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FEMALE SEXUAL DYSFUNCTION AND DISORDERS (T LORENZ AND R NAPPI, SECTION EDITORS)

From Table to Bedroom: Nutritional Status, Dietary Interventions, and Women's Sexual Function

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Abstract

Purpose of Review In this review, we summarize recent empirical evidence assessing the relationship between nutrition and female sexual dysfunction and give a broad interpretation of the effects.

Recent Findings Dietary patterns that ensure adequate intake of shortfall nutrients may help to ameliorate reproductive problems associated with eating disorders, while supplementation in women with low vitamin D status improves sexual functioning. Combination treatments addressing body image concerns and maladaptive eating habits appear to be more effective for some eating disorder subtypes that result in malnutrition. For overweight and obese women, weight loss resulting from dietary changes and/or bariatric surgery tends to improve sexual interest, arousal, and activity. The metabolic perturbations that characterize diabetes mellitus and polycystic ovarian syndrome warrant nutritional interventions, and these lifestyle modifications often improve sexual functioning. Evidence for the use of specific dietary supplements to improve sexual responsivity in women has generally not been supported.

Summary Nutritional status can elicit, exacerbate, or ameliorate sexual problems. Treatment of female sexual dysfunction may be enhanced by a multidisciplinary approach incorporating cutting-edge developments in nutrition science.

Keywords Female sexual dysfunction · Obesity · Diabetes mellitus · Anorexia nervosa · Polycystic ovarian syndrome · Nutrition · Dietary interventions · Dietary supplements

Introduction

It is now well established that sexual functioning can be influenced—either positively or negatively—by health behaviors such as dietary patterns and weight management, and nutrition science is uniquely poised to elucidate such lifestyle factors that impinge upon sexual health. Over the past 85 years, nutrition science has become vastly more interdisciplinary. Founded primarily as a research field to prevent nutrient deficiency-related complications among those with food scarcity [1, 2], nutrition science has now emerged as an invaluable contributor toward understanding the mechanistic underpinnings of chronic diseases on the biochemical, cellular, and organ physiology levels of analysis [3]. The scope of nutritional research has similarly expanded: Not only do researchers and medical practitioners consider how dietary interventions may ameliorate disease, but they also investigate ways that healthful diets may prevent disease development, halt its progression, and improve quality of life (e.g., [4]).

It is within this framework that research examining the relationship between dietary factors, overall diet quality (i.e., macronutrient and micronutrient sufficiency), and sexual function has been conducted. Yet, despite significant advances in nutrition science research, insights into the association between nutrition status and sexual health have been limited. Several factors may account for this knowledge gap. First, given the high prevalence of life-threatening diseases such as cancer, cardiovascular disease (CVD), and diabetes mellitus among westernized countries, research funding to investigate sexual health has been comparatively scarce [5]. Second, many studies have focused on the fecundity/fertility

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aspects of nutrition and reproductive physiology—pregnancy and lactation [6]—rather than ways that marginal deficiencies (or over-nutrition) might impact aspects of the sexual response cycle or modulate sexual interest. Finally, human sexual health research relies upon constructs to represent complex cognitive-affective states such as sexual desire that are either not readily amenable to mechanistic studies or may only be moderately correlated with circulating nutrient metabolites and neuroendocrine substrates [7–9].

Despite these economic and methodologic challenges, a number of well-conducted experiments have begun to elucidate the complex relationships between dietary factors and sexual functioning. This review evaluates and summarizes recent empirical studies relating nutritional status and dietary interventions to sexual function in women, emphasizing those nutrients and dietary patterns that may prevent or ameliorate disease complications commonly associated with female sexual dysfunction (FSD). As nutritional interventions related to conception and pregnancy/gestation have been described extensively elsewhere (e.g., [10]), this review will not comprehensively address those issues.

In order to provide a broad framework for this review, we begin by noting several qualifications. The role of diet and nutrition on sexual health is often evaluated in terms of its effects on cellular and physiological processes. At such levels, diet could affect (improve or decrease) general health, and because aspects of sexual health (e.g., sexual interest) are dependent on overall well-being, sexual health may be affected as well. In other instances, diet may impact general health in ways that impinge upon the same physiological systems involved in sexual response. As examples, reduced/constricted blood flow resulting from diabetes mellitus could also lead to diminished blood flow to genitalia; or diet-related altered endocrine function may affect hormone-dependent genital tissue and response. Finally, albeit rare, diet/nutrition could affect sexual response directly by acting primarily or specifically on sexual tissue, as might be the case for dietary factors that affect PDE-5 activity which, via nitric oxide induction, is responsible for blood flow and erectile response in male and female genital tissue. Thus, diet/nutrition is capable of affecting sexual health through multiple pathways.

Beyond the cellular and physiological effects of diet/nutrition, psychosocial factors may also be affected. Dietary regimes that, for example, lead to malnutrition or being overweight have the potential to affect a person's self-image, often negatively. That is, low energy along with various bodily changes could lead to negative self-evaluation, anxiety, and depression [11]. Furthermore, women whose body type deviates substantially from cultural ideals may be viewed as being less attractive and having lower efficacy, which in turn can negatively affect health, employment opportunities, relationship formation, and medical care [12, 13]. Given that sexual desire and arousal in women are sensitive to psychosocial factors [14–16], restrictive models that assume diet → physiology → sexual function are likely too narrow to capture the potential multivariate effects of diet/nutrition on sexual health [13].

Finally, diet and nutrition are umbrella terms that are themselves multidimensional, and the ways that diet affects bodily processes, general health, and sexual health can depend on such biopsychosocial factors as eating patterns, taste sensitivity, eating disorders, caloric intake, specific nutrient intake, genetic predispositions, and metabolic patterns, to name a few. Although a comprehensive understanding of the relationship between diet/nutrition and sexual function would, ideally, attempt to account for the broad array of variables inherent in the diet/nutrition → sexual health formulation, few studies have been able to address this relationship through such a comprehensive lens.

Given the above constraints, this review is organized along four specific lines of research that have generated reasonably robust conclusions regarding the interface between diet/nutrition and sexual response. Specifically, we evaluate (i) disordered eating patterns, including anorexia nervosa and bulimia, noting how adequate nutritional status may help to improve or restore sexual function; (ii) diet-induced obesity and its deleterious effects on sexuality, describing both nutritional and surgical procedures to improve sexual responsivity; and (iii) metabolic disorders such as diabetes mellitus and polycystic ovarian syndrome, where dietary interventions are not only required to improve health outcomes but may also increase sexual quality of life. Finally (iv), we briefly discuss the possible role of nutraceuticals and dietary supplements on sexual health and well-being—taking a bird's eye view rather than discussing specific herbs and compounds.

Method

We searched the MEDLINE/PubMed, PsycINFO, and PsycARTICLES databases for articles investigating the relationship between nutrition and women's sexual functioning, restricting our searches to articles published in English and from 2000 to present. Particular attention was given to papers published within the past 5 years. Keywords used in our database searches are provided in Table 1. Boolean connectors "AND" and "OR" were also incorporated to refine the search parameters.

Results

Eating Disorders and Malnutrition

A growing body of evidence supports an association between eating disorders and sexual dysfunction in women [17], with

Table 1 Keywords/terms used in bibliographic database searches

Subject terms	Sexual function terms	Disease terms	Nutrition terms
Woman/women	(Sexual) desire	Hyperglycemia	Vitamin deficiency
Female(s)	(Sexual) arousal	Diabetes mellitus	Nutrient deficiency
Rodent(s)	(Sexual) interest	(Type 1) diabetes	Vitamin D
Murine	Sexual function	(Type 2) diabetes	1,25-Dihydroxyvitamin D_3
	Sexual dysfunction	Obese/obesity	(Dietary) fiber
	Orgasm	Overweight	Glycemic/glycemia
	(Vaginal) lubrication	Underweight	Bariatric surgery
	(Sexual) pleasure	Malnutrition	High-fat (diet)
	FSFI	Eating disorder(s)	Diet/dietary
	Depression	Anorexia (nervosa)	Nutrition
	Anxiety	Bulimia (nervosa)	Weight loss
		Polycystic ovarian syndrome	Mediterranean diet
		PCOS	(Nutrition) education

the specific type of eating disorder diagnosis impacting sexual function differentially [17–20]. For example, Pinheiro et al. observed that patients with anorexia nervosa (AN) and bulimia nervosa (BN) experienced significantly lower sexual function—severe loss of libido and higher sexual anxiety—when compared with healthy controls per the Structured Interview for Anorexic and Bulimic Disorders Psychopathology Scale (SIAB-P22)[19]. Furthermore, when comparing AN patients that exhibited either restrictive (RAN) or purging behavior (PAN) against BN patients and eating disorder patients not otherwise specified (EDNOS), greater loss of libido was reported in the RAN and PAN groups. When compared with a normative sample of women from a previous study, eating disorder groups showed lower libido, although groups were not compared statistically. A related study found associations between body shape concern (as assessed by the Eating Disorder Examination Questionnaire) and lower sexual function (assessed by the Female Sexual Function Index (FSFI)) in RAN patients, while emotional eating and subjective binge eating were more strongly related to sexual dysfunction in BN and PAN patients [17]. Specifically, the AN groups (both RAN and PAN) reported a lower total FSFI score when compared with BN, and both AN and BN groups reported significantly lower total FSFI scores compared with healthy controls. All FSFI subdomains were lower in AN patients compared with controls, and all but the pain and desire subscales were lower in BN patients compared with controls. When separating RAN subjects from their PAN counterparts, the RAN group reported significantly lower total FSFI scores. Interestingly, the FSFI sexual desire subdomain did not significantly differ between AN and BN, or RAN versus PAN/BN patients, indicating that desire was low in all eating disorder groups. Furthermore, among RAN patients, a higher concern for body shape was strongly correlated with a lower total FSFI score. Based on their findings, the investigators hypothesized that these patients experienced changes in sexual function—perhaps most strongly in sexual desire—that paralleled changes in their emotional regulation and resultant eating behavior, with over-controlled emotions and eating behaviors common in RAN and dysregulated emotions and eating behaviors characteristic of BN/PAN [17].

Not all studies have shown a difference in sexual function between eating disorder subtypes, although, to their detriment, many have not evaluated the well-known interrelationships among sexual function, body dissatisfaction, and depression. More recently, Gonidakis et al. investigated the role of these clinical variables and found that none of the measures of sexual functioning (desire, arousal, lubrication, orgasm, satisfaction, and pain) was significantly different among eating disorder subtypes and, further, that depression was strongly related to the impaired sexual function in both AN and BN patients when compared with healthy controls [18]. While AN patients reported significantly lower FSFI scores (both total and subdomain) compared with healthy controls, mean differences between BN and control women did not reach statistical significance. Limitations of this study such as the small sample size should be noted. Across all studies, RAN patients experienced greater levels of emaciation and lower total FSFI scores compared with other eating disorder subtypes (PAN, BN, EDNOS) and healthy women. Since healthy women and those with *non*-restrictive eating disorders experience similar levels or prevalence of sexual dysfunction, at least in some studies, factors such as low body weight and malnutrition, observed predominantly in RAN patients, may have a stronger role inducing or exacerbating sexual dysfunction.

The above studies demonstrate that starvation lowers sexual function and inhibits sexual behavior, a finding that has been replicated in animal studies. Animal models have shown that increased activation of orexigenic neuropeptide receptors

plays a role in appetitive and reproductive behavior during starvation. Klingerman et al. [21] showed that food restriction in female Syrian hamsters diverted motivation away from sexual behaviors toward food-seeking behaviors—further supported by Schneider et al. [22], who observed a dose-response relationship between food restriction and re-feeding with the activation of orexigenic neuropeptides and reproductive behaviors. Thus, although the mechanism underlying the relationship between starvation and lower sexual function in humans remains unclear, animal research implicates potential behavioral-neuroendocrine connections as demonstrated above.

Given that malnutrition from disordered eating patterns can interfere with sexual function in women, it is not surprising that weight restoration is associated with increased sexual behavior during the treatment of AN patients [23, 24]. However, changes in all aspects of sexual function are multifactorial, and therefore the challenge is to differentiate the effect of weight restoration on sexual function from other psychosocial factors. For example, body dissatisfaction is a common variable correlated with sexual dysfunction in both women with eating disorders and healthy women [25, 26]. Treatment of female patients with eating disorders focusing on both weight restoration *and* improving body image may well impart greater improvement on sexual function.

Vitamin D Deficiency and Insufficiency

At times, a specific nutrient deficiency can result from inadequate intake rather than general malnutrition. Such is the case with low vitamin D status. Vitamin D is involved in many biological processes vital to growth and development, immune function, and to reducing the risk of chronic diseases [27, 28]. As such, its role in activating genes can occur through multiple pathways, as a conditionally essential nutrient and a bioactive hormone. Moderate evidence shows that low vitamin D status is related to sexual dysfunction in premenopausal women. Krysiak et al. found a strong association in women with deficient levels (< 20 ng/mL) or insufficient levels (20–30 ng/mL) of circulating 25-hydroxyvitamin D (25(OH)D) and impaired sexual functioning compared with healthy women (30–75 ng/mL) [29]. Both groups with low vitamin D status had lower scores across various FSFI parameters as well as more severe depressive symptoms on the Beck Depression Inventory-II (BDI-II). Vitamin D-insufficient women (20–30 ng/mL) showed significant reductions in sexual desire whereas vitamin D-deficient (< 20 ng/mL) women showed reduced overall FSFI scores and in sexual desire, orgasm, and satisfaction subdomains. BDI-II scores were inversely related to sexual function in all groups and may have been a mediating factor for the sexual dysfunction.

This same research group conducted an intervention study to determine whether vitamin D supplementation affects sexual functioning and depressive symptoms in premenopausal women (N = 47; mean age = 30.33) with low vitamin D status [30]. After initial assessment, women with vitamin D insufficiency and deficiency were assigned to either a treatment group providing oral vitamin D supplementation or to a control group. Vitamin D-deficient women were given 4000 IU/day (N = 16), whereas women with vitamin D insufficiency were randomized to receive either 2000 IU/day (N = 17) or no treatment (N = 14). Women with deficiency saw improvements in the overall FSFI score, sexual desire, orgasm, and sexual satisfaction, and women with insufficiency saw improvement in sexual desire when compared with a control group. Concomitant improvements in mood occurred in the vitamin D-deficient treatment group on BDI-II parameters. Further, mean total FSFI scores across all groups had a moderate inverse relationship with the total BDI-II score and total depressive symptoms, with the vitamin D-deficient group having a slightly stronger relationship. Collectively, these findings suggest that the severity of vitamin D deficiency is closely related to the severity of sexual dysfunction in women; however, the study did not separate out the role that improvements in depressive symptoms may have had on sexual function.

The mechanism by which vitamin D status alters sexual function in women remains unclear, although proposed mechanisms include effects on the synthesis of steroid hormones [31–33] and on vascular function [34, 35]. In a cross-sectional study of 73 non-obese, premenopausal women, circulating 25(OH)D and total testosterone levels were positively correlated [31]. As testosterone purportedly affects sexual interest/drive in both men and women, these findings suggest that vitamin D may affect sexual function in non-obese women through increased androgenic activity. Canat et al., in a more comprehensive analysis assessing the relationship between female sexual dysfunction (per FSFI) and vitamin D status (circulating 25(OH)D), included measures of a variety of hormones such as gonadotropins, estradiol, dehydroepiandrotestosterone-SO_4 (DHEA-SO_4), thyroid hormones, sex hormone-binding globulin (SHBG), and both free and total testosterone [32]. Results were mixed: Women with lower overall FSFI scores had significantly lower levels of circulating OH(25)D and lower BDI-II scores ($p < 0.0001$), as demonstrated in previous studies. However, while some hormones tended to be lower in women with lower vitamin D status (thyroid-stimulating hormone, total testosterone, estradiol, luteinizing hormone, DHEA-SO_4, SHBG), none was significantly so, nor was out of normal physiologic ranges. These findings support the relationship between low vitamin D status and female sexual dysfunction but do not confirm a role for endocrine mediation.

While the inverse relationship between vitamin D status and depression score is a consistent finding among the aforementioned studies, the extent to which depression affects

sexual function in the context of low vitamin D status was unclear until recently. Vitamin D supplementation in women with low vitamin D status and sexual dysfunction increased their overall FSFI score, but restoration of normal vitamin D levels accounted for approximately 20% of the overall treatment effect [36]. As seen in other studies, all subscales of the FSFI score had significant inverse relationships with BDI-II scores except for the orgasm and pain subdomains, which were not statistically significant.

Finally, it should be noted that the above studies support a relationship between vitamin D status and sexual function in premenopausal women, but no research has addressed this relationship in perimenopausal or postmenopausal women. Additionally, no studies have examined the longitudinal effects of vitamin D supplementation on improving sexual function in women with low vitamin D status to determine whether the effects persist.

Food Intake and Obesity

Just as low body weight is associated with sexual dysfunction, obesity has also been linked to poor sexual function in women [37, 38]. Obesity-related problems transcend excess food consumption. For obese persons, altered biochemical activity in adipose and other tissue types increases the risk of metabolic syndrome—including dyslipidemia, hypertension, insulin resistance, and a pro-inflammatory milieu—which can adversely impact sexual function. Moreover, obesity frequently presents with comorbid anxiety, depression, and low self-esteem, all of which impinge upon sexual function. Finally, obesity may negatively affect a woman's relationship with her partner, encompassing both partner attraction and sexual engagement issues. To fully understand the obesity-sexual function relationship, such mediating pathophysiologic, psychological, and social/relational variables need to be better integrated into a coherent model [13, 39].

Several studies have supported connections between obesity and sexual dysfunction, with increased sexual problems reported in those with higher body mass index (BMI) values. One sample of over 200 sexually active obese women revealed that 42.9% experienced issues with pain, 48.3% with desire, 35.9% with arousal, and 45% with lubrication [40]. While FSD was common (66% of participants), mediating factors such as body image dissatisfaction or hormonal abnormalities were not investigated. In a similar study, 553 women completed a questionnaire regarding body weight and sexual behavior; obese women were 30% less likely than women of normal BMI to have engaged in sexual intercourse during the previous 12 months [41]. Moreover, BMI was inversely correlated with sexual desire, interest, and activity, with obese participants often feeling limited/restricted in their daily activities. A study of Iranian women generated similar findings, as overweight women reported difficulties with lubrication, arousal, orgasm, and sexual satisfaction [42].

A comprehensive study on the topic by Steffen et al. assessed four domains of sexual function (desire, frequency, satisfaction, and physical health-related limitations on sexual activity) and factors that may be associated in women prior to bariatric surgery [43]. Prior to surgery, nearly half the women were dissatisfied with their sexual life, with 1/3 currently not sexually active. Factors such as older age, antidepressant use, being Caucasian, urinary incontinence, and being unmarried were associated with poorer sexual function in multiple domains, and greater depressive symptoms were associated with poorer sexual function in all domains. Interestingly, BMI was not independently associated with levels of sexual desire or activity. Around 40% of women reported that their lack of sexual activity was due to physical health limitations, including feelings of fatigue/low energy and difficulties with arousal and achieving orgasm.

Not all studies support a simple relationship between obesity and FSD. Esposito and colleagues found an inverse correlation between body weight and sexual functioning (for arousal, lubrication, and orgasm parameters), but only in women who had reported prior sexual problems [44]. That is, no correlation between BMI and sexual functioning emerged for women without previous sexual problems, and thus obesity status may become relevant primarily when sexual dysfunction has already occurred. As noted by the investigators, increased expression of pro-inflammatory mediators such as C-reactive protein was implicated in the relationship between increasing BMI and sexual dysfunction.

Weight Loss Through Diet and Surgical Intervention

Given that obesity has been associated with diminished sexual function, a logical extension is that weight loss in obese women might restore sexual function and, indeed, studies evaluating dietary intervention have shown modest improvement in such women. For example, a very low-calorie ketogenic diet (VLCK) in obese patients with FSD resulted in an improved total FSFI score at maximum ketosis and after the 4-month intervention [45]. Additionally, female participants reported a significant increase in orgasm only at maximal ketosis, followed by increases in sexual arousal and lubrication that persisted through the end of the intervention. These end-of-trial changes paralleled reductions in weight and higher scores for self-esteem. However, findings were limited by the short 4-month follow-up period. The underlying mechanism through which ketosis positively influenced sexual function remains unclear. Experimental studies have shown that the ketone body, beta-hydroxybutyrate, may have protective effects in vascular endothelial cells [46] and alleviate depressive symptoms [47]. Currently, hyperglycemia is proposed to play a role in reduced vaginal lubrication and increased genitourinary

infections in women with diabetes. Improvements in fasting serum glucose levels have been noted in studies evaluating ketogenic diets [48], and the reduction of hyperglycemia may improve vascular and microvascular diabetic complications [49]. However, no studies have evaluated whether diet-induced improvements in sexual function persist. Thus, these effects should be interpreted with caution, as the risk of atherosclerosis may pose an unintended consequence of a ketogenic diet. Future studies should assess long-term effects of ketogenic diets.

In a second example, a randomized clinical trial evaluated the effect of a Mediterranean diet vs a low-fat diet on sexual function in newly diagnosed diabetics who were overweight or obese over 8 years [50]. Women who adhered to a Mediterranean diet experienced greater weight loss, lower systolic blood pressure, lower glycated hemoglobin (HbA1c) scores, and the restoration of more sexual function. While the Mediterranean diet group showed better total FSFI scores, both groups saw sexual improvements from baseline. Though the effects of dietary adherence were modest, they persisted longitudinally. Wekker et al. [51] found similar effects from a 6-month lifestyle intervention focused on physical activity, dietary habits, and behavior modification for weight loss in obese women; while women who received the lifestyle intervention did not differ in weight from the control group, they had non-significant increases in sexual intercourse, interest, orgasm, vaginal lubrication, and overall better sexual function compared with controls on the McCoy Female Sexuality Questionnaire. Although weight loss in the first 6 months did not persist at the 5-year follow-up, the increase in sexual function remained.

Improvement in sexual function has also been noted following bariatric surgery. In one example, a subset of women was evaluated for changes in sexual function, reproductive hormones, and psychosocial status 2 years after bariatric surgery [52]. These women not only experienced significant improvements in the total FSFI score and in arousal, lubrication, desire, and satisfaction subscales, but also reported improvements in quality of life, depressive symptoms, and body image. Significant reductions in total testosterone, estradiol ($p < 0.001$), and DHEA-S ($p < 0.05$), and increases in FSH, LH, and SHBG ($p < 0.001$) were also noted at postoperative year 2. These findings align with previous observations in bariatric patients [53].

Taken together, these studies indicate that interventions to ameliorate obesity—whether through diet or bariatric surgery—improve sexual function in women initially and persist following weight loss. Many physiological and psychological factors likely contribute to these effects, including improved depressive symptoms, body image, and changes in ovarian steroids.

Diet and Metabolism: Diabetes Mellitus

Diabetes mellitus (DM) represents one of the most prevalent chronic diseases in the USA and other westernized countries. According to the American Diabetes Association, nearly 10% of the US population (30.3 million individuals) had DM[1] in 2015 [54]. Moreover, approximately 1.5 million new cases of DM were diagnosed in US adults during 2015, establishing DM as an ongoing public health issue [55]. Lifestyle factors associated with an increased likelihood of developing DM—particularly type 2 DM—include poor weight management, dyslipidemia, persistent hyperglycemia, and physical inactivity [55–57]. Two features of the type 2 diabetic prodrome are insulin resistance, the inability of the systemic tissues to respond properly to physiologic concentrations of insulin [58], and ectopic lipid deposition in skeletal muscle and hepatic tissue, suggesting compromised utilization of fats for energy or substrate mishandling [59]. For this reason, high-fat diets (45–65% of kilocalories from fat) are often employed in rodent models to induce obesity and diabetic-like metabolic dysfunction [60]. Furthermore, human clinical studies suggest that diets lacking in fiber-rich fruits and vegetables and abundant in sugar-sweetened beverages, simple sugars such as fructose, saturated fats, and highly processed foods may increase the likelihood of developing type 2 DM [61–63]. Poorly managed DM, in turn, increases an individual's susceptibility to pathologies such as neuropathy and CVD [64, 65]. Recent research has supported a connection between DM and reduced sexual functioning [66], with both human and rodent studies indicating that lifestyle changes—particularly diet modification—can confer pro-sexual benefits.

Several observational studies have demonstrated a clear link between DM and diminished sexual responsivity. Cortelazzi and colleagues compared FSFI scores between diabetic and non-diabetic premenopausal women [67], with diabetics scoring lower on the total score and on arousal, lubrication, and orgasm subdomains compared with age-matched controls. Moreover, FSD prevalence was significantly higher among diabetic women compared with non-diabetic counterparts (75% vs. 52%, respectively). The investigators also divided participants by the presence or absence of metabolic syndrome, a constellation of risk factors for CVD. Among women with metabolic syndrome, both total FSFI scores and lubrication and orgasm subdomains were significantly lower than their healthy counterparts [67]. Mazzilli et al. similarly evaluated sexual function in premenopausal diabetic women [68], finding that compared with non-diabetic women, women

[1] This value includes both type 1 and type 2 diabetes mellitus, but the American Diabetes Association and Centers for Disease Control and Prevention indicate that the majority of these cases (~ 90% or higher) constitute type 2 diabetes. Importantly, lifestyle modifications—including diet—can be integral to treatment and/or management of both types, as discussed in this review.

with either type 1 or type 2 DM scored significantly lower on the FSFI desire subdomain. Interestingly, type 1 DM also resulted in lower arousal, lubrication, orgasm, and dyspareunia subdomain scores compared with healthy women, but there was no significant difference between women with type 2 DM and controls for those parameters. Total FSFI scores were significantly lower in type 1 diabetic women, whereas overall FSFI scores did not differ between type 2 diabetic women and controls [68]. Thus, the physiological effects of DM may differ depending upon the nature and progression of the disease, as women with type 1 DM reported significantly earlier onset and longer duration of diabetes compared with women with type 2 DM.

In addition to physiologic consequences of DM on sexual functioning, demographic and psychosocial variables may contribute to the risk of diabetes-induced sexual dysfunction. For example, a case-controlled study of sexual function found that Iranian women with type 2 DM had significantly less formal education compared with healthy controls, and a significantly smaller percentage of diabetic women were employed in the workforce [69]. Furthermore, depression and anxiety, variables often associated with sexual problems in the general population [14, 70], have also been implicated in diabetes-induced sexual dysfunction. For example, scores on both the Zung Self-Rating Depression Scale and the Mental Component Summary of the Short-Form 12 Health Survey were significantly correlated with FSFI scores among type 1 diabetic women, and both measures served as predictors of FSFI scores in regression analysis [71]. Similar findings were reported by the large-scale epidemiologic Boston Area Community Health study, as depressive symptoms were associated with worse FSFI scores [72]. Unfortunately, the observational nature of these studies precludes establishing causal relationships: It is unclear whether depression emerges primarily as a *consequence* of diabetic complications—including sexual dysfunction—or, alternatively, preexisting depression arising from a woman's diabetic status (and other factors) decreases her desire to engage sexually and thereby induces dysfunction [66]. Finally, dissatisfaction regarding compromised sexual functioning appears to be prevalent among women with DM. A sexual health screening questionnaire administered to type 2 DM patients at 45 general practices in the Netherlands from 2015 to 2016 revealed that over one-fourth of diabetic women reported sexual dissatisfaction [73]. Importantly, among the sexually dissatisfied women, 47% expressed interest in discussing the matter with their general practitioner [73]. Taken together, the available data suggest that a multidisciplinary clinical approach may be advantageous for treatment of DM, addressing not only nutritional and metabolic complications of the disease (e.g., glycemic management and insulin resistance), but also relevant psychological factors that contribute to quality of life, including sexual satisfaction and function, and mental health issues such as depression [14, 66].

Although dietary approaches to manage and/or prevent DM can vary significantly with regard to cost, duration, or intensity, they are often considered a first-line treatment for DM and its complications [57, 74]. Even minor interventions, such as providing education sessions on evaluating nutrition facts panels [75], may enable women with DM or prediabetes to better identify nutrients of concern. Medical nutrition therapies emphasize diets that concomitantly promote health and elicit adherence by patients—e.g., diets that monitor intake of carbohydrates to prevent large postprandial glycemic fluctuations while still enabling individuals to consume foods that are palatable/appetizing [74, 76]. In a randomized controlled trial comparing training sessions on carbohydrate counting or the plate method with standard-of-care education (controls), within-group reductions in HbA1c were observed for both interventions, and self-efficacy measures increased by the 6-month follow-up evaluation [77]. While few diets have been proposed to *specifically* address diabetes-induced sexual dysfunction, adherence to a Mediterranean dietary pattern (e.g., higher intake of non-starchy vegetables, legumes, nuts, whole grain foods, and fish while minimizing processed meats and saturated fats) appears to improve sexual responsivity among diabetic women [49, 78]. The Mediterranean diet's beneficial effects on sexual function are likely related to its ability to confer weight loss and/or ameliorate diabetic complications such as chronic inflammation and vascular endothelial dysfunction, conditions associated with sexual problems [13, 79].

Recent experiments using diabetic rodent models have illustrated putative mechanisms for improvements in sexual functioning following dietary modification. Comparing 12- and 16-week-old diabetic and non-diabetic Sprague-Dawley rats, Pei and colleagues observed significantly lower vaginal fluid production in diabetic rats relative to their age-matched, non-diabetic counterparts [80]. This reduced lubrication was not associated with significant differences in estradiol concentrations among the groups, but the diabetic rats exhibited decreased expression of aquaporins (AQPs)—protein channels responsible for water transport across cell membranes—in the vaginal epithelium [80]. In a similar study, streptozotocin-induced diabetic rats exhibited significantly elevated blood glucose levels (> 450 mg/dL), reduced vaginal blood flow, and decreased expression of vaginal AQP-2 relative to healthy controls [81]. However, for diabetic rats treated with insulin (3 U/day), these parameters did not differ significantly from non-diabetic controls at 2- and 4-week evaluations. Importantly, several AQPs have also been identified in the human vagina, suggesting that a similar mechanism could induce or augment vaginal lubrication in women [82]. While one experiment found no differences in AQP-2 mRNA expression between postmenopausal, type 2 diabetic women and healthy, age-matched controls [83], further work is needed to determine whether effects may occur in premenopausal women or are impacted by the duration and type of DM. Since insufficient

lubrication is commonly reported among diabetic women (e.g., [73]), restoration of aquaporin expression in the vaginal tissues through dietary and pharmacologic management of diabetes could represent a novel treatment approach for FSD.

Polycystic Ovarian Syndrome and Dietary Intervention

Polycystic ovarian syndrome (PCOS) is an endocrine condition that occurs among 6–10% of women following reproductive maturity [84]. Although some variation exists with regard to clinical presentation, common indicators include disrupted menstrual cycles (oligo-ovulation), elevated androgen production, insulin resistance/hyperinsulinemia, and formation of cysts on the periphery of the ovary ("string-of-pearls" appearance) [85, 86]. Insulin action in the ovaries may further exacerbate androgen levels, as multiple reports have directly implicated insulin in steroidogenic mechanisms [87]. Increased circulating androgens, in turn, can exert male-typical hair growth (hirsutism), acne, and intra-abdominal and visceral fat storage, which could decrease self-esteem or body satisfaction [88]. Due to the increased endocrine and pro-inflammatory activity of visceral adipose tissue relative to subcutaneous fat depots [13, 89], women with PCOS also have greater susceptibility to develop type 2 DM or CVD. In addition to its deleterious effects on fertility and metabolism, PCOS may negatively impact sexual functioning and is amenable to dietary intervention.

An ongoing challenge for PCOS researchers is to determine whether decreased sexual functioning is attributable primarily to the endocrine abnormalities (e.g., disrupted T:E_2 ratios), excess adiposity, or diabetic-like phenotype observed among PCOS patients, and whether PCOS imparts greater burden on sexual responsivity than the combination of its constituent symptoms. For example, a recent systematic review and meta-analysis did not find a significant association between PCOS and a diagnosis of FSD, but a subgroup analysis of FSFI domains revealed significantly lower arousal and lubrication scores among women with PCOS compared with healthy controls [90]. In a similar vein, Noroozzadeh and colleagues did not find significantly lower total or subdomain FSFI scores in PCOS patients relative to controls, but sexual dysfunction in both groups was relatively high (44.4% vs. 36.1% in controls, respectively) [91]. With regard to circulating hormones, elevated androgens were not associated with lower FSFI domains among women with PCOS, but prolactin was inversely correlated with the orgasm subdomain [91]. Interestingly, some reports have suggested that higher circulating androgens may actually be *protective* against PCOS-induced sexual dysfunction rather than contributing to its emergence [92, 93].

Due to these somewhat equivocal hormone findings, clinicians have shifted their research focus to the impact of PCOS on body weight and adiposity. In a case-control study comparing obese women with or without PCOS, an increased waist-to-hip ratio (WHR) was associated with a lower score on the Female Sexual Quotient (SQ-F) instrument, irrespective of PCOS status [94]. A separate regression analysis revealed that both WHR and depression were associated with SQ-F scores at or below the threshold for sexual dysfunction risk (≤ 60) [94]. Comparing women with PCOS to healthy controls, Benetti-Pinto and colleagues found women with PCOS to have significantly higher BMI values, younger age, and greater number of sexual intercourse events per month [95]. Importantly, however, women with PCOS also reported lower general quality-of-life scores per the World Health Organization Quality of Life (WHOQOL-BREF) instrument. Moreover, women with PCOS had significantly lower total FSFI scores and sexual satisfaction subscores compared with controls. BMI values were also inversely correlated with all WHOQOL-BREF subcategories except environment, as well as the orgasm subdomain of the FSFI [95]. Similar findings were reported by Kogure et al., as both waist circumference and BMI were positively correlated with depression; moreover, a significantly greater percentage of women with sexual dysfunction were classified as depressed compared with those without sexual problems (46.2% vs. 23.5%) [96]. Taken together, these studies stress the necessity to examine relationships between body image dissatisfaction, affective disorders, and sexual dysfunction, as these factors may interact within the PCOS phenotype and influence sexual health far more than endocrine substrates alone [14].

Current dietary guidelines for women with PCOS emphasize weight reduction and glycemic management, similar to recommendations for type 2 DM [97]. Dietary regimens prescribing 500–600 kcal/day deficits have been shown to reduce BMI and circulating testosterone while improving insulin sensitivity [98, 99]. Unfortunately, the cardiometabolic benefits arising from such diets have not yet been empirically related to changes in sexual function (e.g., pre-post evaluation of FSFI parameters) in these studies. Ongoing work is needed to better clarify the relationship between PCOS, its mediating comorbidities, and sexual dysfunction.

Dietary Supplements

Dietary supplements have become a thriving business throughout the USA and much of the rest of the world. Nutraceuticals—one form of dietary supplements—are products derived from food sources that presumably have additional physiological benefits beyond the nutritional value of the food. From a regulatory perspective in the USA, all nutraceuticals and dietary supplements fall under the same classification, being largely unregulated and therefore exempt of having to verify the claims from their presumed beneficial effects. Consequently, purported effects of dietary

supplements are often not well substantiated from an empirical perspective [5].

Herbal (plant-derived) supplements have had a long history of use, particularly in cultures that subscribe heavily to traditional medical practices; early support for their use typically emanated from the local lore. Such supplements—and there are hundreds, perhaps even thousands, available worldwide—have been used to prevent disease, to cure various disorders, and to improve general physical and psychological health. A number of these supplements are also purported to impart pro-sexual effects. For example, a limited body of evidence supports a pro-sexual role for plant derivatives such as Tongkat Ali, ginseng, and horny goat weed—some presumably exerting effects on endocrine (particularly androgen) function, others affecting genital blood flow capacity through vascular smooth muscle response and/or nitric oxide activity (the neurotransmitter involved in stimulation of erectile tissue). Still other supplements such as maca and St. John's Wort are purported to have indirect effects on sexual functioning by ameliorating comorbid conditions, including menopausal symptoms and depression, which often interfere with sexual responsivity. However, for nearly all the herbal supplements that have undergone any depth of analysis, positive effects are reported primarily in men. Studies in women either have yielded inconsistent or null results, or simply have not been conducted or reported. Such effects may be related to possible biases reflecting the cultural context in which the studies were carried out, where women's sexuality is strongly curtailed by social scripts [100]. Alternatively, they may reflect a true lack of results in women where psychosocial factors tend to play a more prominent role in sexual responsivity. Thus, at this juncture, evidence supporting any particular herbal supplement, or combination of supplements, as strong mediators or promoters of sexual responsivity in women is either unconvincing or not available.

One class of dietary supplements—phytoestrogens—have received particular attention with regard to women's sexual and reproductive health. Phytoestrogens are plants containing naturally occurring estrogen such as beans, soybeans, peas, lentils, and whole grains and seeds, especially flaxseed, rye, and millet. From a theoretical perspective, phytoestrogens may provide relief from menopausal symptoms and reduce osteoporosis, heart disease, and breast cancer risk by slowing cell growth and preventing inflammation [101]. Phytoestrogens act by modulating estrogen receptors, but because their action is rather weak, effects tend to be inconsistent across individuals due to the many other mitigating factors (e.g., source, amount, absorption, metabolism, overall health status, and age). While eating foods rich in phytoestrogen has helped menopausal women in reducing hot flashes and vaginal dryness, data are insufficient to recommend any particular source, amount, or frequency of phytoestrogen intake. To date, as far as we could ascertain, no studies have demonstrated positive effects of phytoestrogens on sexual responsivity in women. Rodent studies suggest that, depending on a variety of parameters, phytoestrogens have the potential to mildly increase or actually interfere with sexual responsivity [102, 103]. Although in moderation phytoestrogens appear to be safe, heavy intake may have adverse effects such as abnormal uterine bleeding [104].

Discussion and Conclusions

Regulatory mechanisms involved in food intake, diet selection, and metabolism clearly have the potential to affect sexual function in women. These effects are mainly indirect—operating through multiple pathways and often influencing general health by compromising underlying cellular and physiological systems that also impinge on or mediate sexual responsivity (Table 2). Despite the variety of ways through which diet and nutrition can affect women's sexual function, we outline four broad unifying interpretations with respect to such relationships.

First, malnutrition and low nutrient status are factors likely to disrupt sexual function. Malnutrition represents a dire condition regarding the organism's survival, so sexual response—important to genetic survivability rather than individual survivability—assumes a lower priority. Classic experimental studies on animals well over half a century ago successfully generated need/motivation hierarchies, with sexual motivation (in humans, libido, or sexual desire) generally requiring a minimum level of basic health for activation [105]. Thus, findings indicating that malnutrition and low vitamin D status diminish overall sexual response as well as its subcomponents (e.g., desire, arousal, and orgasm) are to be expected, as sexual desire/motivation is blunted. Because arousal and orgasmic capacity pivot heavily on sexual interest/desire, they too would show decrements. Indeed, bodily distress induced by starvation results in significant amounts of cortisol release [106], and cortisol is associated with attenuated sexual response in both men and women [107, 108].

Second, as manifest in the relationship between cortisol and sexual function, effects of diet on sexual response are likely mediated in part by endocrine and neural processes, although details of the underlying mechanisms are often complex and poorly delineated. In women, for example, it is uncertain whether obesity has significant effects on gonadal steroids such as estrogen, and although estrogen levels appear to increase along with weight, effects on sexual response are inconsistent and further complicated by menopausal status. In addition, in contrast with obesity and sexual function in

Table 2 Overview of health conditions described in this review

Disease/ condition	Effects on general health	Effects on sexual function	Nutritional interventions
Eating disorders (anorexia, bulimia)	Undernutrition may lead to vitamin and mineral deficiencies, poor bone health, and muscle wasting; anemia; comorbid anxiety or depression	Lower total FSFI scores among all eating disorders relative to healthy controls; comparing eating disorder subtypes, anorexia yields more severe sexual dysfunction than bulimia or EDNOS	Ensure adequate caloric, macronutrient, and micronutrient intakes; therapies should address contributing psychosocial factors
Vitamin D deficiency	Impaired growth and development; deficiency associated with depressive symptoms; risk of bone resorption/deterioration due to dysregulated parathyroid hormone	Deficiency associated with lower total FSFI and desire, lubrication, arousal, orgasm, and satisfaction subdomains	Vitamin D-rich foods include fatty fish (e.g., salmon, mackerel), portabella mushrooms, and fortified milks and juices; dietary supplements may be utilized
Obesity	Increased risk of cardiovascular disease and type 2 diabetes mellitus; poor blood circulation; pro-inflammatory conditions; lower self-esteem and body satisfaction	Reduced blood flow to genitals may impair physiologic arousal; greater sexual dissatisfaction; decreased sexual engagement; insufficient lubrication	Dietary patterns should reduce hyperglycemia, blood pressure parameters, and body weight; in cases of morbid obesity, bariatric surgery may be recommended
Diabetes mellitus	Elevated risk of cardiovascular disease; inability to control blood glucose (hypoglycemia or hyperglycemia); may contribute to depression or anxiety	Present with lower total FSFI scores and lower arousal, lubrication, and orgasm subdomains; decreased expression of aquaporin proteins in vaginal tissue; decreased satisfaction by self-report	Choose whole grain, high-fiber, and unprocessed foods to reduce glycemic fluctuations; diets should address overweight/obesity when present
Polycystic ovarian syndrome	Formation of painful cysts; acne and male-typical hair (hirsutism); insulin resistance; high gonadal androgens; elevated risk of overweight/obesity	Irregular menstrual cycles and oligo-ovulation; may have normal sexual desire or high frequency of intercourse, but lower orgasm and satisfaction on FSFI	Low glycemic index to manage insulin resistance and blood glucose; lower calories to reduce adiposity and body weight

men where a possible relationship has been drawn between weight and nitric oxide availability, a similar relationship has not been demonstrated convincingly in women [13]. Nevertheless, obesity in both men and women—and PCOS in women—is often tied to metabolic syndrome and associated with a number of comorbidities, including dyslipidemia, chronic inflammation, diabetes, insulin resistance, and CVD. As fluctuations in inflammatory biomarkers, particularly C-reactive protein, appear to modulate sexual responsivity throughout the menstrual cycle even among healthy women [109], these factors warrant ongoing investigation. Such comorbidities—rather than DM or PCOS directly—may be the culpable entity for decreased sexual function in women, as discussed in the "Diet and Metabolism: Diabetes Mellitus" section.

Third, sexual desire and arousal in women are strongly driven by contextual factors (partner, emotional intimacy, situation, etc.), perhaps more so than to biological factors, which often assume a secondary role [110]. Indeed, because diet may affect body shape, psychological factors related to body image, sexual anxiety, self-esteem and efficacy, and attractiveness (all of which can affect relationship function) likely play an important role in the connection between diet/nutrition and sexual function—that is, women's sexuality and responsivity are typically affected by such psycho-relational variables [111]. Additionally, disease states (e.g., obesity, malnutrition, metabolic syndrome) are sometimes associated with depression and anxiety, which are also known to independently impact sexual response in women [14, 70]. Although a number of recent research studies have adopted a multivariate approach to understanding the diet-sexual function link, such methodologies need to become routine.

Finally, no dietary panacea has been identified to improve or retain healthy sexual functioning in women. Aspects of a balanced Mediterranean-type diet, known to promote general health, also appear to indirectly promote sexual health. But no single dietary supplement, or combination of supplements, consistently provides positive effects on sexual desire, arousal, orgasm, or satisfaction in women.

In conclusion, sexual functioning in women can be affected by diet/nutritional status, and accordingly, changing to a healthier diet and nutritional status may positively affect sexual function. Such effects are typically mediated through third variables, being generally tied to the overall health and well-being of the individual.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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