome: A systematic review and meta-analysis. *PLoS One*. 2025; 20: e0313571.
71. Trace SE, Thornton LM, Runfola CD, Lichtenstein P, Pedersen NL, Bulik CM. Sleep problems are associated with binge eating in women. *Int J Eat Disord*. 2012; 45: 695-703.
72. Zerón-Ruggerio MF, Doblas-Faxeda S, Díez-Hernández M, Izquierdo-Pulido M. Are emotional eating and other eating behaviors the missing link in the relationship between inadequate sleep and obesity? A systematic review. *Nutrients*. 2023; 15: 2286.
73. Ciano C, King TS, Wright RR, Perlis M, Sawyer AM. Longitudinal study of insomnia symptoms among women during perimenopause. *J Obstet Gynecol Neonatal Nurs*. 2017; 46: 804-813.
74. Tomada I. Lipedema: From women's hormonal changes to nutritional intervention. *Endocrines*. 2025; 6: 24.
75. Bini J, Parikh L, Lacadie C, Hwang JJ, Shah S, Rosenberg SB, et al. Stress-level glucocorticoids increase fasting hunger and decrease cerebral blood flow in regions regulating eating. *Neuroimage Clin*. 2022; 36: 103202.
76. Katzer K, Hill JL, McIver KB, Foster MT. Lipedema and the potential role of estrogen in excessive adipose tissue accumulation. *Int J Mol Sci*. 2021; 22: 11720.
77. Bauer AT, von Lukowicz D, Lossagk K, Aitzetmueller M, Moog P, Cerny M, et al. New insights on lipedema: The enigmatic disease of the peripheral fat. *Plast Reconstr Surg*. 2019; 144: 1475-1484.
78. Wright T, Babula M, Schwartz J, Wright C, Danesh N, Herbst K. Lipedema reduction surgery improves pain, mobility, physical function, and quality of life: Case series report. *Plast Reconstr Surg Glob Open*. 2023; 11: e5436.

79. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. *Nat Rev Endocrinol*. 2018; 14: 301-316.
80. Shulhai AM, Rotondo R, Petraroli M, Patianna V, Predieri B, Iughetti L, et al. The role of nutrition on thyroid function. *Nutrients*. 2024; 16: 2496.
81. Fowler N, Adler S, Najarian T, Rowsemit C, Safer D. Maladaptive hypothyroidism, or the famine response, after bariatric surgery: TSH not the gold standard for detection. *Surg Obes Relat Dis*. 2016; 12: s118-s119.
82. Fothergill E, Guo J, Howard L, Kerns JC, Knuth ND, Brychta R, et al. Persistent metabolic adaptation 6 years after “The Biggest Loser” competition. *Obesity*. 2016; 24: 1612-1619.
83. Kharrazian D, Herbert M, Lambert J. The relationships between intestinal permeability and target antibodies for a spectrum of autoimmune diseases. *Int J Mol Sci*. 2023; 24: 16352.
84. Iacovides S, Maloney SK, Bhana S, Angamia Z, Meiring RM. Could the ketogenic diet induce a shift in thyroid function and support a metabolic advantage in healthy participants? A pilot randomized-controlled-crossover trial. *PLoS One*. 2022; 17: e0269440.
85. Nath H, Samtiya M, Dhewa T. Beneficial attributes and adverse effects of major plant-based foods anti-nutrients on health: A review. *Hum Nutr Metab*. 2022; 28: 200147.
86. Yasmeen F, Pirzada RH, Ahmad B, Choi B, Choi S. Understanding autoimmunity: Mechanisms, predisposing factors, and cytokine therapies. *Int J Mol Sci*. 2024; 25: 7666.
87. Rajendiran A, Tenbrock K. Regulatory T cell function in autoimmune disease. *J Transl Autoimmun*. 2021; 4: 100130.
88. Stys PK, Tsutsui S, Gafson AR, 't Hart BA, Belachew S, Geurts JJ. New views on the complex interplay between degeneration and autoimmunity in multiple sclerosis. *Front Cell Neurosci*. 2024; 18: 1426231.
89. Kruglikov IL, Scherer PE. Is the endotoxin-complement cascade the major driver in lipedema? *Trends Endocrinol Metab*. 2024; 35: 769-780.
90. Mazzucca CB, Raineri D, Cappellano G, Chiocchetti A. How to tackle the relationship between autoimmune diseases and diet: Well begun is half-done. *Nutrients*. 2021; 13: 3956.
91. Mazur A, Frączek P, Tabarkiewicz J. Vitamin D as a nutri-epigenetic factor in autoimmunity-a review of current research and reports on vitamin D deficiency in autoimmune diseases. *Nutrients*. 2022; 14: 4286.
92. Wessels I, Rink L. Micronutrients in autoimmune diseases: Possible therapeutic benefits of zinc and vitamin D. *J Nutr Biochem*. 2020; 77: 108240.
93. Sahebari M, Rezaieyazdi Z, Khodashahi M. Selenium and autoimmune diseases: A review article. *Curr Rheumatol Rev*. 2019; 15: 123-134.
94. Lerner A, Shoenfeld Y, Matthias T. Adverse effects of gluten ingestion and advantages of gluten withdrawal in nonceliac autoimmune disease. *Nutr Rev*. 2017; 75: 1046-1058.
95. Huang XS, Dai N, Xu JX, Xiang JY, Zheng XZ, Ke TY, et al. MRI quantitative assessment of the effects of low-carbohydrate therapy on Hashimoto’s thyroiditis. *Endocr Connect*. 2024; 13: e230477.
96. Reddel S, Putignani L, Del Chierico F. The impact of low-FODMAPs, gluten-free, and ketogenic diets on gut microbiota modulation in pathological conditions. *Nutrients*. 2019; 11: 373.
97. Norwitz NG, Soto-Mota A. Case report: Carnivore-ketogenic diet for the treatment of inflammatory bowel disease: A case series of 10 patients. *Front Nutr*. 2024; 11: 1467475.

98. Gargano D, Appanna R, Santonicola A, De Bartolomeis F, Stellato C, Cianferoni A, et al. Food allergy and intolerance: A narrative review on nutritional concerns. *Nutrients*. 2021; 13: 1638.
99. Amato AC, Amato LL, Benitti D, Amato JL. Assessing the prevalence of HLA-DQ2 and HLA-DQ8 in lipedema patients and the potential benefits of a gluten-free diet. *Cureus*. 2023; 15: e41594.
100. Kelso JM. Unproven diagnostic tests for adverse reactions to foods. *J Allergy Clin Immunol Pract*. 2018; 6: 362-365.
101. Amato AC, Benitti DA. Lipedema can be treated non-surgically: A report of 5 cases. *Am J Case Rep*. 2021; 22: e934406-1-e934406-8.
102. Cui A, Xiao P, Ma Y, Fan Z, Zhou F, Zheng J, et al. Prevalence, trend, and predictor analyses of vitamin D deficiency in the US population, 2001-2018. *Front Nutr*. 2022; 9: 965376.
103. Pereira-Santos M, Costa PD, Assis AD, Santos CD, Santos DD. Obesity and vitamin D deficiency: A systematic review and meta-analysis. *Obes Rev*. 2015; 16: 341-349.
104. Liu X, Baylin A, Levy PD. Vitamin D deficiency and insufficiency among US adults: Prevalence, predictors and clinical implications. *Br J Nutr*. 2018; 119: 928-936.
105. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. *Am J Health Promot*. 1997; 12: 38-48.
106. Kirk J, MacDonald A, Lavender P, Dean J, Rubin G. Can treatment adherence be improved by using Rubin's four tendencies framework to understand a patient's response to expectations. *Biomed Hub*. 2017; 2: 1-12.
107. Pool E, Delplanque S, Coppin G, Sander D. Is comfort food really comforting? Mechanisms underlying stress-induced eating. *Food Res Int*. 2015; 76: 207-215.
108. Al-Wardat M, Clarke C, Alwardat N, Kassab M, Salimei C, Gualtieri P, et al. The difficulties in emotional regulation among a cohort of females with lipedema. *Int J Environ Res Public Health*. 2022; 19: 13679.
109. Van Strien T, Frijters JE, Bergers GP, Defares PB. The Dutch eating behavior questionnaire (DEBQ) for assessment of restrained, emotional, and external eating behavior. *Int J Eat Disord*. 1986; 5: 295-315.
110. Mason TB, Pacanowski CR, Lavender JM, Crosby RD, Wonderlich SA, Engel SG, et al. Evaluating the ecological validity of the Dutch eating behavior questionnaire among obese adults using ecological momentary assessment. *Assessment*. 2019; 26: 907-914.
111. Adams RN, Athinarayanan SJ, McKenzie AL, Hallberg SJ, McCarter JP, Phinney SD, et al. Depressive symptoms improve over 2 years of type 2 diabetes treatment via a digital continuous remote care intervention focused on carbohydrate restriction. *J Behav Med*. 2022; 45: 416-427.
112. Danan A, Westman EC, Saslow LR, Ede G. The ketogenic diet for refractory mental illness: A retrospective analysis of 31 inpatients. *Front Psychiatry*. 2022; 13: 951376.
113. Calabrese L, Frase R, Ghaloo M. Complete remission of depression and anxiety using a ketogenic diet: Case series. *Front Nutr*. 2024; 11: 1396685.
114. Kempa S, Gross M, Oliinyk D, Siegmund A, Müller M, Prantl L, et al. Health implications of lipedema: Analysis of patient questionnaires and population-based matched controls. *Life*. 2024; 14: 295.
115. Gold SM, Köhler-Forsberg O, Moss-Morris R, Mehnert A, Miranda JJ, Bullinger M, et al. Comorbid depression in medical diseases. *Nat Rev Dis Primers*. 2020; 6: 69.

116. Fetzer A, Fetzer S. Lipoedema UK Big Survey 2014 Research Report [Internet]. London, UK: Lipoedema UK; 2016. Available from: <https://lnni.org/sites/default/files/UK-Big-Surey-version-web%20-%20Sept%2016.pdf>.
117. Kraus RH. All about lipoedema [Internet]. German: Lymph & Gesundheit; 2015. Available from: <https://www.humanmed.com/wp-content/uploads/2019/03/Lymph und Gesundheit 01-2015.pdf>.
118. Galmiche M, Déchelotte P, Lambert G, Tavalacci MP. Prevalence of eating disorders over the 2000-2018 period: A systematic literature review. *Am J Clin Nutr*. 2019; 109: 1402-1413.
119. Wright TF, Herbst KL. A young woman with excessive fat in lower extremities develops disordered eating and is subsequently diagnosed with anorexia nervosa, lipedema, and hypermobile Ehlers-Danlos Syndrome. *Am J Case Rep*. 2021; 22: e930840-1-e930840-7.
120. Carmen M, Safer DL, Saslow LR, Kalayjian T, Mason AE, Westman EC, et al. Treating binge eating and food addiction symptoms with low-carbohydrate Ketogenic diets: A case series. *J Eat Disord*. 2020; 8: 2.
121. Norwitz NG, Hurn M, Forcen FE. Animal-based ketogenic diet puts severe anorexia nervosa into multi-year remission: A case series. *J Metab Health*. 2023; 6: a84.
122. Eisenberg Colman MH, Quick VM, Lipsky LM, Dempster KW, Liu A, Laffel LM, et al. Disordered eating behaviors are not increased by an intervention to improve diet quality but are associated with poorer glycemic control among youth with type 1 diabetes. *Diabetes Care*. 2018; 41: 869-875.
123. Schlundt DG, Rea MR, Kline SS, Pichert JW. Situational obstacles to dietary adherence for adults with diabetes. *J Am Diet Assoc*. 1994; 94: 874-879.
124. Heo S, Lennie TA, Moser DK, Okoli C. Heart failure patients' perceptions on nutrition and dietary adherence. *Eur J Cardiovasc Nurs*. 2009; 8: 323-328.
125. Elfhag K, Rössner S. Who succeeds in maintaining weight loss? A conceptual review of factors associated with weight loss maintenance and weight regain. *Obes Rev*. 2005; 6: 67-85.
126. Lemstra M, Bird Y, Nwankwo C, Rogers M, Moraros J. Weight loss intervention adherence and factors promoting adherence: A meta-analysis. *Patient Prefer Adherence*. 2016; 10: 1547-1559.
127. Rotberg B, Junqueira Y, Gosdin L, Mejia R, Umpierrez GE. The importance of social support on glycemic control in low-income Latinos with type 2 diabetes. *Am J Health Educ*. 2016; 47: 279-286.
128. Dudek JE, Białaszek W, Ostaszewski P. Quality of life in women with lipoedema: A contextual behavioral approach. *Qual Life Res*. 2016; 25: 401-408.
129. Christoffersen V, Tennfjord MK. Younger women with lipedema, their experiences with healthcare providers, and the importance of social support and belonging: A qualitative study. *Int J Environ Res Public Health*. 2023; 20: 1925.
130. Falck J, Rolander B, Nygårdh A, Jonasson LL, Mårtensson J. Women with lipoedema: A national survey on their health, health-related quality of life, and sense of coherence. *BMC Womens Health*. 2022; 22: 457.
131. Berkman L, Epstein AM. Beyond health care-socioeconomic status and health. *N Engl J Med*. 2008; 358: 2509-2510.
132. Braveman P, Egerter S, Williams DR. The social determinants of health: Coming of age. *Annu Rev Public Health*. 2011; 32: 381-398.

133. Fetzer A. Women in dire need: The far-reaching impact of lipoedema on women's lives. *Br J Community Nurs.* 2020; 25: S6-S9.
134. Gibbs J, Cappuccio FP. Common nutritional shortcomings in vegetarians and vegans. *Dietetics.* 2024; 3: 114-128.
135. Athinarayanan SJ, Roberts CG, Adams RN, Volk BM, Phinney SD, Volek J, et al. 410-P: Two-year (2y) eGFR slope in people with type 2 diabetes (T2D) receiving a very low carbohydrate diet (VLCD) intervention. *Diabetes.* 2023; 72: 410-P.
136. Rojas-Morales P, Pedraza-Chaverri J, Tapia E. Ketone bodies for kidney injury and disease. *Adv Redox Res.* 2021; 2: 100009.
137. Yamahara K, Yasuda-Yamahara M, Kuwagata S, Chin-Kanasaki M, Kume S. Ketone body metabolism in diabetic kidney disease. *Kidney360.* 2024; 5: 320-326.
138. Yurista SR, Nguyen CT, Rosenzweig A, de Boer RA, Westenbrink BD. Ketone bodies for the failing heart: Fuels that can fix the engine? *Trends Endocrinol Metab.* 2021; 32: 814-826.
139. Nielsen R, Møller N, Gormsen LC, Tolbod LP, Hansson NH, Sorensen J, et al. Cardiovascular effects of treatment with the ketone body 3-hydroxybutyrate in chronic heart failure patients. *Circulation.* 2019; 139: 2129-2141.
140. Needham N, Campbell IH, Grossi H, Kamenska I, Rigby BP, Simpson SA, et al. Pilot study of a ketogenic diet in bipolar disorder. *BJPsych Open.* 2023; 9: e176.
141. Hall KD, Ayuketah A, Brychta R, Cai H, Cassimatis T, Chen KY, et al. Ultra-processed diets cause excess calorie intake and weight gain: An inpatient randomized controlled trial of ad libitum food intake. *Cell Metab.* 2019; 30: 67-77.e3.
142. Steele EM, O'Connor LE, Juul F, Khandpur N, Baraldi LG, Monteiro CA, et al. Identifying and estimating ultraprocessed food intake in the US NHANES according to the Nova classification system of food processing. *J Nutr.* 2023; 153: 225-241.
143. Johnston CS, Tjonn SL, Swan PD, White A, Hutchins H, Sears B. Ketogenic low-carbohydrate diets have no metabolic advantage over nonketogenic low-carbohydrate diets. *Am J Clin Nutr.* 2006; 83: 1055-1061.
144. Norwitz NG, Soto-Mota A, Kaplan B, Ludwig DS, Budoff M, Kontush A, et al. The lipid energy model: Reimagining lipoprotein function in the context of carbohydrate-restricted diets. *Metabolites.* 2022; 12: 460.
145. Soto-Mota A, Flores-Jurado Y, Norwitz NG, Feldman D, Pereira MA, Danaei G, et al. Increased low-density lipoprotein cholesterol on a low-carbohydrate diet in adults with normal but not high body weight: A meta-analysis. *Am J Clin Nutr.* 2024; 119: 740-747.
146. Norwitz NG, Feldman D, Soto-Mota A, Kalayjian T, Ludwig DS. Elevated LDL cholesterol with a carbohydrate-restricted diet: Evidence for a "lean mass hyper-responder" phenotype. *Curr Dev Nutr.* 2022; 6: nzab144.
147. Mardinoglu A, Wu H, Bjornson E, Zhang C, Hakkarainen A, Räsänen SM, et al. An integrated understanding of the rapid metabolic benefits of a carbohydrate-restricted diet on hepatic steatosis in humans. *Cell Metab.* 2018; 27: 559-571.e5.
148. Vilar-Gomez E, Athinarayanan SJ, Adams RN, Hallberg SJ, Bhanpuri NH, McKenzie AL, et al. Post hoc analyses of surrogate markers of non-alcoholic fatty liver disease (NAFLD) and liver fibrosis in patients with type 2 diabetes in a digitally supported continuous care intervention: An open-label, non-randomised controlled study. *BMJ Open.* 2019; 9: e023597.

149. Dowla S, Pendergrass M, Bolding M, Gower B, Fontaine K, Ashraf A, et al. Effectiveness of a carbohydrate restricted diet to treat non-alcoholic fatty liver disease in adolescents with obesity: Trial design and methodology. *Contemp Clin Trials*. 2018; 68: 95-101.
150. Antonio J, Ellerbroek A, Silver T, Vargas L, Tamayo A, Buehn R, et al. A high protein diet has no harmful effects: A one-year crossover study in resistance-trained males. *J Nutr Metab*. 2016; 2016: 9104792.
151. Cheng Y, Zheng G, Song Z, Zhang G, Rao X, Zeng T. Association between dietary protein intake and risk of chronic kidney disease: A systematic review and meta-analysis. *Front Nutr*. 2024; 11: 1408424.
152. Unwin D, Unwin J, Crocombe D, Delon C, Guess N, Wong C. Renal function in patients following a low carbohydrate diet for type 2 diabetes: A review of the literature and analysis of routine clinical data from a primary care service over 7 years. *Curr Opin Endocrinol Diabetes Obes*. 2021; 28: 469-479.
153. Höhn S, Dozières-Puyravel B, Auvin S. History of dietary treatment from Wilder's hypothesis to the first open studies in the 1920s. *Epilepsy Behav*. 2019; 101: 106588.
154. Newmaster K, Zhu Z, Bolt E, Chang RJ, Day C, Mhanna A, et al. A review of the multi-systemic complications of a ketogenic diet in children and infants with epilepsy. *Children*. 2022; 9: 1372.
155. Faerber G. Nutritional therapy for lipedema and obesity - results of a guideline-based treatment concept. *Vasomed*. 2017; 29: 122-123.