HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a behavioral health professional or Florida nurse, please return the included Answer Sheet/ Evaluation.) Your postmark or facsimile date will be used as your completion date.
- Receive your Certificate(s) of Completion by mail, fax, or email.

Faculty

Diane Thompson, RN, MSN, CDE, CLNC, has an extensive history in nursing and nursing education. She possesses a strong background in diabetes and cardiac care, starting her professional career at the cardiac care area of the Cleveland Clinic in Cleveland, Ohio. Ms. Thompson took the knowledge and experience she learned from the Cleveland Clinic and transferred it into the home health arena in rural Ohio, after which she moved to Florida and obtained further knowledge while working as a PRN nurse in all areas, including medical/surgical, intensive care, emergency, critical care, and cardiology. With a desire to have a specific area to concentrate her profession, Ms. Thompson accepted a position as a pneumonia case manager, which led into a diabetes case manager career. (A complete biography appears at the end of this course.)

Faculty Disclosure

Contributing faculty, Diane Thompson, RN, MSN, CDE, CLNC, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planners

Jane C. Norman, RN, MSN, CNE, PhD Alice Yick Flanagan, PhD, MSW

Director of Development and Academic Affairs Sarah Campbell

Division Planners/Director Disclosure

The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for nurses, social workers, counselors, and therapists in all practice settings with a desire to better understand the issue of sexual dysfunction in patients with diabetes.

Accreditations & Approvals



In support of improving patient care, NetCE is jointly accredited by the Accreditation Council for Continu-JOINTLY ACCREDITED PROVIDER® ing Medical Education (ACCME),

INTERPROFESSIONAL CONTINUING EDUCAT

the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

As a Jointly Accredited Organization, NetCE is approved to offer social work continuing education by the Association of Social Work Boards (ASWB) Approved Continuing Education (ACE) program. Organizations, not individual courses, are approved under this program. Regulatory boards are the final authority on courses accepted for continuing education credit.

NetCE has been approved by NBCC as an Approved Continuing Education Provider, ACEP No. 6361. Programs that do not qualify for NBCC credit are clearly identified. NetCE is solely responsible for all aspects of the programs.

Copyright © 2021 NetCE

A complete Works Cited list begins on page 22.

NetCE • Sacramento, California

Mention of commercial products does not indicate endorsement.

Designations of Credit

NetCE designates this continuing education activity for 5 ANCC contact hours.

NetCE designates this continuing education activity for 6 hours for Alabama nurses.

NetCE designates this continuing education activity for 3 pharmacotherapeutic/pharmacology contact hours.

AACN Synergy CERP Category A.

Social workers completing this intermediate-to-advanced course receive 5 Clinical continuing education credits.

NetCE designates this continuing education activity for 1.5 NBCC clock hours.

Individual State Nursing Approvals

In addition to states that accept ANCC, NetCE is approved as a provider of continuing education in nursing by: Alabama, Provider #ABNP0353 (valid through 07/29/2025); Arkansas, Provider #50-2405; California, BRN Provider #CEP9784; California, LVN Provider #V10662; California, PT Provider #V10842; District of Columbia, Provider #50-2405; Florida, Provider #50-2405; Georgia, Provider #50-2405; Kentucky, Provider #7-0054 (valid through 12/31/2025); South Carolina, Provider #50-2405; West Virginia, RN and APRN Provider #50-2405.

Individual State Behavioral Health Approvals

In addition to states that accept ASWB, NetCE is approved as a provider of continuing education by the following state boards: Alabama State Board of Social Work Examiners, Provider #0515; Florida Board of Clinical Social Work, Marriage and Family Therapy and Mental Health, Provider #50-2405; Illinois Division of Professional Regulation for Social Workers, License #159.001094; Illinois Division of Professional Regulation for Licensed Professional and Clinical Counselors, License #197.000185; Illinois Division of Professional Regulation for Marriage and Family Therapists, License #168.000190.

About the Sponsor

The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare. Our contributing faculty members have taken care to ensure that the information and recommendations are accurate and compatible with the standards generally accepted at the time of publication. The publisher disclaims any liability, loss or damage incurred as a consequence, directly or indirectly, of the use and application of any of the contents. Participants are cautioned about the potential risk of using limited knowledge when integrating new techniques into practice.

Disclosure Statement

It is the policy of NetCE not to accept commercial support. Furthermore, commercial interests are prohibited from distributing or providing access to this activity to learners.

Course Objective

The purpose of this course is to provide healthcare providers with the information necessary to identify and address sexual problems in patients with diabetes.

Learning Objectives

Upon completion of this course, you should be able to:

- 1. Identify the prevalence of diabetes in the United States and risk factors for its development.
- 2. Describe the basics of sexual physiology in both men and women.
- 3. Identify possible causes of sexual dysfunction in patients with diabetes.
- 4. Evaluate the impact of various lifestyle interventions on sexual functioning in patients with diabetes.
- 5. Compare and contrast available pharmacologic treatments for sexual dysfunction.
- 6. Discuss other possible treatments for sexual dysfunction.
- 7. Outline the psychosocial impact of sexual dysfunction on patients with diabetes.



Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also

included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

As the number of diabetes cases in the United States continues to rise, the associated complications of the disease have become major public health issues. The complication of sexual dysfunction is often not discussed or addressed, although it is a relatively common occurrence among patients with type 1 or type 2 diabetes.

Human sexuality is a dynamic and multifaceted construct consisting of interplay between interpersonal, biologic, psychologic, and cultural factors. Sexuality impacts many aspects of life, and an individuals' sexual self-schema is an evolving concept [1]. For patients experiencing sexual dysfunction, the issue can have major repercussions, from conflict in their relationships to loss of their perceived identify and self-esteem. Feelings of loss, sadness, and tension are common.

Primary education often covers the topic of diabetes without addressing the impact of sexual dysfunction on adults with the disease and their partners. However, healthcare professionals are in a unique position to provide education, support, empathy, and encouragement to these patients, allowing them to lead the best possible life, with minimal stressors as a result of the disease process. A thorough understanding of the relationship between diabetes and sexual dysfunction will allow healthcare professionals to improve the quality of life of patients living with diabetes. Screening of sexual dysfunction should become a part of the routine care of patients with diabetes.

OVERVIEW OF DIABETES

DIABETES EPIDEMIOLOGY

Diabetes, known clinically as diabetes mellitus, is a progressive disease process affecting the fuel metabolism functioning within the body [2]. According to the American Diabetes Association (ADA), the prevalence of diabetes has increased eightfold since 1958, with the sharpest increase occurring in the 2000s [3]. As of 2018, 10.5% of the U.S. population, or 34.2 million Americans, had diabetes [4].

#94973 Sexual Dysfunction in Patients with Diabetes

Unfortunately, 7.3 million of these individuals were unaware of their diabetes diagnosis [4]. Diabetes has been considered epidemic since the 1970s, and the percentage of Americans expected to have diabetes or prediabetes is estimated to reach 15.5% and 30%, respectively, by the year 2030 [5].

The scope of the problem is vast and diverse, particularly among geographic regions. In 2011, the Centers for Disease Control and Prevention identified a "diabetes belt" in the United States, consisting of 644 counties in 15 states, where 11.7% of the adult population has diagnosed diabetes, compared with an 8.5% average in other counties (Figure 1) [6]. Although this represents a particularly dense geographic concentration of disease, there are many other counties and groups of counties outside of this belt with prevalences as high or higher. Many of the counties outside of the "diabetes belt" with especially prevalent diabetes have high Native American populations; one such example are several counties in northeastern Arizona, northwestern New Mexico, and southern Utah [3].

Genetics, race, age, and lifestyle significantly influence the onset and progression of the disease process [7]. Although all races and ethnicities can develop diabetes, the prevalence is greatest among non-Hispanic blacks, Mexicans, and Native Americans/ Alaska Natives [4; 8; 9; 10]. The incidence of diagnosed diabetes is estimated to be 11.7% among non-Hispanic blacks 18 years of age and older, compared with the overall U.S. rate of 8.2%. The prevalence of diabetes among persons of Hispanic descent who are 18 years of age or older is 12.5% [4]. Among the subdivisions of Hispanic groups, diabetes prevalence rates are 8.3% for Central/South Americans, 6.5% for Cubans, 12.4% for Puerto Ricans, and 14.4% for Mexicans. In addition to being at high-risk for diabetes, Mexican Americans are 40% more likely to die from the disease than their non-Hispanic white counterparts [4]. However, Native Americans/ Alaska Natives present the greatest risk for the development of type 2 diabetes; their risk is nearly three times greater than that of white Americans [10]. It is estimated that approximately 14.7% of Native Americans/Alaska Natives 18 years of age and older have type 2 diabetes [4]. The highest prevalence of



diabetes in the United States is observed in certain Native American groups of the Southwest, where an estimated 22.2% of the population has the disease [4]. The highest rate of diabetes for any population (worldwide) has been reported to occur in the Pima Indians of Arizona [11].

The most rapid increase in diabetes prevalence in the last decade has been among adolescents. Historically, children and adolescents with hyperglycemia have been diagnosed with type 1 diabetes, a result of the body being unable to produce adequate amounts of insulin. However, it is now estimated that as many as 46% of juvenile-onset cases of diabetes are type 2 [12]. Furthermore, it has been predicted that children born in this millennium will have a one in three chance of developing diabetes in their lifetime; among high-risk ethnic groups, the estimate is as high as one in two [13].

DIAGNOSIS

As discussed, the most common types of diabetes are type 1 and type 2. However, gestational diabetes is also relatively common and is a source of significant morbidity and mortality. Gestational diabetes is first recognized in pregnancy, usually around the 24th week of gestation, and typically resolves after the birth of the child [3]. Other less common types of diabetes include [14; 15]:

 Maturity-onset diabetes of the young (MODY): A genetic, autosomal-dominant defect of the pancreatic beta cells, resulting in insulin deficiency and decreased insulin release without the presence of insulin resistance and obesity. This form of diabetes typically develops in patients younger than 25 years of age. It is a different clinical entity than type 2 diabetes of the adolescent, which presents with insulin resistance.

DIAGNOSTIC CRITERIA FOR TYPE 2 DIABETES			
Stage	Fasting Plasma Glucose Level	Two-Hour Postprandial Plasma Glucose Level	Glycosylated Hemoglobin (HbA _{1c}) Level
Euglycemia	<100 mg/dL	<140 mg/dL	-
Prediabetes	≥100 mg/dL but <126 mg/dL	≥140 mg/dL but <200 mg/dL	-
Diabetes	≥126 mg/dL	≥200 mg/dL	≥6.5%
Source: [3; 14; 15]			Table 1

- Diabetes related to diseases of the exocrine pancreas, such as cystic fibrosis, and various endocrine diseases, such as Cushing syndrome, acromegaly, and chromocytoma
- Drug-induced diabetes resulting from the use of certain medications, particularly high-dose corticosteroids

All adults older than 45 years of age should be screened for type 2 diabetes every three years or every three years if they have any risk factors [3]. In addition, individuals of any age who are at risk for or are suspect of having diabetes should be screened. Established risk factors for type 2 diabetes include [16]:

- Age older than 45 years
- Body mass index (BMI) greater than or equal to 25 kg/m^2
- Family history of type 2 diabetes
- Habitual physical inactivity
- Race/ethnicity (e.g., African American, Hispanic American, Native American, Alaska Native, or Pacific Islander)
- Impaired glucose tolerance (IGT) or elevated fasting glucose
- Previous history of gestational diabetes or giving birth to a child weighing more than 9 pounds

- Hypertension (i.e., blood pressure greater than 140/90 mm Hg in adults)
- Abnormal lipid levels (i.e., high-density lipoprotein [HDL] level <35 mg/dL and/ or triglyceride level >250 mg/dL)
- Polycystic ovarian syndrome
- History of vascular disease
- Acanthosis nigricans (most common among individuals of African descent)

The diagnostic criteria for type 2 diabetes are fairly straightforward and are based on fasting plasma glucose, postprandial plasma glucose levels, or glycosylated hemoglobin (HbA_{1c}) testing (Table 1). After a diagnosis of type 2 diabetes has been definitively made, education on self-care management is necessary in order to obtain euglycemia and prevent complications related to the detrimental effects of hyperglycemia [3]. It is estimated that as many as 90% of patients with type 2 diabetes will require oral medications to achieve adequate glucose control within five years of diagnosis [3]. When glucose levels cannot be adequately controlled with oral medications, the use of injectable medications is necessary. If elevated blood glucose levels are untreated and continue to rise, the result can be hyperosmolar hyperglycemic nonketotic syndrome (HHNS) and ultimately death [17].

AN OVERVIEW OF SEXUAL PHYSIOLOGY

Human sexuality is increasingly recognized as an important aspect of an individual's health and quality of life throughout the lifespan. Sexual activity has been associated with health benefits and longevity [18]. However, older adults engaging in sexual activity has long been a taboo, allowing for the perpetuation of myths regarding sexuality later in life. In fact, a regular sex life can continue throughout life. Data derived from the National Social Life, Health, and Aging Project indicate that more than half of individuals 75 to 85 years of age are sexually active, and physical health is significantly correlated with sexual activity and many aspects of sexual function, regardless of age [18].

In order to understand sexual dysfunction in patients with diabetes, it is important to have a solid comprehension of the normal functioning of the male and female reproductive systems. In theory, men and women experience similar physiologic changes (i.e., vasodilation) in response to sexual arousal. However, men are believed to follow a general linear pattern during sexual activity: excitement, arousal, plateau, orgasm, and resolution. Women, on the other hand, are thought to follow a nonlinear model of sexual response including emotional intimacy, sexual stimuli, and emotional and physical satisfaction [19].

Sexual maturation and function in women involve the secretion of hormones, primarily estrogen and androgens [20]. Estrogen is an umbrella term that encompasses three similar hormones: estradiol, estrone, and estriol. The presence of estrogen induces the cervical mucosa to produce abundant fluid secretions, which in addition to providing lubrication, enhances the survival and mobility of sperm [21]. The presence of estrogen also protects the vaginal tissues by facilitating nitric oxide synthesis, the enzyme involved in the control of vaginal and clitoral arterial blood flow. When estrogen levels decrease, women experience difficulties with vaginal lubrication, low sexual desire, painful intercourse, and/or difficulties with orgasm [19]. Androgens, which are primarily considered a male sex hormone, are also a part of normal female sexuality. In women, androgens activate sebaceous glands, which play a role in activation of sexual desire and libido functions [21].

Male sexual functioning is centered on the erectile reflex. Erectile tissue consists of vascular chambers, supplied with blood via arterioles, within the corpora cavernosa and corpus spongiosum [20]. Typically, the arterioles are constricted, resulting in minimal blood flow through the erectile tissues. However, in the presence of sexual stimulation, the arterioles dilate and fill with blood, expanding the erectile tissue and resulting in erection. The process of formation and maintenance of an erection is under the control of the autonomic nervous system, but it can be stimulated or inhibited by central nervous system input, such as stress, medications, and visual stimuli [21]. Impotence is defined as the inability to consistently maintain sufficient rigidity for sexual intercourse and may be the result of arterial, venous, neurogenic, or psychogenic causes [22].

EVDENCE-BASED
PRACTICEThe National Health Care for the
Homeless Council concludes that
clinicians should assess all male patients
with diabetes for erectile dysfunction.
(https://nhchc.org/wp-content/uploa
ds/2019/08/2013DiabetesGuidelines_FINAL_20130612.pdf. Last accessed March 23, 2021.)Level of Evidence: Expert Opinion/Consensus
Statement

Diabetes can impact all areas of sexual function due to the presence of vascular impairments, endothelial dysfunction, neurologic derangements, and hormonal changes [1]. The exact cause of sexual dysfunction can be difficult to elucidate and is most likely a result of a combination of these factors.

POSSIBLE CAUSES OF SEXUAL DYSFUNCTION IN PATIENTS WITH DIABETES

VASCULAR DISEASE

Blood flow is directly related to driving pressure and inversely related to arteriolar resistance, which is dependent on the net effects of systemically circulating substances, such as catecholamines, angiotensin, and prostaglandins [23]. Vascular endothelial thickening and its consequences are most associated with chronic cardiovascular diseases such as coronary artery disease and peripheral vascular disease, the presence of which greatly increases the risk for myocardial infarction and stroke [1]. In patients with diabetes, atherosclerosis is often present, as evidenced by fatty streaking, intimal plaques, and calcification of vessels. Changes in platelet activity, with an increase in adhesiveness and tendency to aggregation, have been observed in patients with diabetes, although it is not clear whether this is a primary alteration as a consequence of diabetes or if it occurs secondary to occlusive arterial disease [24].

When the vasculature is weakened due to narrowing related to fatty streak formation or rupture, the result is ischemia. Ischemia is the reversible cellular injury that occurs when tissue demands for oxygen exceed the supply. The result is an imbalance in oxygen supply and demand that results in tissue hypoxia, decreased energy substrate, and the buildup of toxic metabolites. Ultimately, ischemia results in alteration in tissue function [23].

This process of weakening vasculature and alteration of tissue function can lead to obstruction of the genital arteries and consequent symptomatic sexual dysfunction in both men and women [1]. Diffuse atherosclerosis, a common finding in patients with diabetes, may affect the penile, clitoral, or vaginal vasculature in addition to the circulatory beds of the heart, brain, and lower extremities. There may be a discrete narrowing in the external iliac artery that diverts the blood supply from penile circulation [25].

#94973 Sexual Dysfunction in Patients with Diabetes

In women, estrogen acts as a vasoprotector, which diminishes the effects of atherosclerotic disease on female sexuality in the childbearing years. However, as estrogen levels drop, often during perimenopause and menopause, arterial blood flow to the pelvis may be compromised. This is termed clitoral and vaginal vascular insufficiency syndrome and may cause delayed vaginal engorgement, diminished vaginal lubrication, pain or discomfort with intercourse, diminished vaginal sensation, diminished vaginal orgasm, and diminished clitoral sensation or orgasm [26; 27]. There is some evidence that hormone replacement therapy in postmenopausal women increases clitoral blood flow, but this must be weighed against the possible risks associated with the therapy [28].

Although erectile dysfunction is associated with cardiovascular risk factors and atherosclerosis, it is not known whether the presence of erectile dysfunction is predictive of future cardiovascular events. In one study, all-cause deaths occurred in 11.3% of individuals who reported erectile dysfunction at baseline, but in only 5.6% of individuals who reported no or mild erectile dysfunction [29].

Autonomic Neuropathy

Autonomic neuropathy significantly impacts the survival and quality of life of an individual with diabetes. The autonomic nervous system consists of the afferent and efferent systems, involving both the parasympathetic and sympathetic nervous systems, and may involve any organ within the body. Disturbances in the autonomic nervous system may be functional (e.g., gastroparesis, ketoacidosis) or organic (e.g., lost nerve fibers) [30]. With autonomic neuropathy, there is damage to the autonomic, motor, and/or sensory nerves as a result of metabolic or vascular derangement in individuals with long-standing diabetes [31].

Studies of men with diabetes who experience erectile dysfunction have suggested that neurologic abnormalities, primarily autonomic neuropathy, are present in up to 80% of the cases [25]. The primary abnormalities are related to the autonomic nervous system, which is responsible for engorgement [25]. Neurologic impotence, usually in the form of erectile dysfunction or retrograde ejaculation, can result from diabetic autonomic neuropathy [31].

The erectile tissue and neurologic innervation of the female genitalia are homologous to the male, which may contribute to the observation that women with diabetes have more arousal phase dysfunction [25]. In women without dysfunction, vaginal lubrication is initiated by increased blood flow through the vaginal capillary plexus. During this process, arterial dilation occurs [19]. In women with peripheral nervous system disease, such as that seen with diabetes, the sexual response cycle is stunted, resulting in decreased lubrication, vaginal wall thickening, and difficulty or inability to achieve orgasm [27].

OBESITY

Individuals with diabetes (particularly type 2) tend to be overweight or obese, and this may be a confounding factor for patients experiencing sexual dysfunction. Vascular, endothelial, neurogenic, endocrine, and psychologic factors may all play a role [32]. Obesity and sexuality is a prevailing area of study for researchers, although many studies have been small in scale and focus primarily on the obese male with erectile dysfunction or obese women awaiting bariatric surgery. One study of 12,364 French men and women between 18 and 69 years of age revealed that obese men and women were at a greater risk of negative sexual outcomes than their nonobese counterparts [33]. The research uncovered the fact that obese women were 30% less likely to report a sexual partner in the previous 12 months than women of a healthy weight. Obese men were 70% less likely to report more than one partner in the same time period and greater than 2.6 times more likely to report erectile dysfunction than their nonobese counterparts [33]. However, the study did not determine the cause of sexual inactivity/dysfunction, and the actual etiology may be physical or psychologic (or both) in nature. When an individual views him/herself as visually unappealing, the emotion may be internalized and result in sexual avoidance, even when the individual is in a committed relationship [32].

Obesity is often the result of insulin resistance in diabetes and is associated with dyslipidemia and endothelial and smooth muscle dysfunction, each of which is associated with sexual dysfunction [34]. A strong inverse relationship has been identified between the incidence of metabolic syndrome and testosterone levels (total and unbound, or "free") as well as sex hormone-binding globulin levels. The association is strongest for the dyslipidemia and waist circumference components of metabolic syndrome when compared with elevated triglycerides, hypertension, or glucose intolerance [35]. As such, diminished levels of testosterone should also be considered, along with vascular and neuropathic etiologies, when evaluating erectile dysfunction in overweight patients with poorly controlled diabetes [32].

CASE STUDY

Patient T is large man, 44 years of age, who is admitted to the emergency department with complaints of nausea, vomiting, and excessive urination. He and his wife had been out riding their motorcycles over the past weekend and eating a high-fat diet, as they do most weekends. They decided to come to the emergency department suspecting food poisoning. He is a white male with seasonal allergies and hypertension, but no other significant medical history. His surgical history is positive for an appendectomy at 15 years of age without complications. His family history is positive for type 2 diabetes, coronary artery disease, cerebrovascular accident, hyperlipidemia, hypertension, and obesity. Upon physical assessment, Patient T is alert and oriented. His height is 5 feet 10 inches; weight 239 pounds without shoes; BMI 34.4 kg/m²; blood pressure 146/82 mm Hg on medications; pulse 83 beats per minute, regular rate and rhythm; and oral temperature 37 degrees Celsius. His lungs are clear to auscultation, and heart sounds are clear, without rubs or murmurs auscultated. The abdomen is soft and nontender in all quadrants. Peripheral pulses are present at +2 at all extremities. Patient T's feet are free from lesions, with a positive Babinski reflex, and all extremities are warm to touch and responsive to monofilament test. Laboratory results include:

- HbA_{1c}: 8.1% (estimated average glucose: 186 mg/dL)
- Random blood glucose: 321 mg/dL
- Blood urea nitrogen (BUN): 22 mg/dL
- Creatinine: 0.9 mg/dL
- Alanine transaminase: 16 U/L
- HDL: 31 mg/dL
- Low-density lipoprotein (LDL): 122 mg/dL
- Triglycerides: 201 mg/dL
- Microalbumin: 312 mcg/mg

The patient reports that the only medications he is currently taking are over-the-counter cetirizine (Zyrtec) and chlorthalidone 25 mg/day for hypertension.

The emergency physician diagnoses Patient T with new-onset type 2 diabetes and refers him to the inpatient diabetes educator for survival skills education. He is discharged on metformin 1000 mg twice daily and blood glucose monitoring twice a day for the next month. In addition, Patient T is instructed to follow-up with his primary care provider within the next 72 hours for further diabetes evaluation.

The certified diabetes educator meets with the patient and his wife to provide information on metformin, a biguanide. Education focuses on the drug's mechanism of action, lifestyle modification (especially diet), and recognition and treatment of hyperglycemia.

Patient T is provided with a blood glucose monitor and instructed on the frequency, use, and importance to the management of diabetes. He is informed of the discharge order to monitor his glucose levels twice daily. The diabetes educator encourages him to alternate the times of his monitoring to obtain the greatest amount of information to guide management decisions. Patient T and his wife ask many questions and are able to verbalize the instructions given.

#94973 Sexual Dysfunction in Patients with Diabetes

At the conclusion of the visit, Patient T's wife timidly asks if there are any other things diabetes could affect. The educator begins to list the many possible chronic complications, but the wife stops her and states that the patient has recently had problems performing. Patient T, mortified, states he is fine, but his wife disagrees, stating she loves him and wants their physical relationship back. When asked how long the problem had been occurring, the patient states that the problems began in the last month. The educator provides information regarding the impact of stress, elevated glucose levels, diet, and obesity on erectile function.

As a first step, the educator encourages Patient T to obtain better glycemic control, improve his diet, and manage any stress he may be experiencing. Because these are all modifiable conditions, they should be addressed first and may resolve the sexual dysfunction. If the condition remains a persistent issue, the patient is instructed to discuss further options (e.g., medication) with his primary care provider. Patient T and his wife are agreeable to this plan and appear more comfortable and relaxed.

TREATMENT OPTIONS

In the treatment of sexual dysfunction, the first and most important goal is to identify and treat any reversible cause(s). Education is an essential part of this process, as patient investment and compliance with lifestyle changes and treatments is necessary [29]. Patients and their significant others should have a solid understanding of diabetes-related and other causes of sexual dysfunction and of the available treatment options [7]. Due to the more overtly physiologic nature of male sexual dysfunction, many options exist for the treatment of sexual dysfunction in men. However, the same cannot be stated for women. In both sexes, the appropriate first step is to address modifiable factors, such as controlling of blood glucose levels, adoption of a healthy diet, and counseling [32]. In men, first-line therapy for erectile dysfunction (the most common cause of male sexual dysfunction) consists of pharmacotherapy with a phosphodiesterase-5 inhibitor (i.e., sildenafil, vardenafil, or tadalafil) and/or testosterone replacement

in hypogonadal men [36; 37]. Other mechanical and surgical options are available [37]. Women also have some medical treatment options, although education and psychotherapy (e.g., individual and couple therapy, cognitive-behavioral therapy, physiotherapy) are the most common approaches [38]. As with all patients with diabetes, education regarding diet (e.g., adopting the Mediterranean diet), exercise (aerobic and anaerobic exercise), control of blood glucose levels, and smoking cessation should be provided and reinforced regularly [32].

LIFESTYLE INTERVENTIONS

The first step in addressing sexual dysfunction in most patients is to make changes in one's lifestyle, particularly for women, for whom pharmacologic and surgical options are limited. This includes obtaining adequate rest, engaging in effective stress management techniques, and regular exercise [38]. Regular physical activity is protective against the development of sexual problems in patients with diabetes [36; 39]. Weight loss may also be helpful for some patients. In fact, obesity nearly doubles the risk of erectile dysfunction, and even modest improvement in weight may result in better sexual functioning [36]. Smoking is associated with an increase in the risk of erectile dysfunction, and given the implications of smoking for all patients, cessation should be encouraged.

Engaging in noncoital intimacy (e.g., sensate-focus exercises) and enhancing stimulation and eliminating routine, with the use of erotic materials, masturbation, and devices, may improve sexual response, particularly among women [40]. Some women have experienced success with pelvic floor muscle training (Kegel exercises), a process for strengthening the pubococcygeus and levator ani muscles [41]. With this training, the individual should alternate constriction and release of the muscles of the pelvic floor. These exercises should be done rapidly 10 to 20 times [31].

Steps should also be taken to decrease pain associated with intercourse by changing positions, ensuring full arousal, or practicing biofeedback [40]. Topical lubricants can improve the comfort of sex, especially for those experiencing vaginal dryness, and many over-the-counter products are available [32]. Lubricants add temporary moisture to vaginal tissue, allowing for easier penetration, but these products do not increase blood flow to the genitals and may not improve disorders of desire. Only wateror silicone-based (not oil-based) products should be utilized. Silicone-based lubricants are not absorbed by the skin, resulting in longer efficacy compared to water-based formulations. However, because these products are not absorbed, they must be washed completely off with soap and water following sexual activity [19].

PSYCHOSOCIAL INTERVENTIONS

Marriage counseling or sex therapy may be required for cases in which sexual dysfunction has been long standing in the relationship [7]. In severe cases, individuals have reported the absence of a sexual physical relationship with their significant other for more than 10 years. Truth, honesty, and openness are essential goals for therapy in order to initiate the healing process. Because the task may seem insurmountable to the couple, encouragement regarding the re-establishment of a healthy relationship will be fundamental [32].

Discussion of the issues related to sexual dysfunction can potentiate an already fragile state. Stress increases relationship friction and can worsen sexual dysfunction; therefore, management of stress is crucial [32]. Stress is subjective in nature, and a patients' self-described stress level should not be discounted. Members of the healthcare team have an important role assisting patients and their partners to modify their appraisals of typical and atypical stressors related to diabetes and complications associated with the disease process. Providing individuals with more effective coping strategies is often necessary [42].

PHARMACOTHERAPY

When education and control of modifiable factors do not result in improvements or resolution, medical treatments will be required [32]. In general, pharmacotherapy is used for male sexual dysfunction, but research into drugs for female sexual dysfunction is ongoing. Prior to the initiation of any therapeutic option, the individual should be mandated to refrain from the use of alcohol and all forms of tobacco. The patient's current medications should also be assessed for the presence of medication that might contribute to sexual dysfunction [30]. If possible, these medications should be eliminated or replaced.

The ability of a man to initiate and maintain an erection is dependent on the presence of nitric oxide and cyclic guanosine monophosphate. Phosphodiesterase-5 enzyme inhibitors used to address erectile dysfunction, including sildenafil, vardenafil, tadalafil, and avanafil, act by increasing nitric oxide and cyclic guanosine monophosphate levels, both of which may be diminished in men with diabetes [30]. These medications are absolutely contraindicated in individuals being treated with nitroglycerine or other nitrate-containing medications due to the potential for severe hypotension and fatal cardiac events [7].



The National Institute for Health and Care Excellence recommends that clinicians consider a phosphodiesterase-5 inhibitor to treat problematic erectile dysfunction in men with type 2 diabetes, initially choosing the drug with the lowest acquisition cost

and taking into account any contraindications.

(https://www.nice.org.uk/guidance/ng28. Last accessed March 23, 2021.)

Level of Evidence: Expert Opinion/Consensus Statement

Phosphodiesterase-5 enzyme inhibitors have also been studied for improvements in sexual arousal and functioning in women, although their use is offlabel. One systematic review and meta-analysis found significant increases in adverse events with these agents compared with placebo, but concluded that

#94973 Sexual Dysfunction in Patients with Diabetes

they were a relatively safe and potentially effective treatment modality for female sexual dysfunction [43]. Additional research is necessary before they can be recommended [44].

Sildenafil

Sildenafil, marketed in the United States as Viagra, is typically given in tablet form in dosages ranging from 20 mg to 100 mg [45; 46]. The usual dose is 50 mg taken one hour (range: 30 minutes to four hours) before sexual activity. Sildenafil acts to increase the effect of nitric oxide by inhibiting phosphodiesterase-5, which is responsible for degradation of cyclic guanosine monophosphate in the corpus cavernosum [45]. When sexual stimulation produces local release of nitric oxide, inhibition of phosphodiesterase-5 by sildenafil causes increased levels of cyclic guanosine monophosphate in the corpus cavernosum, resulting in smooth muscle relaxation and inflow of blood. The medication is only effective in the presence of sexual stimulation. The effect of sildenafil on sexual arousal in women has been studied but is unclear, and data from clinical trials are limited.

The most common adverse reactions are headache and dyspepsia [46]. Other less common side effects include flushing, insomnia, diarrhea, myalgia, epistaxis, dyspnea, abnormal vision (e.g., color changes, light sensitivity, blurred vision), pyrexia, erythema, paresthesia, nasal congestion, and increased liver enzymes [46]. In rare cases, myocardial infarction, hemorrhage, and transient ischemic attack have been reported [45; 46]. If severe reactions or vision or hearing changes develop, the patient should be advised to contact his healthcare provider as soon as possible.

Possible drug-drug interactions can occur with beta-blockers, loop and potassium-sparing diuretics, cytochrome P450 inducers, rifampin, delavirdine, protease inhibitors, hepatic isoenzyme inhibitors, antiretroviral medications, and isosorbide [45]. High-fat meals may reduce absorption, so patients should be advised to take sildenafil on an empty stomach. Grapefruit may increase the drug level while delaying absorption and should be avoided.

Patient teaching for those taking sildenafil should focus on the avoidance of adverse events and safe administration. First, individuals must be cautioned to avoid use of nitrates or advise their primary care or emergency care providers of the use of this medication. Patients should also be aware of the potential cardiac risk with sexual activity, especially in the presence of cardiovascular risk factors. If symptoms such as chest pain, dizziness, or nausea occur during sexual activity, the activity should be halted and a healthcare provider be contacted. Erections lasting greater than four hours and priapism (i.e., painful erection lasting longer than six hours) may occur, and immediate medical attention is required in these cases to prevent permanent penile tissue damage. Finally, education regarding the prevention of sexually transmitted infections is necessary, as sildenafil does not prevent the spread of these diseases.

Vardenafil

Vardenafil (Levitra, Staxyn) is given in an entericcoated or oral disintegrating tablet taken by mouth as a single dose, as needed, one hour prior to sexual activity [45]. Dosage range is 5–20 mg and based on effectiveness and tolerance, with a maximum of 20 mg daily [46]. The medication should be taken on an empty stomach for maximum efficacy.

Vardenafil acts by increasing cyclic guanosine monophosphate levels, prolonging smooth muscle relaxation, and promoting blood flow into the corpus cavernosum [45]. Potential adverse reactions include headache, dizziness, flushing, decrease or loss of hearing, tinnitus, rhinitis, sinusitis, dyspepsia, nausea, back pain, and flu-like symptoms [46]. A transient decrease in supine blood pressure may also occur. Possible drug-drug interactions have been noted with alpha-blockers, nitrates, antiarrhythmics (e.g., quinidine, procainamide, amiodarone, sotalol), erythromycin, indinavir, itraconazole, ketoconazole, and ritonavir [45]. As with sildenafil, high-fat meals may reduce peak drug levels. The patient education needs for vardenafil are similar to those outlined for sildenafil. Evaluation of the individual's cardiac risk prior to the initiation of the medication is necessary. Other general topics should include risk of priapism, vision/hearing changes, safe and effective administration practices, and when to contact a healthcare provider.

Tadalafil

Tadalafil, which is sold as Cialis, Alyq, and Adcirca in the United States, is available in enteric-coated tablets. The typical dose is 10 mg daily taken at least 30 minutes prior to sexual activity, which is titrated to a greater dose as needed [45; 46]. Creatinine clearance must be assessed by the healthcare provider prior to initiating the medication. Unlike the other medications, tadalafil may improve erectile function for up to 36 hours after a single dose [46].

As with sildenafil and vardenafil, tadalafil increases cyclic guanosine monophosphate levels, prolongs smooth muscle relaxation, and promotes blood flow into the corpus cavernosum. Adverse reactions may include dizziness, headache, flushing, myalgia, decrease or loss of hearing, nasal congestion, tinnitus, dyspnea, back pain, limb pain, hypertension, and dyspepsia [46]. Tadalafil has been associated with interactions with alpha-blockers, nitrates, erythromycin, itraconazole, ketoconazole, ritonavir, and rifampin [46]. Dosing should be adjusted or the medication discontinued if taken with protease inhibitors, potent CYP3A4 inhibitors, or potent CYP3A4 inducers. Coadministration with nitrates may cause a serious decrease in blood pressure, leading to an increased risk of myocardial infarction or stroke [45]. Patients should be advised to seek immediate medical attention if chest pain develops after taking the medication. Alcohol use may increase the incidence of certain side effects, including headache, dizziness, orthostatic hypotension, and tachycardia; avoidance of alcohol is advised. Grapefruit should also be avoided.

Information regarding the transmission and prevention of sexually transmitted infections should be provided. Additional patient education may focus on appropriate administration, recognition of adverse effects, and times to contact a healthcare provider.

Avanafil

Avanafil is a second-generation phosphodiesterase-5 enzyme inhibitor that was approved for use in April 2012 [47]. The usual initial dose is 100 mg, taken 15 minutes before sexual activity [46]. The recommended dose with concomitant alpha blocker or CYP34A inhibitor use is 50 mg [46]. Although avanafil does potentiate nitroglycerin-induced hypotension, the effects of the agent on heart rate and blood pressure are less than those of the first-generation phosphodiesterase-5 enzyme inhibitors. Nonetheless, its use is not recommended in patients taking nitrates [46]. The side effects of avanafil are similar to the effects observed with other erectile dysfunction drugs, with headaches and flushing being the most common. Grapefruit potentiates the effect and toxicity of avanafil, and alcohol should also be avoided. Avanafil may be taken with food, including foods with fat. Studies have shown that this agent is effective in men with erectile dysfunction, including those with diabetes, and that it has a low rate of discontinuation (2.8%) due to adverse effects even at the maximum dose of 200 mg, which most men eventually progressed to in clinical trials [48; 49].

Agents for Female Sexual Dysfunction

In 2009, flibanserin was submitted for approval by the U.S. Food and Drug Administration (FDA) for the treatment of hypoactive sexual desire disorder in women. This medication acts by blocking serotonin, which has been shown to inhibit sexual function. Post hoc analysis of data from studies of flibanserin's antidepressant properties found that the agent significantly improved self-reported sexual function, although this was not replicated in later direct studies [50; 51]. The difference could be partly attributed to the different populations studied (i.e., the general public compared to women with major depressive disorder). In 2010, the FDA's Reproduc-

#94973 Sexual Dysfunction in Patients with Diabetes

tive Health Drugs Advisory Committee voted that flibanserin was not significantly more effective than placebo and that the potential benefits did not outweigh the risk of adverse events [51]. In 2013, the FDA again denied approval of flibanserin after the pharmaceutical company resubmitted a new drug application with data from 14 additional clinical trials; the same reasons for denial were cited [52]. However, after additional data were provided, in 2015 the FDA approved flibanserin to treat hypoactive sexual desire disorder in premenopausal women [53]. The drug includes a boxed warning due to an increased risk for severe hypotension and syncope when taken along with alcohol. One 100-mg tablet is taken daily at bedtime [46].

Androgen Therapy

An estimated 30% of men with erectile dysfunction fail to respond to first-line drugs, and low testosterone levels maybe a contributing factor [54]. Androgen therapy, usually in the form of testosterone therapy, may be used in the treatment of male and female dysfunction, although its use in women is controversial and off-label [32; 40]. Although available data support the role of testosterone therapy for women, its use is limited by the lack of approved formulations and long-term safety data [55]. Benefits have been noted for women who are postmenopausal and not taking estrogen replacement [56]. Older age is associated with lower levels of testosterone.

Testosterone replacement, often in the form of a transdermal gel or a patch, may be utilized, with the goal of increasing desire and stimulation. Transdermal testosterone is a 1% gel in 25 mg or 50 mg per unit dose packaged in a 1.25 gram per non-aerosol metered pump or a 1.62% gel in 20.25 mg or 40.5 mg per unit dose [45]. It is applied to the shoulder or upper arm, where it can be covered by a short-sleeved shirt, being careful to use gloves for application. The skin should be clean, dry, and intact. Gel is typically applied in the morning. The maximum dosages of the 1% and 1.62% gels are 100 mg and 81 mg, respectively [46]. The patch is available in 2-mg and

4-mg strengths, but the initial dose is usually 4 mg (as a single patch) [46]. The dose is then adjusted according to serum testosterone levels. The patch should be placed on the clean, dry skin of the back, abdomen, upper arm, or thigh at night, with the site rotated to avoid irritation [46]. Other preparations are available.

In men, possible adverse reactions to topical testosterone include stroke, asthenia, depression, headache, gastrointestinal bleeding, prostatitis, prostate abnormalities, urinary tract infections, cholestatic hepatitis, reversible jaundice, hypernatremia, hyperkalemia, hypercalcemia, hyperphosphatemia, hypercholesterolemia, pruritus, acne, allergic contact dermatitis, gynecomastia, breast tenderness, and flulike symptoms [45]. In women, side effects include decreased HDL levels, acne, hirsutism, clitorimegaly, and voice deepening [40].

Concurrent use of topical testosterone and corticosteroids may increase edema, and use with insulin may alter insulin dosage requirements [45]. Adverse interactions have also been noted with oral anticoagulants. Oxyphenbutazone levels may increase when utilized in combination with testosterone gel or patch, and propranolol clearance may increase when utilized in combination with testosterone gel or patch [45]. When applying the gel, it is important to prime the pump by pumping three times and discarding the gel prior to the first use. For the best results, patients should refrain from bathing or swimming for five hours after application.

When used to treat sexual dysfunction in individuals with diabetes, topical testosterone may decrease glucose levels and alter symptoms of hypoglycemia. Patients should be advised to report this and other possible side effects, including priapism, nausea and vomiting, changes in skin color, ankle edema, or sudden weight gain, to their care provider. In addition, patients' female partners should be monitored for signs of virilization, such as acne or changes in body hair distribution.

Estrogen Replacement

Estrogen plays an important role in normal female sexual functioning by maintaining the integrity of the female genital tissue, and low estrogen levels can create an excessively sensitive vaginal environment, whereby touch that was once pleasurable becomes annoying, painful, or irritating [19]. Low levels of serum estrogen can also cause vaginal wall atrophy, thinning of the vaginal mucosa, and an elevated pH level, which leads to changes in the vaginal flora and increases the risk for vaginal and urinary tract infections [32]. The major cause of low estrogen levels is menopause, and most women will experience a change in sexual function during this period [27]. Sexual complaints have been associated with serum estrogen levels less than 50 pg/mL.

Estrogen hormone replacement therapy has been used for years to treat symptoms of menopause, but more recent research has indicated that its use may place women at increased risk for stroke and certain cancers [57; 58]. However, estrogen replacement can improve sexual functioning and satisfaction, including clitoral sensitivity, increased libido, and improvements in urogenital atrophy [59]. Estrogen may be taken alone or in conjunction with progesterone or testosterone. It is important to weigh the possible benefits against the risks of hormone replacement.

Intracavernosal or Intraurethral Alprostadil

For patients who do not respond to the first-line therapies of lifestyle change, pharmacotherapy, and/or testosterone replacement, intracavernosal or intraurethral alprostadil may be effective in improving erectile functioning. This second-line therapy consists of the injection of alprostadil, a prostaglandin, into the corpora cavernosa or the insertion of a suppository containing alprostadil into the urethra. The active ingredient is absorbed in to the penile tissue, facilitating smooth muscle relaxation and aiding in tumescence, an effect that lasts approximately 30 to 60 minutes [25]. The dosage should be individualized according to response to dose, etiology of erectile dysfunction, and agent being used [46]. After the initial appointment establishes the correct dose, the patient may selfadminister alprostadil 10 to 15 minutes prior to sexual activity up to three times per week, with at least 24 hours between doses. If the medication is administered intraurethrally, the patient should be advised to urinate prior to insertion.

Oral stimulation should be avoided while using this medication and administration method. If the patient's female partner experiences vaginal bleeding or itching or if she may be pregnant, barrier contraception (e.g., a condom) should be used during intercourse [32; 46].

Patients tend to prefer the intracavernosal method over the intraurethral administration as it is better tolerated and more effective [36]. Common side effects with intraurethral administration of alprostadil include penile pain, urethral burning or bleeding, dizziness, and testicular pain, while the intracavernosal administration is associated with penile pain, prolonged erection, injection site hematoma, and headache [36; 46]. With either medication, prolonged erections and priapism are serious concerns. If a rigid erection lasts longer than four hours, the patient should be instructed to contact his healthcare provider.

VACUUM PUMP DEVICES

Vacuum pump devices or constrictors are a viable alternative to medication therapy or medication failure. They are non-invasive, have few side effects, and are generally well tolerated [17]. To use, the vacuum tube is lubricated and placed over the penis, with a constriction band situated over the end. A battery- or hand-operated pump is initiated, and a vacuum is produced. Sitting back or lying down may improve the tightness of the seal. For patients with larger abdomens who are unable to visualize the pelvic area, assistance applying the pump may be necessary. When significant tumescence is produced, the band is moved to the base of the penis, the vacuum is released, and the cylinder is removed.

#94973 Sexual Dysfunction in Patients with Diabetes

The band can safely remain in place for 30 minutes. These devices do not produce a full erection, and the base will remain flaccid; however, sufficient rigidity is obtained for sexual activity in 80% to 90% of cases [25].

Thorough education regarding appropriate application and use of vacuum devices is essential for successful outcomes and prevention of injury. Patients should be encouraged to practice the application process to gain confidence and to use sufficient lubrication to avoid friction injury. It may be necessary for patients to remove hair from their pubic area in order to obtain the tightest seal possible.

PROSTHESES

The implantation of an inflatable penile prosthesis is a surgical option for the treatment of impotence in men who have not responded to first- or secondline therapies [17]. The prostheses are implanted by a urologist as a pair and are made primarily of a silicone polymer. The three main types of prostheses are malleable, inflatable, and mechanical [25]. The cost varies significantly based on the type of prosthesis selected.

After it is implanted, the individual or his significant other may inflate the prosthesis by pressing on the pump, which transfers fluid from the reservoir to the cylinders within the penis. The implant may be deflated after sexual activity by pressing on the deflation valve at the base of the device. This will cause the device to return the fluid from the implant to the reservoir [32].

Patients should be instructed to watch for signs and symptoms of infection and to alert their healthcare provider of any discharge or seepage from the tip of the penis. In addition, patients should be aware of potential signs of complications, such as mechanical failure, extrusion of the device, pain, and bruising. These discoveries should be communicated to a primary care provider without delay [25].

PSYCHOSOCIAL IMPACT OF SEXUAL DYSFUNCTION

Sexual intimacy is a taboo subject in many cultures, and men and women may feel uncomfortable discussing it, even with healthcare providers [32]. In addition, some patients are less engaged in discussing health issues, particularly conditions like diabetes, depression, or sexual dysfunction. However, if left untreated, diabetes and sexual dysfunction can have significant negative ramifications on mental and physical health. This is an important consideration, as psychologic stress can exacerbate existing issues, including sexual dysfunction, leading to a cycle of despair and dysfunction. In one study, men and women with diabetes and sexual dysfunction reported more depressive symptoms than those without sexual dysfunction [60]. Emotional factors that may interfere with sexual arousal, causing or worsening sexual dysfunction, include [61]:

- Poor communication or conflict with a partner
- Depression
- Anxiety
- Stress
- Fatigue

Sexual and emotional issues do not just impact the individual. They can impair personal relationships and generate challenges of trust, intimacy, and closeness. Patients or partners may experience feelings of distance or withdrawal emotionally as well as physically. Partners of patients with diabetes and sexual dysfunction may not experience enjoyment or may dread being unable to bring their partner to orgasm. This can lead to issues of negative self-worth, fears of abandonment or betrayal, and loss of intimacy [32]. By presenting clear information regarding how sexual health can be impacted by diabetes, stress, cardiovascular issues, and low hormone levels, healthcare professionals can help patients successfully manage this significant personal issue [61]. Sexuality and virility are important aspects of an individual's self-perception and beliefs about one's role in society. This can be compounded in cultures that highly value youth, masculinity/femininity, and/or virility/fertility (including many Western cultures). Healthcare professionals may assess patients for impaired self-esteem with interview techniques and quality of life questionnaires [32].

Individuals with diabetes have an increased risk of depression compared to the general public. As many as 10% to 28% of individuals with diabetes meet the criteria for comorbid depression prior to being diagnosed with sexual dysfunction [62; 63]. In women with diabetes, in particular, depression is a significant predictor of sexual dysfunction, as is the quality of the partner relationship [27; 60]. To a lesser extent, depression and psychologic problems impair diabetic men's sexuality as well [64]. Symptoms of depression include [25]:

- Apathy and self-imposed social isolation
- An inability to perform activities of daily living
- Disruption of sleep patterns
- Memory impairment
- Mood swings
- Frustration
- Despair/hopelessness
- Suicidal ideation

In addition to the organic impact of depression on sexual arousal and function, the medications used to treat depression can also cause impaired sexual response [27; 65]. Antidepressants associated with the greatest rates of sexual side effects include selective serotonin reuptake inhibitors (e.g., paroxetine, sertraline), serotonin-norepinephrine reuptake inhibitors (e.g., venlafaxine), tricyclic antidepressants (e.g., amitriptyline, clomipramine), and monoamine oxidase inhibitors (e.g., isocarboxazid) [66]. If possible, antidepressants with fewer sexual side effects, such as bupropion, should be selected for patients with diabetes. Clinical guidelines for the treatment of depression have been established and may be applied, with few alterations, to patients with diabetes diagnosed with major depressive disorder. However, the most effective approach and treatment for individuals with diabetes and minor subclinical depression (dysthymia) are less clear, although it should be addressed fully before it advances to major depression [62]. In many cases, these patients will benefit from referral to a mental health expert for psychotherapy, support groups, and/or pharmacologic intervention.

Some individuals with diabetes will have a decreased interest in sexual intimacy due to feelings of constant fatigue. This may be the result of physical or psychologic factors (or a combination). If fatigue occurs secondary to depression, antidepressant treatment should improve the symptom.

Often, patients experiencing sexual dysfunction may be angry, anxious, or self-loathing. These types of feelings make it difficult for the individual to clearly communicate with his or her significant other. If relationship problems are present, referral to a counselor, therapist, or psychologist for individual and couple's counseling is indicated. The couple may also be provided with techniques to improve their sexual relationship, including [32]:

- Redefining pleasure in the relationship
- Mood-setting techniques
- Cuddling
- Scheduled intimacy
- Erotic media

Providing education regarding medications or alternate forms of counseling has been proven beneficial for the management of depression and/or anxiety, and this should result in improvements in sexual function [32]. Individuals should be advised to contact their healthcare provider if they experience depressed mood or anxiety for more than two weeks [61].

#94973 Sexual Dysfunction in Patients with Diabetes

Patient teaching for successful understanding and management of psychologic distress stemming from sexual dysfunction should include the following key points [32]:

- A good sexual relationship requires more than a pill.
- Open communication is imperative.
- Relationship building and bonding may be required.
- Counseling regarding individual expectations may be needed.
- A positive and encouraging attitude is essential for both individuals.
- Keep the end result in the forefront of the discussion.
- Encourage alternate ways for expression of pleasure.

CASE STUDIES

CASE STUDY 1

Patient K is an active white man, 75 years of age, presenting to his physician's office for his three-month diabetes evaluation. He has a positive history of diabetes for the past 20 years, and a 28-year history of hypertension and hypercholesterolemia. Past surgical history is positive for bilateral knee replacement 10 years ago, two angioplasties with stents within the past five years, and non-emergent coronary artery bypass surgery two years ago. He continues to smoke despite multiple attempts to stop and strong advisement by all providers involved in his care.

Currently, his blood pressure is 152/84 mm Hg, and his pulse is 78 beats per minute, regular rate and rhythm. He is 5 feet 10 inches tall and weighs 252 pounds. Laboratory analysis reveals the following results:

- HbA_{1c}: 8.0% (normal range: 4.6% to 7.1%)
- Total cholesterol: 178 mg/dL (normal range: <200 mg/dL)

- LDL: 108 mg/dL (normal range: <130 mg/dL)
- HDL: 43 mg/dL (normal range: 30-75 mg/dL)
- Triglycerides: 188 mg/dL (normal range: 40–170 mg/dL)
- BUN: 13 mg/dL (normal range: 6-23 mg/dL)
- Creatinine: 1.2 mg/dL (normal range: 0.6–1.5 mg/dL)
- Potassium: 4.3 mEq/L (normal range: <8 mEq/L)
- Sodium: 38 mEq/L (normal range: 10-40 mEq/L)

The patient's current medications include:

- Metformin: 2,000 mg daily in two divided doses
- Glimepiride: 4 mg each morning
- Pioglitazone: 30 mg each morning
- Digoxin: 0.5 mg daily
- Atenolol: 50 mg daily
- Ezetimibe: 10 mg daily
- Aspirin: 81 mg daily

Patient K's wife of 46 years, Mrs. K, accompanies him to the visit. While reviewing the results of the patient's laboratory tests and blood glucose results, Dr. G detects tension between the patient and his wife. When his wife attempts to ask a question regarding Patient K's blood glucose levels, he snaps at her to leave him alone and stop nagging. Mrs. K leaves the office in tears. Patient K apologizes to Dr. G for the outburst and states that he has not been sleeping well. When asked how often this was happening, Patient K states only a few times a month.

Over the next 18 months, Patient K and his wife continue to attend his scheduled appoints without fail. The tension in the couple's relationship continues, but Dr. G feels that he should not pry. However, at the next visit Dr. G notes that Patient K is more withdrawn than usual and is avoiding all eye contact with Mrs. K as she sits on a stool in the corner of the room rather than in the seat next to the patient, as she usually does. Furthermore, Mrs. K is not engaging in any of the comforting gestures he has come to expect from her (e.g., rubbing Patient K's back and hand).

Dr. G reviews Patient K's medical record and notes a weight gain of 20 pounds and an increase in his HbA_{1c} (from 8.0% to 9.2%). Even more tension and perceived friction is evident between the patient and his wife. When Dr. G asks about Patient K's activities, the only response is a shrug from the patient's shoulders and a roll of the eyes from Mrs. K. Dr. G can no longer ignore these behaviors. He has known the couple for more than 20 years and has noted a dramatic change just in the last two years. He closes Patient K's chart and tells the couple what he has been witnessing.

Both the patient and his wife begin to cry. Patient K states that it is a personal problem they are handling, and he is uncomfortable talking about it. Dr. G asks Mrs. K to have a seat in the waiting room. After the wife has left the room, Dr. G asks for details, reassuring Patient K that everything they discuss will be confidential and that he will not be judged. Eventually, Patient K confides that he has been a poor husband and does not know how to make his wife happy. Dr. G asks if either of them is seeing other people. Patient K responds that he is not, and while he does not think Mrs. K is, he would not blame her if she was. He also states that he is not "a real man." Dr. G presses the patient regarding what has made him feel this way. After several moments, Patient K admits that he has been unable to achieve an erection for the last 20 months, despite a previously healthy sex life and continuing to find his wife attractive.

Dr. G assures the patient that many men experience erectile dysfunction and that, with treatment, he should be able to experience a healthy sex life with his wife once again. Dr. G and Patient K discuss the many treatment options available, addressing benefits and potential drawbacks of each. In addition, Dr. G emphasizes the importance of lifestyle changes in improving sexual functioning, encouraging the patient once again to quit smoking and lose weight. These changes may also help control Patient K's HbA1c, which has been rising despite treatment. If his level remains high, insulin therapy may be considered. Due to Patient K's reluctance to add another medication to his regimen, he decides to try a vacuum pump device. The patient and his wife meet with an educator for information regarding safe application of the device and conditions requiring healthcare provider notification. Although the couple is initially timid and appears embarrassed, the educator puts them at ease and the education session progresses. Patient and Mrs. K are encouraged to go home and practice.

After six months, Patient K returns to Dr. G's office with his wife. Unfortunately, even with significant practice, the couple remains unable to achieve a fulfilling sex life. Dr. G assesses the patient's testosterone level to determine if this is a contributing factor. The result is 205 pg/mL (normal range: 44–244 pg/mL), effectively ruling out a hormonal etiology. Although the vacuum pump device allows for a functional sexual relationship, they miss the spontaneity they once enjoyed. As a result, Patient K expresses interest in investigating the available pharmacologic options.

Following an in-depth discussion of each agent, Patient K ultimately decides to utilize sildenafil. Dr. G provides the couple with education regarding the drug interactions and possible adverse effects, taking time to answer any questions and to emphasize the continued importance of lifestyle interventions. At the end of the visit, Patient K and his wife feel comfortable with the new arrangement and commit to calling if any further questions arise or if adverse effects are experienced.

#94973 Sexual Dysfunction in Patients with Diabetes

In six months, Patient K returns to his primary care provider for follow-up. When Dr. G enters the examination room, he is met by a more confident appearing patient. He is calm, at ease, and sitting with a relaxed smile on his face. Patient K tells Dr. G that his relationship with Mrs. K is improving, and they have been able to engage in sexual activity regularly. In addition, Patient K has lost 25 pounds and has cut back on his smoking. His HbA_{1c} level is normal on medications, and he seems very happy.

CASE STUDY 2

Patient N is a postmenopausal Latina woman, 59 years of age. She has a history of depression (2 years), fibromyalgia (11 years), diabetes (12 years), hypertension (3 years), osteoarthritis (6 years), and hypercholesterolemia (6 years). She has two adult children, both born by cesarean delivery. Her past surgical history is positive for bilateral knee replacement (nine years ago), cholecystectomy (20 years ago), and appendectomy (47 years ago). She has a family history of diabetes, cardiovascular disease, hypertension, stroke, and prostate and breast cancer.

Patient N uses alcohol (beer, wine, and liquor) occasionally and socially, consuming approximately three drinks per week or less. She has no history of tobacco use. Her diet consists primarily of convenience foods due to a lack of desire to cook and availability of the items. She has gained 20 pounds over the past year, and she denies engaging in any form of exercise.

At her routine gynecologic visit, Patient N is free of initial complaints. Although she has a strong professional relationship with her gynecologist, Patient N presents with a flat affect and withdrawn behavior. Dr. J questions the patient regarding her disposition, but she dismisses the behavior as "nothing." Dr. J continues to pursue the cause of the mood change and inquires regarding Patient N's relationship with her husband of 37 years. Patient N begins crying and states that she has been separated from her husband for the past five months, a fact that is all her own fault.

Dr. J comforts Patient N and asks her to describe what happened. At first, the patient is reluctant to discuss the problems, but Dr. J reassures Patient N that many couples experience problems and it is nothing to be ashamed of. He lets the patient know that he would like to help her. While continuing crying, Patient N claims she is no longer desirable to her husband. She admits to a noticeable change in her attitude toward sexual intimacy, pain with intercourse, and vaginal dryness, all of which have occurred gradually over the past six years. Patient N states that she still loves her husband and finds him attractive, but no longer knows how to demonstrate that love.

Dr. J assures the patient that this is a common complaint for many women, especially those who are postmenopausal and/or diabetic. Dr. J tells Patient N that when women progress through menopause, their estrogen levels decrease, and estrogen plays an important role in sexual health and desire in women. Furthermore, Dr. J educates the patient regarding the neuropathic aspect of diabetes and sexual function.

Initially, Dr. J advises Patient N to exercise and adopt a healthier diet to promote better glycemic management and weight loss. Patient N agrees to try this approach and to contact her primary care provider for assistance. Dr. J also encourages her to inquire about possible adjustment of her depression medication during this period in her life, which the patient also agrees to.

Patient N feels encouraged to talk with her husband regarding their situation and determine if the relationship was something they wanted to salvage or dissolve. Although she believes she already knows the answer and is confident to take the first step, she is unsure of what to say. Dr. J encourages the patient to engage in a frank conversation regarding what she is going through and determine if her husband is willing to attend counseling. Patient N returns for a follow-up visit in six months, and Dr. I notes a slightly brighter affect to the patient's demeanor. Dr. J evaluates Patient N's progress and finds that she and her husband are meeting with a therapist to attempt to overcome their issues. During therapy, Mr. N stated that he felt responsible for Patient N's lack of sexual desire. Although Patient N and her husband have started to work past some of their issues, pain with intercourse and persistent vaginal dryness continue to be problems. Dr. J suggests utilizing an over-the-counter, silicone- or water-based lubricant. He cautions the couple to avoid oil-based products and to be cautious with application due to the potential risk for falls. Enhancing the sensual experience (through erotic massage or viewing erotic materials) is also suggested.

Patient N continues to follow-up with Dr. J for the next six months and reports progression in her sexual relationship with her husband. She states that while things are not perfect, she and her husband are committed to finding their optimal comfort level with each other.

CONCLUSION

Unfortunately, sexual dysfunction is common among individuals living with diabetes. The greatest defenses are controlling blood glucose, addressing cardiac risk factors, establishing a healthy blood pressure level, and maintaining an open and honest relationship [7]. However, in many cases, more intensive intervention, in the form of psychotherapy, pharmacotherapy, or surgery, may be necessary. The most important points for healthcare providers are to ensure that patients feel comfortable and secure in discussing sexual issues and to provide clear and accurate information regarding diabetes, sexual functioning, and available treatment options.

FACULTY BIOGRAPHY

Diane Thompson, RN, MSN, CDE, CLNC, has an extensive history in nursing and nursing education. She possesses a strong background in diabetes and cardiac care, starting her professional career at the cardiac care area of the Cleveland Clinic in Cleveland, Ohio. Ms. Thompson took the knowledge and experience she learned from the Cleveland Clinic and transferred it into the home health arena in rural Ohio, after which she moved to Florida and obtained further knowledge while working as a PRN nurse in all areas, including medical/surgical, intensive care, emergency, critical care, and cardiology. With a desire to have a specific area to concentrate her profession, Ms. Thompson accepted a position as a pneumonia case manager, which led into a diabetes case manager career.

Ms. Thompson has been employed in diabetes care since 2001, when she was hired as a diabetes case manager. After the completion of 1000 hours of education to diabetes patients, Ms. Thompson earned her certification as a diabetes educator in 2003. Since 2006, Ms. Thompson has been the Director of Diabetes Healthways at Munroe Regional Medical Center in Ocala, Florida. As the director of the diabetes center, Ms. Thompson is responsible for the hospital diabetes clinicians, hospital wound care clinicians, and out-patient education program. Ms. Thompson has also lectured at the local, state, and national level regarding diabetes and the hospital management of hyperglycemia. Ms. Thompson is a member of the ADA, AADE, Florida Nurses Association, and the National Alliance of Certified Legal Nurse Consultants.

#94973 Sexual Dysfunction in Patients with Diabetes

Ms. Thompson acknowledges her family as her greatest accomplishment. She is a wife of 26 years and a mother of a daughter and son, of which she is very proud. Ms. Thompson credits her husband for the support needed to see a goal and achieve it. He has been by her side through nursing school and completion of her Bachelor's degree and Master's degree, which she was awarded in 2015 from Jacksonville University in Florida.

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or controlbased. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

Works Cited

- 1. Perez K, Gadgil M, Dizon DS. Sexual ramifications of medical illness. Clin Obstet Gynecol. 2009;52(4):691-701.
- 2. American Association of Diabetes Educators. The Art and Science of Diabetes Self-Management Education: A Desk Reference for Healthcare Professionals. 4th ed. Chicago, IL: American Association of Diabetes Educators; 2017.
- 3. American Diabetes Association. Standards of medical care in diabetes-2021. Diabetes Care. 2021;44(Suppl 1):S1-S244.
- Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2020. Available at https://www.cdc.gov/diabetes/ pdfs/data/statistics/national-diabetes-statistics-report.pdf. Last accessed March 18, 2021.
- Rowley WR, Bezold C, Arikan Y, Byrne E, Krohe S. Diabetes 2030: insights from yesterday, today, and future trends. *Popul Health* Manag. 2017;20(1):6-12.
- 6. Barker LE, Kirtland KA, Gregg E, Geiss I, Thompson T. Geographic distribution of diagnosed diabetes in the United States: a diabetes belt. Am J Prev Med. 2011;40(4):434-439.
- 7. Westerfield J, Holcomb S, Jensen S (eds). Current Trends in Diabetes Management: A Guide for the Healthcare Professional. 7th ed. Nashville, TN: Healthways; 2008.
- 8. American Diabetes Association. Statistics about Diabetes. Available at https://www.diabetes.org/resources/statistics/statistics-about-diabetes. Last accessed March 18, 2021.
- 9. U.S. Department of Health and Human Services Office of Minority Health. Diabetes and Hispanic Americans. Available at https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=63. Last accessed March 18, 2021.
- 10. U.S. Department of Health and Human Services Office of Minority Health. Diabetes and American Indians/Alaska Natives. Available at https://www.minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=33. Last accessed March 18, 2021.
- Acton KJ, Burrows NR, Moore K, Querec L, Geiss LS, Engelgau MM. Trends in diabetes prevalence among American Indian and Alaska Native children, adolescents, and young adults. Am J Public Health. 2002;92(9):1485-1490.
- 12. Temneanu OR, Trandafir LM, Purcarea MR. Type 2 diabetes mellitus in children and adolescents: a relatively new clinical problem within pediatric practice. *J Med Life*. 2016;9(3):235-239.
- 13. Colberg S, Friesz M. Diabetes Free Kids: A Take-Charge Plan for Preventing and Treating Type 2 Diabetes in Children. New York, NY: Avery; 2005.
- 14. Goldstein BJ, Müller-Wieland D (eds). Type 2 Diabetes: Principles and Practice. 2nd ed. New York, NY: Informa Healthcare; 2008.
- 15. Childs BP, Cypress M, Spollett G (eds). Complete Nurse's Guide to Diabetes Management. 4th ed. Alexandria, VA: American Diabetes Association; 2017.
- 16. National Institute of Diabetes and Digestive and Kidney Diseases. Risk Factors for Type 2 Diabetes. Available at https://www.niddk. nih.gov/health-information/diabetes/overview/risk-factors-type-2-diabetes. Last accessed March 18, 2021.
- 17. Edelman SV, Henry RR. Diagnosis and Management of Type 2 Diabetes. 11th ed. New York, NY: Professional Communications; 2011.
- 18. Lindau ST, Gavrilova N. Sex, health and years of sexually active life gained due to good health: evidence from two United States population based cross sectional surveys of ageing. *BMJ*. 2010;340(810):1-11.
- 19. Feldhaus-Dahir M. Treatment options for female sexual arousal disorder: part II. Urol Nurs. 2010;3(4):247-251.
- 20. Lyn S. Lange Smart Charts: Physiology. New York, NY: Lange; 2004.
- 21. Moktar A, Rodway GW, Huether SE. Structure and function of the reproductive systems. In: Huether SE, McCance KL (eds). *Understanding Pathophysiology*. 6th ed. St. Louis, MO: Mosby; 2016: 779-801.
- 22. Fode M, Sønksen J, McPhee SJ, Ohl DA. Disorders of the male reproductive tract. In: Hammer GD, McPhee SJ(eds). Pathophysiology of Disease: An Introduction to Clinical Medicine. 7th ed. New York, NY: McGraw Hill; 2014: 651-676.
- 23. West CM, Pelter MM. Ischemia. In: Carrieri-Kohlman V, Lindsey AM, West CM (eds). Pathophysiological Phenomena in Nursing: Human Response to Illness. 3rd ed. St. Louis, MO: Saunders; 2003: 413-438.
- 24. Fisher M, Shaw KM. Diabetes and the heart. In: Shaw KM, Cummings MH (eds). *Diabetes: Chronic Complications*. 3rd ed. West Sussex: Wiley; 2012: 165-189.
- 25. Cummings MH. Diabetes and sexual health. In: Shaw KM, Cummings MH (eds). *Diabetes: Chronic Complications*. 3rd ed. West Sussex: Wiley; 2012: 141-164.
- 26. Goldstein I, Berman JR. Vasculogenic female sexual dysfunction: vaginal engorgement and clitoral erectile insufficiency syndromes. Int J Impot Res. 1998;10(Suppl 2):S84-S90.
- 27. Berman JR. Physiology of female sexual function and dysfunction. Int J Impot Res. 2005;17:S44-S51.
- 28. Alatas E, Yagci B, Oztekin O, Sabir N. Effect of hormone replacement therapy on clitoral artery blood flow in healthy postmenopausal women. J Sex Med. 2008;5(10):2367-2373.
- 29. Böhm M, Baumhäkel M, Teo K, et al. Erectile dysfunction predicts cardiovascular events in high-risk patients receiving telmisartan, ramipril, or both: the ongoing telmisartarn alone and in combination with ramipril global endpoint trial/telmisartan randomized assessment study in ACE intolerant subjects with cardiovascular disease. *Circulation*. 2010;121(12):1439-1446.

- 30. Vinik AI, Vinik EJ. Diabetic neuropathies. In: Mensing C, Cornell S, Halstenson C (eds). The Art and Science of Diabetes Self-Management Education: A Desk Reference for Healthcare Professionals. 3rd ed. Chicago, IL: American Association of Diabetes Educators; 2014.
- 31. Venes D (ed). Taber's Cyclopedic Medical Dictionary. 22nd ed. Philadelphia, PA: FA Davis Company; 2013.
- 32. Roszler J. Sex and Diabetes and Much, Much, More! Paper presented at: American Association of Diabetes Educators Annual Conference. 2010; San Antonio, TX.
- 33. Goldbeck-Wood S. Obesity and poor sexual health outcomes. BMJ. 2010;340(19):1-5.
- 34. Fabbri A, Greco E, Aversa A. Erectile dysfunction. In: Leslie RD, Pozzilli P (eds). *Diabetic Complications*. London: Martin Dunitz; 2003: 55-72.
- 35. Brunton SA, Sadovsky R. Late-onset male hypogonadism and testosterone replacement therapy in primary care. J Fam Pract. 2010;59(7 Suppl):1-8.
- 36. Heidelbaugh JJ. Management of erectile dysfunction. Am Fam Physician. 2010;81(3):305-312.
- 37. Rew KT, Heidelbaugh JJ. Erectile dysfunction. Am Fam Physician. 2016;94(10):820-827.
- 38. Frank JE, Mistretta P, Will J. Diagnosis and treatment of female sexual dysfunction. Am Fam Physician. 2008;77(5):635-642.
- Esposito K, Maiorino MI, Bellastella G, Giugliano F, Romano M, Giugliano D. Determinants of female sexual dysfunction in type 2 diabetes. Int J Impot Res. 2010;22(3):179-184.
- 40. Phillips NA. Female sexual dysfunction: evaluation and treatment. Am Fam Physician. 2000;62(1):127-136.
- 41. Bø K. Pelvic floor muscle training in treatment of female stress urinary incontinence, pelvic organ prolapse and sexual dysfunction. *World J Urol.* 2012;30(4):437-443.
- 42. Ruggiero L, Wagner J, De Groot M. Understanding the individual: emotional and psychological challenges. In: Mensing C, Cornell S, Halstenson C (eds). The Art and Science of Diabetes Self-Management Education: A Desk Reference for Healthcare Professionals. 3rd ed. Chicago, IL: American Association of Diabetes Educators; 2014.
- 43. Gao L, Yang L, Qian S, Li T, Han P, Yuan J. Systematic review and meta-analysis of phosphodiesterase type 5 inhibitors for the treatment of female sexual dysfunction. *Int J Gynaecol Obstet.* 2016;133(2):139-145.
- 44. Chivers ML, Rosen RC. Phosphodiesterase type 5 inhibitors and female sexual response: faulty protocols or paradigms? J Sex Med. 2010;7(2 Pt 2):858-872.
- 45. Springhouse (ed). Nursing 2010 Drug Handbook. Philadelphia, PA: Lippincott, Williams & Wilkins; 2009.
- 46. LexiComp Online. Available at https://online.lexi.com. Last accessed March 18, 2021.
- U.S. Food and Drug Administration. FDA Approves Stendra for Erectile Dysfunction. Available at https://wayback.archive-it. org/7993/20170112023943/http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm302140.htm. Last accessed March 18, 2021.
- 48. Sanford M. Avanafil: a review of its use in patients with erectile dysfunction. Drugs Aging. 2013;30(10):853-862.
- 49. Wang H, Yuan J, Hu X, Tao K, Liu J, Hu D. The effectiveness and safety of avanafil for erectile dysfunction: a systematic review and meta-analysis. *Curr Med Res Opin.* 2014;30(8):1565-1571.
- 50. Kennedy S. Flibanserin: initial evidence of efficacy on sexual dysfunction, in patients with major depressive disorder. *J Sex Med.* 2010;7(10):3449-3459.
- Hitt E. FDA Advisory Committee Votes Against Flibanserin for Hypoactive Sexual Disorder. Available at https://www.medscape.com/ viewarticle/723896. Last accessed March 18, 2021.
- 52. Sprout Pharmaceuticals. Sprout Pharmaceuticals Appeals FDA Decision on New Drug Application for Flibanserin to Treat Hypoactive Sexual Desire Disorder in Premenopausal Women. Available at https://www.prnewswire.com/news-releases/sprout-pharmaceuticalsappeals-fda-decision-on-new-drug-application-for-flibanserin-to-treat-hypoactive-sexual-desire-disorder-in-premenopausal-women-235380991.html. Last accessed March 18, 2021.
- U.S. Food and Drug Administration. FDA Approves First Treatment for Sexual Desire Disorder. Available at https://wayback.archiveit.org/7993/20170112023753/http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm458734.htm. Last accessed March 18, 2021.
- 54. Khera M, Bhattacharya RK, Blick G, Kushner H, Nguyen D, Miner MM. Improved sexual function with testosterone replacement therapy in hypogonadal men: real-world data from the Testim Registry in the United States (TRIUS). J Sex Med. 2011;8(11):3204-3213.
- 55. Davis SR, Worsley R, Miller KK, Parish SJ, Santoro N. Androgens and female sexual function and dysfunction: findings from the Fourth International Consultation of Sexual Medicine. *J Sex Med.* 2016;13(2):168-178.
- 56. Davis SR, Moreau M, Kroll R, et al. Testosterone for low libido in postmenopausal women not taking estrogen. N Engl J Med. 2008;359(19):2005-2017.
- Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. JAMA. 2002;288(3):321-33.

- 58. Women's Health Initiative. Available at https://www.nhlbi.nih.gov/science/womens-health-initiative-whi. Last accessed March 18, 2021.
- 59. Elder JA, Braver Y. Female Sexual Dysfunction. Available at https://teachmemedicine.org/cleveland-clinic-female-sexual-dysfunction/. Last accessed March 18, 2021.
- 60. Enzlin P, Mathieu C, Van den Bruel A, Vanderschueren D, Demyttenaere K. Prevalence and predictors of sexual dysfunction in patients with type 1 diabetes. *Diabetes Care*. 2003;26(2):409-414.
- 61. American Diabetes Association. Sexual Implications of Emotional Health. Available at https://www.diabetes.org/resources/men/ sexual-implications-emotional-health. Last accessed March 18, 2021.
- 62. Solowiejczyk J. Diabetes and depression: some thoughts to think about. Diabetes Spectrum. 2010;23(1):11-15.
- 63. Khaledi M, Haghighatdoost F, Feizi A, Aminorroaya A. The prevalence of comorbid depression in patients with type 2 diabetes: an updated systematic review and meta-analysis on huge number of observational studies. *Acta Diabetol.* 2019;56(6):631-650.
- 64. Giugliano F, Maiorino M, Bellastella G, Gicchino M, Giugliano D, Esposito K. Determinants of erectile dysfunction in type 2 diabetes. Int J Impot Res. 2010;22(3):204-209.
- 65. Bostwick JM. A generalist's guide to treating patients with depression with an emphasis on using side effects to tailor antidepressant therapy. *Mayo Clin Proc.* 2010;85(6):538-550.
- 66. Kennedy SH, Rizvi S. Sexual dysfunction, depression, and the impact of antidepressants. J Clin Psychopharmacol. 2009;29(2):157-164.

Evidence-Based Practice Recommendations Citations

- Kalinowski A, Tinker T, Wismer B, Meinbresse M. Adapting Your Practice: Treatment Recommendations for Patients who are Homeless with Diabetes Mellitus. Nashville, TN: Health Care for the Homeless Clinicians' Network; 2013. Available at https://nhchc.org/wp-content/uploa ds/2019/08/2013DiabetesGuidelines_FINAL_20130612.pdf. Last accessed March 23, 2021.
- National Institute for Health and Care Excellence. *Type 2 Diabetes in Adults: Management*. London: National Institute for Health and Care Excellence; 2015. Available at https://www.nice.org.uk/guidance/ng28. Last accessed March 23, 2021.