



Review Article

Male sexual dysfunction and comorbidity

Snehil Gupta¹, Akash Kumar², Ashish Pakhre¹

¹ Assistant Professor, ²Senior Resident, Department of Psychiatry, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India

Date of Submission :

16 April 2022

Date of Acceptance :

17 May 2022

Keywords:

Male sexual dysfunction, Anxiety, Depression, Substance use, Personality disorder

Abstract

Introduction: Male sexual dysfunction is prevalent among individuals with psychiatric or physical comorbidities. Psychiatric disorders per se can cause male sexual dysfunctions; psychotropic medications used in their treatment can also result in male sexual dysfunctions. Thus, having sound knowledge about these variables would assist clinicians in comprehensive assessment and management. This paper aims to review existing literature on male sexual dysfunctions with co-morbid psychiatric and physical illnesses, including their management.

Methodology: PubMed and Google Scholar databases were searched, along with bibliographic- and grey literature search, to obtain relevant records. We described the findings of the review narratively.

Results: A total of 34 records were eligible for the current review. Male sexual dysfunctions are frequent with psychiatric (e.g., psychotic disorders, depression, substance use disorders) and physical (neurological-, cardiovascular-, and genitourinary

conditions) illnesses. Medications, both psychotropic, e.g., selective-serotonin-reuptake inhibitors, antipsychotics and non-psychotropic, e.g., beta-blockers, thiazides, are equally implicated in male sexual dysfunction. Therefore, treating underlying co-morbid illnesses,

reducing/discontinuing the offending drugs, and switching to an agent with lesser adverse sexual effects are the cornerstone of the management. Furthermore, using medications, e.g., phosphodiesterase inhibitors, devices like prostheses and implants, and correction of genito-urinary conditions are also equally important.

Conclusion: Better knowledge and understanding of sexual dysfunctions among co-morbid psychiatric or physical illnesses, adequate assessment, and formulation of a comprehensive treatment plan are crucial to addressing these comorbidities.

Corresponding author: Dr. Ashish Pakhre

Email: sjmc.ashish@gmail.com

How to cite the article: Gupta, S., Kumar, A., & Pakhre, A. (2022). Male sexual dysfunction and comorbidity.

Indian Journal of Health, Sexuality and Culture, 8(1), 12–30.

DOI: 10.5281/zenodo.6806176

This article is distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Introduction

Male sexuality is a complex physiological process involving the interplay of multiple bodily systems like the nervous systems, genitourinary systems and cardiovascular systems. Additionally, it is influenced by socio-cultural and psychosocial factors (Kandeel et al., 2001). The different factors affecting sexual function involve partner's sexual functions or general physical condition, relational aspects, e.g., poor communication, disparities in desire for sexual activity, history of sexual or emotional abuse, or psychiatric comorbidities such as depression, anxiety, etc., cultural or religious factors such as prohibitions concerning sexual activity (American Psychiatric Association, 2013). Besides these factors, aging results in the expected decline in the sexual responsiveness of an individual (Chung, 2019).

The male sexual cycle is divided into the excitement, orgasmic, and resolution phases. The excitement phase entails desire and erection, the orgasmic step entails ejaculation, while the resolution phase involves the general feeling of well-being and enhanced intimacy (Sadock et al., 2017; Wylie and Kenney, 2010).

The dysfunction in one phase of the sexual cycle may increase the risk of developing sexual dysfunctions in another domain, e.g., low sexual desire may result in an insufficient erection. However, these dysfunctions may also be completely independent, like the inability to attain erection despite an adequate or high degree of sexual attraction as the case in various organic or psychological disorders (Rowland et al., 2021).

Sexual dysfunction is a significant cause of poor quality of life (QoL), and treatment can be challenging if comorbidities or underlying aetiologies are not identified and managed. Some mental disorders (e.g., depression, schizophrenia) have sexual dysfunctions as manifestations of the disease itself, where treatment of primary diagnosis can lead to spontaneous improvement in sexual dysfunctions. Furthermore, medications used to treat these primary diagnoses (e.g., SSRIs for depression or beta-blockers for hypertension) can cause sexual dysfunctions or worsen them. In such cases, sexual dysfunction can cause poor

compliance, complicating the management (Ghormode et al., 2019; Montejo et al., 2018).

Despite the topic's significance, overall, there is a lack of literature differentiating various aspects of the male sexual dysfunction vs. female sexual dysfunction; literature tends to describe them together, which otherwise can have critical clinical implications (Kok, 2004). Moreover, the available literature is limited to studying only one/or two sexual dysfunctions, which can lead to missed diagnosis of other sexual dysfunctions. Additionally, if medical and psychiatry comorbidities are not assessed appropriately, the incidence and prevalence of sexual dysfunctions may be over or underestimated. Likewise, they can be wrongly attributed to the primary physical or mental disorders or the medications used. Furthermore, these co-morbid conditions can adversely affect the management of sexual dysfunctions (Polland et al., 2018).

Therefore, there is a need for an active comprehensive assessment of all sexual dysfunctions, not just relying on patient's reporting, rather evaluating underlying or co-morbid conditions to improve patient's quality of life and compliance to treatment.

Methodology: A literature search was undertaken by screening PubMed and Google Scholar databases. Search terms used were male sexual dysfunctions, erectile dysfunction (ED), hypoactive sexual desire disorders, ejaculation problems, premature ejaculation (PME), delayed ejaculation, anorgasmia, disorders of orgasm (for sexual dysfunctions); psychiatric disorders/illnesses, mental issues, mental disorders (for psychiatric comorbidities); and medical comorbidities, physical illnesses/disorders (for medical comorbidities).

Findings: The search resulted in 822 articles. Upon title and abstract screening and subsequent full texts screening, only 34 articles were relevant for the review. The highest number of the studies were related to sexual dysfunctions with co-morbid cardiovascular disorders (n=9), followed by endocrinological disorders (n=7), including metabolic syndrome and androgen deficiency states, chronic medical disorders as a whole

(n=4), treatment of sexual dysfunctions in chronic medical illnesses (n=4), urogenital and age-related sexual dysfunction (n=1 each). Concerning the mental disorders and co-morbid sexual disorders (n=9), the highest number of the studies were on depression (n=3), followed by mental illnesses as a whole (n=3), schizophrenia (n=2) and psychotropic-induced sexual dysfunctions (n=1).

A. Male sexual dysfunction and co-morbid medical conditions

A recent systematic review and meta-analysis from Ethiopia involving both institute-based and community-based participants showed the pooled prevalence of sexual dysfunction to be 68.04% (Abosetugn and Yehualashet, 2021). Likewise, another meta-analysis reported the pooled prevalence of erectile dysfunction in diabetes mellitus to be 71.45% (Shiferaw et al., 2020). However, here authors did not describe the setting of the study. Similarly, a recent meta-analysis involving 34 studies conducted on chronic kidney disease patients reported an overall prevalence of erectile dysfunction to be 76% (Pizzol et al., 2021). In medical conditions, assessment and management are challenging and need detailed knowledge of various medical illnesses and pathophysiology. It is equally important to rule out psychogenic factors leading to sexual dysfunctions in patients suffering from medical diseases.

Etiological aspects of sexual dysfunction with co-morbid medical illness

Medical illnesses can affect sexual functioning in various ways and have myriad explanations. It is crucial to note that many patients may have a multifactorial etiology for sexual dysfunctions. Other conditions that can substantially affect sexual function are advanced age, chronic diseases, malnutrition, medication side effects, nicotine, drug and alcohol use, and abuse.

One of the more difficult challenges clinicians faces when treating erectile disorder (ED) is ruling out conditions most likely attributable to medical factors. Apart from psychological factors, ED can have several physiological etiologies. Acquired ED has been associated with

biological factors, including diabetes, cardiovascular diseases (CVDs), neurological illnesses, etc. It is important to understand that whether erectile dysfunction is caused by psychological factors or medical disorders.

Additionally, there are modifiable risk factors for acquired ED, such as sedentary lifestyle, diabetes, etc., that should be considered. Finally, the treatment of medical conditions threatens the development of sexual dysfunctions. For example, cytotoxic drugs, hormonal agents, and cardiovascular medications have been implicated in various sexual dysfunctions.

Pathophysiology of sexual dysfunction and medical diseases

Optimal sexual functioning can be affected by various implicating factors related to medical illnesses. Ejaculation can be compromised due to interruption in the nerve supply to the genitalia; such complications can occur in surgeries in the abdominal region, where traumatic injury can occur to lumbar sympathetic ganglia (Clayton and Ramamurthy, 2008). Prostatectomy or any genitourinary surgery in males can cause failure in ejaculation as a complication. Many neurodegenerative diseases like multiple sclerosis, diabetic neuropathy, and alcoholic neuropathy can affect the autonomic nervous system, affecting ejaculation. Ejaculation is regulated by the Hypogastric (sympathetic) nerve and Pudendal (parasympathetic) nerve. There is a loss of fast conducting peripheral sensory nerves and reduced steroid secretion with aging, which causes delayed ejaculation in elderly males. In males, the inability to experience orgasm may stem from neurological disorders affecting the lumbosacral spine or pain and paraesthesia from external genitalia (Clayton and Ramamurthy, 2008; Imprialos et al., 2018; Zemishlany and Weizman, 2008).

Neurological disorders

Neurodegenerative disorders like Alzheimer's disease, frontotemporal dementia, amyotrophic lateral sclerosis, dementia with Lewy Bodies, multiple system atrophy, cortico-basal degeneration, progressive supranuclear palsy, Huntington's disease can result in a disturbance in autonomic

function, pain, and interruption in sensory-motor coordination. It is also understood that sexual problems can be due to medications used to treat neurodegenerative disorders and movement disorders (Malcher et al., 2021). Spinal cord injury can affect or reduce nerve impulses from the brain to the penis and lead to ED. Pelvic injuries can cause nerve disruption and cause ED.

Cardio-vascular disorders

Hypertension leads to increased peripheral sympathetic activity, heightened vasoconstrictor tone, and reduced endothelium-dependent vasodilation. Changes in the cyclooxygenase pathway can play a crucial role as they can cause an increase in reactive oxygen species and cause more damage to normal endothelial functioning. It is to be emphasized that many disease states will have endothelial-dependent vasodilation in dysfunctional form. Hypertension can affect sexual function in many ways, including causing endothelial abnormalities, and reduced vasodilatory capacity occurs as structural alterations in vascular and corporal remodeling.

Endocrinological conditions

Sexual dysfunctions are common, particularly among individuals with diabetes mellitus, hypothyroidism, and an androgen deficient state (Burger and Papalia, 2006; Clayton and

Ramamurthy, 2008). In males with SD, who has diabetes, hardening and narrowing of blood vessels supplying the erectile tissue of genitalia occur. Furthermore, diabetes mellitus directly affects erection through the nervous system.

Uro-genital disorders

In rectal cancer patients receiving proctectomy for treatment, sexual dysfunction is commonly seen. It is noticed that males report long-standing distress even after years of surgery. ED can occur due to interruption in the inferior hypogastric plexus, and disruption in the superior hypogastric plexus leads to ejaculatory problems (Shivananda and Rao, 2016).

The male endocrine system is affected by chronic kidney diseases, resulting in diminished testosterone levels. Low testosterone levels occur due to hypogonadotropic hypogonadism. There is also reduced libido and altered body image and fertility. Hormonal actions are affected as progressive renal dysfunction continues to occur. Metabolism of hormones or excretion by kidneys is altered. Due to chronic renal dysfunction, circulating binding proteins are changed, and concentration is disturbed. Hyperprolactinemia is also observed in chronic kidney disease patients, resulting in ED, reduced libido, gynecomastia, and infertility (Edey, 2017).

Table 1: Sexual dysfunctions related to chronic medical illness

Mechanism	Medical Conditions and Factors
Influence on libido due to nonhormonal medications	Narcotics can depress desire through gonadotropin suppression. SSRIs reduce desire and response
Alteration in sexual desire due to diseases	Typically reduced due to hyperprolactinemia and anemia of chronic renal failure. It may be increased in some brain disorders (Kluver-Bucy syndrome, frontal lobe lesions).
Influence of pain on sexual desire and response	Pain d/t medical condition (e.g., neurological/ cancer pain) are potent sexual distraction
Disease-causing interruption in genital response	ED from multiple sclerosis, hypertension, orgasmic disorder from multiple sclerosis
Effect of antiandrogen treatment on sexual desire	Gonadotropin-Releasing Hormone (GnRH) therapy in prostate cancer
Disruption of genital response from surgery	Radical prostatectomy and ED
Disruption of sexual desire and response from chemotherapy	Testicular failure after intensive chemotherapy for hematopoietic transplantation

d/t: due to, ED: erectile dysfunctions, SSRIs: selective serotonin reuptake inhibitors

B. Psychiatric comorbidities with sexual dysfunctions

Literature suggests a bidirectional association between sexual dysfunction and different mental health disorders. Sexual dysfunction is more prevalent in individuals with psychiatric illnesses (about 50%) compared to the general population and those with medical conditions. Further, among psychiatric disorders, sexual dysfunction is more common in schizophrenia (about 75%), followed by bipolar disorders (>50%), depressive

disorders (40 to 50 %), and anxiety disorders (about 20%) (Abdelatti et al., 2020).

When comparing sexual dysfunctions among mental disorders, sexual dysfunctions affecting orgasm and satisfaction were more common in schizophrenia than in bipolar disorders, depressive disorders, and anxiety disorders. In contrast, the incidence of ED and hypoactive sexual desire disorders was similar among different mental disorders (Abdelatti et al., 2020). Table 2 lists the typical sexual dysfunctions usually co-morbid with various psychiatric

Table 2: Common sexual dysfunctions (Sexual dysfunctions) co-morbid with psychiatric disorders

Psychiatric disorders	Comorbid Sexual dysfunctions	Remarks
Psychosis	<ul style="list-style-type: none"> Reduced desire, ED, PME^{1,2} 	
Bipolar disorder	<ul style="list-style-type: none"> Hypersexuality during mania / hypomania Decreased libido during depressive phase 	<ul style="list-style-type: none"> May be a manifestation of underlying psychopathology or disinhibited behaviour
Depression	<ul style="list-style-type: none"> Common sexual dysfunctions - sexual arousal disorders, ED, lower subjective arousal Fewer minutes of NPT, penile rigidity Sexual desire disorders: decreased libido and sexual desire Some reports of increased libido sexual desire Less satisfaction with sexual activities 	<ul style="list-style-type: none"> The severity of illness correlates with the prevalence of SD³
OCD	<ul style="list-style-type: none"> Lower sexual arousal, PME, ED, and sexual dissatisfaction 	<ul style="list-style-type: none"> Fewer studies on men
GAD	<ul style="list-style-type: none"> Affects all phases of the sexual response cycle 	<ul style="list-style-type: none"> Performance anxiety and cognitive distortions about sexuality are common.
Panic disorders	<ul style="list-style-type: none"> PME, ED, sexual aversion, MHSDD, orgasmic disorder 	<ul style="list-style-type: none"> Impact of socio- cultural factors is more pronounced.
Social phobia	<ul style="list-style-type: none"> Most common - PME, Lower frequency of orgasm, decreased arousal, less sexual satisfaction 	
PTSD	<ul style="list-style-type: none"> Most common: ED and increased sexual frequency; Others- PME, MHSDD, Sexual avoidance, dissatisfaction, Lower sexual desire, arousal, activity, satisfaction 	<ul style="list-style-type: none"> Past traumatic events often result in Sexual dysfunctions Lack of trust in the partner and perceived vulnerabilities are common attributes of sexual dysfunctions in these population
Behavioral & psychological symptoms of dementia (BPSD)	<ul style="list-style-type: none"> Sexual disinhibition⁴ 	<ul style="list-style-type: none"> Due to memory and cognitive decline

ED: erectile dysfunction, PME: premature ejaculation, NPT nocturnal penile tumescence, MHSDD: Male hypoactive sexual desire disorder, OCD: Obsessive compulsive disorder, GAD: Generalized anxiety disorders, PTSD: posttraumatic stress disorder,

1. Macdonald et al., 2003 2. Malik, 2008 3. Clayton et al., 2014 4. Sadock et al., 2017

Sexual dysfunction in schizophrenia or psychosis may be an independent phenomenon associated with the core psychopathology like negative-, cognitive-, positive symptoms (delusion/hallucination) (Sadock et al., 2017) or antipsychotic-induced (Bitter et al., 2005). Additionally, substance use like nicotine or alcohol in these patients may further affect sexual function (Macdonald et al., 2003; Malik, 2008).

Mood disorders, including bipolar and depressive disorders, also have high comorbidity with sexual dysfunction (Kennedy et al., 1999; Waldinger, 2015). Any sexual conditions may arise in depression, and the most common is loss of libido (Clayton et al., 2014; Laurent and Simons, 2009a). However, some patients with depressive disorders may have increased libido (a typical feature), indicating a mixed episode or bipolarity. Sexual dysfunction in mood disorders can be due to anhedonia in a depressive episode and hypersexuality or disinhibition as a manifestation of a mania or hypomania episode. Sexual disinhibition may also be seen in a background of memory impairment and confusion in cases of pseudodementia or dementia (Nordvig et al., 2019). In bipolar disorders, patients usually have alternating decreased desire and hypersexuality according to the current phase of illness. Furthermore, sexual dysfunctions in mood disorders may be related to antidepressants, mood stabilizers, or agents like benzodiazepines, anticholinergics, and anticonvulsant drugs (La Torre et al., 2014a).

Similarly, any sexual problem may arise with anxiety disorders, but decreased sexual desire and sexual aversion are more prevalent. Concerning anxiety-spectrum disorders, generalized anxiety disorders (GAD) can affect all stages of the sexual cycle (Johnson et al., 2004; Laurent and Simons, 2009a), while obsessive-compulsive disorders (OCD) (Monteiro et al., 1987) and panic disorders (Figueira et al., 2001) are often associated with decreased sexual desire and sexual aversion. Moreover, these may also result in decreased arousal, pain, and reduced satisfaction. Social phobia may diminish sexual desire and causes PME, but it may also impair other phases of the sexual cycle (Bodinger et al., 2002; Laurent and Simons, 2009a). Post-

traumatic stress disorder (PTSD) has been linked to sexual aversion, pain, ED, and PME (Kotler et al., 2000; Solursh and Solursh, 2011). While there is a dearth of systematic research relating sexual functioning to anxiety disorders, most data demonstrate significant correlations between sexual dysfunction and multiple aspects of anxiety (Laurent and Simons, 2009a).

C. Psychotropic medications and sexual dysfunctions

Although psychotropic medications can improve sexual dysfunctions by correcting underlying psychopathologies, they also risk precipitating or worsening sexual dysfunction. The susceptibility and type of sexual adverse effects vary from the class of drugs and from person to person. Most of the sexual dysfunctions caused by them are reversible and resolve after the cessation of the offending agent. Nevertheless, again, clinical trial's assessment of sexual adverse effects is limited by the lack of validated questionnaires and proper controls in studies (Khin et al., 2015). Sexual functions result from intricate interactions between the cardiovascular, musculoskeletal, sympathetic, and parasympathetic nervous systems of the human body. Additionally, various drugs can affect sexual function by one or the other mechanism (Kandeel et al., 2001). Table. 4 lists the major categories of psychotropics and sexual dysfunctions associated with them.

Among antipsychotics, the most crucial cause for various sexual dysfunctions is hyperprolactinemia, esp. with first-generation antipsychotics, while sexual dysfunctions are less common with prolactin-sparing antipsychotics (Aizenberg et al., 1995; Raja, 1999; Serretti and Chiesa, 2011; Smith, 2003). Consequently, the risk of sexual dysfunction is highest with risperidone and haloperidol and lesser with agents like aripiprazole and quetiapine (Baggaley, 2008; Bitter et al., 2005; Montalvo et al., 2013; Peluso et al., 2013). Similarly, asenapine (Ajmal et al., 2014), brexpiprazole (Citrome, 2015), cariprazine (Nasrallah et al., 2017), and lurasidone (Citrome et al., 2012) are not known to cause sexual dysfunctions.

Among antidepressant medications, selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), and monoamine oxidase inhibitors (MAOI) are well known for affecting all stages of the sexual cycle, the most common being delayed ejaculation (Sadock et al., 2017; Torre et al., 2013). These sexual dysfunctions are often dose-dependent and reversible (Clayton et al., 2014; Wagner et al., 2018). The incidence and the type of sexual dysfunctions among different antidepressants vary depending on the drug's pharmacological profile. Drugs like Bupropion, mirtazapine and mianserine, reboxetine, are milnacipran safer in this regard (Cleare et al., 2015; Reichenpfader et al., 2014). Some of these adverse effects are even clinically utilized to treat sexual dysfunctions, for instance, dapoxetine's use in PME (McMahon, 2012) or use of trazodone for ED (Montejo et al., 2018).

Another important class of psychotropics is mood stabilizers, including drugs like lithium and anticonvulsants like valproate, carbamazepine, etc. Lithium monotherapy is not commonly associated with significant sexual dysfunctions. However, sexual dysfunction can occur with it, particularly when used with other drugs, e.g., benzodiazepines, whereas anticonvulsants can cause decreased libido due to their testosterone lowering potential (Lossius et al., 2007).

However, it should be underscored that most of the data on anticonvulsants related sexual dysfunctions pertaining to their use on patients with epilepsy and as we know, epilepsy can have an independent effect on sexual dysfunction. Thus, the independent effect of these agents in patients without epilepsy needs further studies (La Torre et al., 2014b).

Anxiolytics can adversely affect sexual functioning. Benzodiazepines such as clonazepam can cause sexual dysfunctions secondary to sedation and muscle relaxation. However, considering their frequency of use, the risk is only small. In contrast, some anxiolytics like buspirone may improve sexual dysfunctions especially in cases associated with significant anxiety (Gitlin, 2003).

Literature suggests that both illicit (opioids, marijuana, cocaine, stimulants, etc.) and licit substance (alcohol, tobacco smoking) use (in males) can result (Table 4) in significant sexual dysfunction (Johnson et al., 2004). The opioids are associated with high rates of sexual dysfunction, both while being used and after the cessation. Sexual dysfunctions can also occur during the opioid substitution therapy (methadone & buprenorphine) and opioid-antagonist treatment (Naltrexone) (Nik Jaafar et al., 2013; Ramdurg et al., 2012; Sathe et al., 2001).

Table 3: Effect of medications on sexual functioning

Medications	Effect on sexual functioning
Cardiovascular medications: antihypertensives, antiarrhythmics, beta-blockers, calcium channel blockers, diuretics, lipid-lowering medications, vasodilators, combination agents	Erectile dysfunction, Decreased libido in both genders and Ejaculatory or orgasmic delay or inhibition
Chemotherapeutic agents: antineoplastic, cytotoxic agents, anti-metabolites, alkylating agents, hormones, immunomodulators	These drugs have high toxicity; however, their impact on sexual functioning is poorly studied. Decreased libido is a frequent complication of chemotherapeutic agents.
Medications used in urogenital system: drugs used for urinary incontinence, benign prostatic hypertrophy prostatic and/or cancer	Finasteride is associated with ED or delayed ejaculation. Imipramine (TCA), used in enuresis and occasionally in incontinence, commonly cause ED and other impairment of sexual functioning
Medications used in neurology: antiepileptics, antiparkinsonian medications, anti-migraine medications	Decreased libido. Carbamazepine affects levels of sex hormones and SHBG. Antiparkinsonian drugs may result in hypersexuality

ED: erectile dysfunction, SHBG: sex hormone-binding globulin, TCA: tri-cyclic antidepressants

Likewise, agents like cocaine, cannabis (marijuana), and psychostimulants (3,4-Methylenedioxyamphetamine (MDMA)), although initially can enhance some aspects of the sexual functioning of an individual, in the long run, they can result in sexual dysfunctions in the form of erectile dysfunction, decreased libido, and anorgasmia (Johnson et al., 2004; McElrath, 2005; Sadock et al., 2017; Zemishlany et al., 2001). Alcohol use can have short and long-term effects on different phases of the sexual cycle (mostly leading to ED), with an overall prevalence of sexual dysfunction being 40-95% (Grover et al., 2014). Similarly, tobacco smoking can lead to ED either by its independent effect or by enhancing the pathological changes due to other systemic diseases like cardiovascular diseases, hypertension, and diabetes mellitus (Kovac et al., 2015).

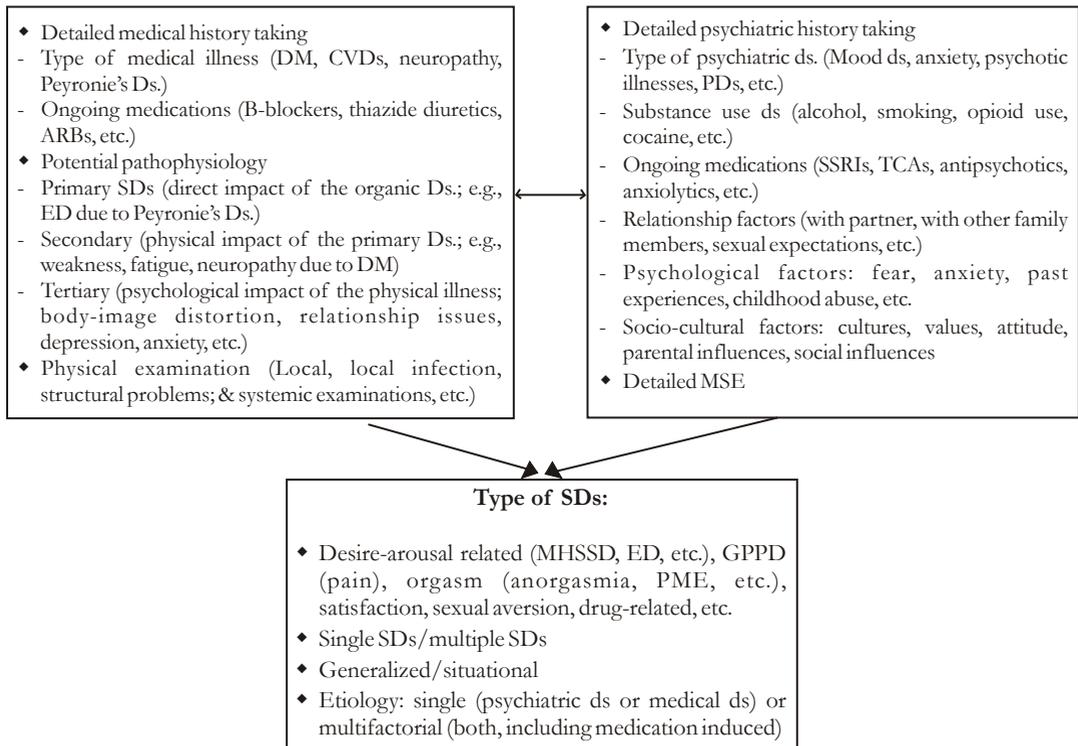
Commonly used agents like antihistaminic and anticholinergic drugs may also lead to sexual

dysfunctions by blocking cholinergic receptors, which play an essential role in erection. Lastly, the alpha and beta receptor antagonists affect sexual function by decreasing the sympathetic tone and vascular changes (Sadock et al., 2017).

Assessment and management of the sexual dysfunction in individuals with co-morbid medical/psychiatric illnesses

Assessment: A thorough evaluation should start with establishing rapport with the patient, including being sensitive to his socio-cultural background and exploring his belief system. The clinician must provide adequate time and support to the patient to share his difficulties. Furthermore, confidentiality must be maintained at all costs; partners/significant others can be involved in treatment if the patient wishes to (Figure 1).

Figure 1: Flow-diagram of the assessment of sexual dysfunction in individuals with medical/psychiatric comorbidities



ARBs: angiotensin-receptor blockers, DM: diabetes mellitus, MAOI: monoamine oxidase inhibitors, MHSSD: male hypoactive sexual desire disorders, MSE: mental state examination, PDs: personality disorders, PME: premature ejaculation, SDs: sexual dysfunctions, SSRIs: selective serotonin reuptake inhibitors, TCAs: tri-cyclic antidepressants,

First and foremost is enquiring about the sexual functioning (or dysfunction) of all the individuals with chronic medical conditions or co-morbid psychiatric disorders, particularly considering the high prevalence of sexual dysfunctions in these patients (Figure 1).

Furthermore, sexual dysfunctions should be considered a continuum with medical and psychiatric disorders rather than having a dual notion (Basson and Gilks, 2018). The cornerstone of a comprehensive assessment includes detailed medical and psychiatric history taking, including psychoactive substance (PAS) use, and conducting a thorough physical and mental state examination, respectively. A close look at their medical records, including those of allied disciplines (e.g., urologists, neurologists, endocrinologists, etc.), and being aware of the impact of the co-morbid medical/psychiatric illnesses and their medications on sexual dysfunctions are vital. A detailed physical examination, both local (e.g., any structural abnormality, infection) and systematic examinations (peripheral pulse, neurological examination, etc.), is imperative.

A detailed psychiatric history must incorporate early childhood experiences, including abuse, and personality traits (emotionally unstable, narcissistic, anxious-avoidant, or anankastic, etc.) (Clayton and Ramamurthy, 2008; Zemishlany and Weizman, 2008). Additionally, the Mental State Examination should explore the co-morbid mood-, anxiety-, or substance use disorders. Furthermore, cognitive distortions (e.g., body-image concerns), cognitive functioning, judgment, and insight about the ongoing illnesses (or motivation to quit substances) must also be adequately assessed.

Additionally, the meaning of sexuality for the patients and how current sexual dysfunctions have affected various domains of his life must be explored. Furthermore, their treatment outcome expectancies should be part of a comprehensive assessment.

Proper liaising with specialists of allied disciplines (e.g., neurologist, urologist) would help the mental health professionals/psycho-

sexual medicine specialists conduct a proper assessment and formulate a robust treatment plan.

Additionally, a detailed inquiry about the psychological, cognitive, socio-cultural, relational, and QoL aspects of the patients about sexuality and sexual dysfunctions are vital. Involving a partner early in the treatment process, as the patient wishes to, can have both short and long-term positive effects (Zemishlany and Weizman, 2008).

Identifying the cause of sexual dysfunction has a considerable impact on the diagnosis. Sexual dysfunctions can be the direct effect of the underlying physical/psychiatric illness (Primary Sexual Dysfunctions) or secondary to the physical effects of the underlying disease, e.g., weakness, neuropathy, easy fatiguability of the depression, etc. (Secondary Sexual Dysfunctions) or an outcome of the psychological impact of the physical illness, e.g., body-image distortions, relationship issues, performance anxiety, etc. (Tertiary Sexual Dysfunctions) (Clayton and Ramamurthy, 2008).

Sexual dysfunction has multifactorial etiologies, or they are outcomes of complex interaction among several variables. Apart from the bio-psychological factors, socio-cultural factors also play a huge role in determining an individual's sexual function (or dysfunction) and the latter's implications in one's life. The Diagnostic and Statistical Manual-5 of mental disorder (DSM-5) also highlights this aspect when it describes how socio-cultural factors can determine the clinical manifestations of various sexual disorders, the perceived level of morbidity among the individuals, their motivation to seek treatment for those problems, and the kinds of treatment one may be willing to receive (American Psychiatric Association, 2013). Thus, identifying these interrelationships is an essential part of the assessment and subsequent management.

Questionnaire-based assessment of sexual functioning (e.g., sexual functioning questionnaire) may assist a health professional in a thorough exploration of sexual functioning across different domains (Smith et al., 2002).

Furthermore, it aids in identifying cooccurring sexual dysfunctions, e.g., ED with PME, decreased desire associated with the arousal problems, genital pain/penetration problems, and sexual dissatisfaction. Thus, ensuring any crucial aspect of sexual issues is not missed (Zemishlany and Weizman, 2008).

Management: Managing sexual dysfunction with co-morbid physical/ psychiatric illnesses is often challenging for clinicians. However, there are some general principles that, if followed, can help in the comprehensive management and attaining a good outcome.

- 1) Adequate psychoeducation to the patient about the nature of the condition, treatment, course, and outcome
- 2) Employing a multi-disciplinary approach (involving specialists of allied disciplines)
- 3) Addressing patient's/partner's concerns, (his) intra and (their) interpersonal issues, and treatment expectancies
- 4) Removing modifiable risk factors like offending medications, psychoactive substance use, psychosocial issues, local pathologies, etc.
- 5) Treating by considering the cultural values of the patient and his meaning of normal sexual functioning
- 6) Unfounded or unrealistic expectations from the treatment should be addressed then and there itself
- 7) Stepped care approach: choosing a less invasive treatment first (psychosocial interventions, lifestyle modifications, etc.) then, depending upon the response, going for more intensive therapies (medications, devices, and surgeries)

The management of common physical illnesses co-morbid with the sexual dysfunctions has been described below (Table 5):

Cardiovascular disorders: Sexual dysfunctions, particularly ED, often herald underlying cardiovascular diseases (Reffellmann and Kloner, 2006). Anti-hypertensives, particularly non-selective sympatholytic drugs, e.g., propranolol, angiotensin receptor blockers (enalapril, etc.)

and thiazide diuretics can worsen ED (al Khaja et al., 2003). Similarly, nitrate should be avoided in individuals requiring phosphodiesterase inhibitors (e.g., Sildenafil) for treating ED. With PDEIs, nitrate can result in significant hypotension, precipitating unstable angina or myocardial infarction. However, cardio-selective beta-blockers and Angiotensin-Converting Enzyme Inhibitors are safer options. Additionally, phosphodiesterase inhibitors such as sildenafil or tadalafil effectively manage ED in these individuals.

Neurological disorders: Sexual dysfunctions arise secondary to decreased genital sensation, absent lubrication, decreased desire secondary to gonadotropin deficiency, etc. Phosphodiesterase inhibitors are usually less effective in these conditions (Demirkiran et al., 2006; Rees et al., 2007). Testosterone supplementations, lubricants, dopamine agonists (e.g., ropiranoole), and invasive procedures such as intra-cavernous vasodilators (papaverine, prostaglandins, etc.), and vacuum tumescence are effective. It is also crucial that the clinicians attend to the psychosocial problems arising secondary to neurological conditions in patients through proper psychoeducation and psychotherapies (Clayton and Ramamurthy, 2008). Finally, early rehabilitation and addressal of stroke patients' nutritional, cognitive, and emotional needs can ameliorate their sexual dysfunctions (Rees et al., 2007).

Endocrinological diseases: ED is prevalent in individuals with Diabetes Mellitus (secondary peripheral neuropathy, body-image distortions, intra-/interpersonal issues, co-morbid depression, etc.), thyroid disorders, and androgen deficiency (Bhasin et al., 2007). Adequate glycaemic control, achieving a euthyroid state, and testosterone replacement therapy are effective treatment options for these conditions, respectively (Table 5). Furthermore, the associated psychological problems could be managed with evidence-based non-pharmacological interventions such as Cognitive Behavioural Therapy for co-morbid mild-moderate depression and body-image distortions and couple therapy for marital issues. PDEIs can also be added for erectile dysfunctions.

Genito-urinary conditions: Prostatitis, Peyronie's disease, chronic renal failure (CRF), etc., are frequently associated with sexual dysfunction (Clayton and Ramamurthy, 2008; Soykan et al., 2005). Treating underlying infection/inflammation, using PDEIs, encouraging coital activities, particularly in Peyronie's disease where spontaneous improvement is likely (Basson and Schultz, 2007; Mynderse and Monga, 2002), correcting the hormonal or metabolic abnormalities (in case of CRF), and whenever required medications (PDEIs for ED) or other non-invasive procedures are key steps.

Metabolic syndrome or obesity: Decreased desire and ED are common among individuals suffering from metabolic syndrome or obesity (Lee et al., 2012). Lifestyle modifications (e.g., smoking cessation, proper diet); PDIEs (for ED), testosterone replacement therapy, and aromatase inhibitors, e.g., Letrozole (for hypogonadism); psychosocial interventions (for underlying fear, anxiety, cognitive distortions, etc.); and surgical procedures, whenever required, such as bariatric surgery, the intra-penile prosthesis can significantly improve sexual functioning and QoL (Vaishnav et al., 2022).

As highlighted above, co-morbid psychiatric disorders or psychological problems have a bi-directional relationship with sexual dysfunction. Some of the essential considerations while managing these individuals have been enumerated in Table 5.

Depression: Commonly used antidepressants such as SSRIs, TCAs, and MAOIs further worsen sexual functioning (lead to ED, delayed ejaculation, anorgasmia, etc.). Hence, management of sexual dysfunctions in co-morbid depression is decreasing the dose of the offending agent, drug holiday, and switching to a drug with favorable sexual functioning profiles such as mirtazapine, mianserin, trazodone/nefazodone, bupropion, or addition of buspirone (5HT_{1a} partial agonist) or cyproheptadine (5HT_{2A} antagonist) (Laurent and Simons, 2009b) are crucial strategies. Furthermore, PDEIs (sildenafil 25mg OD/BD or Tadalafil 10-20mg OD to be used before the act) are particularly useful for ED.

Anxiety and related disorders: Social anxiety disorders often result in performance anxiety leading to ED and PME (Laurent and Simons, 2009b). Similarly, past experiences of individuals with PTSD predispose them to several sexual dysfunctions; even anxiolytic induced (e.g., clonazepam) sexual dysfunctions are common among them. Likewise, for depression, mirtazapine, buspirone, and PDEIs are effective medications for these symptoms. Additionally, psychodynamic psychotherapy (to allay the unconscious conflicts), Cognitive Behavioural Therapy, Behavioural Therapy (e.g., relaxation therapy, systematic desensitization, etc.), and couple therapy can effectively manage sexual dysfunction with co-morbid anxiety disorders (Zemishlany and Weizman, 2008).

Schizophrenia and other psychotic diseases: Negative and cognitive symptoms of schizophrenia and antipsychotic medications used in its treatment can lead to sexual dysfunction. Managing underlying symptoms through pharmacological or non-pharmacological intervention, or through both can lead to reversal of sexual dysfunctions. However, antipsychotic medications, particularly first-generation antipsychotics (e.g., haloperidol, chlorpromazine) can cause or worsen sexual dysfunctions in these individuals. In contrast, SGAs have the lesser potential of causing them, albeit within-class variations, with clozapine having a comparable risk to FGAs. Risperidone (moderate risk) and olanzapine, quetiapine, and aripiprazole (least risk) are safer alternatives. Likewise, treatment of sexual dysfunction with co-morbid depression, decreasing the dose, switching to antipsychotics with lesser sexual adverse effects, adding PDEIs, and couple therapy is the cornerstone of the management (Zemishlany and Weizman, 2008).

Personality disorders: Sexual disorders are common in individuals with personality disorders, particularly with emotionally unstable personality disorders and narcissistic PD. Sexual dysfunctions emanate from past unpleasant experiences, intra/interpersonal psychological issues, and co-morbid mood or anxiety disorders (Zemishlany and Weizman, 2008). Attending to these psychological issues, coupled with psychological interventions for the personality

issues such as psychodynamic psychotherapy, dialectic behavioral therapy, CBT, etc., or the addition of PDEIs are valuable strategies to address sexual dysfunction.

Substance use disorders: Apart from the direct effect of the substances on the sexual functioning of users, psychosocial (e.g., relationship problems with the spouse, adverse cognitive consequences) and physical complications (e.g., Human Immunodeficiency Virus/Acquired Immuno-deficiency Syndrome, Sexually Transmitted Diseases, neuropathy associated with alcohol use) with them can also precipitate or worsen the sexual disorders (Palha and Esteves, 2008). Sexual dysfunctions, if not adequately managed, can lead to frequent relapses in substance use.

Attaining abstinence from substances through various pharmacological or non-pharmacological means, e.g., family therapy or marital therapy, additional PDEIs, and treating underlying mood or anxiety disorders & co-morbid physical illnesses are cornerstones of management.

Others: Both physical and psychological complications of eating disorders such as body-image distortion, overvalued ideas about sexual activities, and cognitive distortions can result in various sexual dysfunctions (Castellini et al., 2016). Non-pharmacological interventions such as psycho-education about sexuality and systematic desensitization are helpful treatment options for these individuals (Zemishlany and Weizman, 2008).

Table 4: Psychotropics, associated sexual dysfunction, and underlying mechanisms

Psychotropics	Sexual dysfunction	Mechanism of action (MOA)
Antipsychotics	<ul style="list-style-type: none"> • Phenothiazines: lower dose: delayed orgasm, higher dose: normal orgasm without ejaculation¹ • Haloperidol: Sexual dysfunction in about 70% of patients and Sexual dysfunctions similar to phenothiazines² • Risp. & palip.: Sexual dysfunction in 60 -70% of patients^{2,3}: ejaculatory problems like retrograde ejaculation⁴ • Olanz. : Sexual dysfunction in >50% of patients priapism⁵ • Clzp. - ED and ejaculation difficulty, disorders of arousal, priapism • Sulpiride/amisul.: Sexual dysfunction prevalence equal to other SGA⁶ • Thioxanthenes: arousal & orgasmic issues⁷ 	<ul style="list-style-type: none"> • Hyperprolactinemia d/t Dopamine antagonism : decreased libido • Anticholinergic effects : disorders of arousal • Blockade of peripheral alpha 1 receptor : ED, ejaculation • Block of both alpha 1 and cholinergic receptors : priapism • AP induced sedation and weight gain : reduced sexual desire
Antidepressant	<ul style="list-style-type: none"> • SSRIs: high rates of Sexual dysfunctions across all the SSRIs, Higher frequency of Sexual dysfunctions (>30%) with fluoxetine, fluvoxamine, paroxetine and sertraline⁸ • TCA: More common with clomi, amitrp. & imi.; less common with secondary amines (desi., nortryp.) • MAOIs: incidence is 20-42%⁹ • Agomelatine: no significant Sexual dysfunctions⁹ • Bupropion: no significant Sexual dysfunctions¹⁰ • Duloxetine: can affect all stages of sexual cycles. • Mirtaz., rebox., traz., milnacpr., mians. Sexual dysfunctions< SSRIs¹¹ • Venlafaxine - can affect all stages • Vilazodone: can involve all stages but low risk • Vortioxetine: can affect arousal & orgasm¹² 	<ul style="list-style-type: none"> • Serotonergic agents: inhibit orgasm • Alpha 1 blockade: DE, Trazodone: alpha1 block: priapism • others: sedation, hormonal changes, disturbance of cholinergic/adrenergic balance, peripheral α -adrenergic agonism, inhibition of NO
Mood stabilizer	<ul style="list-style-type: none"> • MHSDD • Anorgasmia (gabapentin) • Li: reports of Sexual dysfunctions with concomitant use of other agents. • CBZ: decreased libido • Ox-CBZ- less likely to be associated with sexual dysfunctions 	<ul style="list-style-type: none"> • Lithium: not well understood • Anticonvulsants: lowers free testosterone level due to enzyme induction
	<ul style="list-style-type: none"> • Valproate: lower rate of sexual dysfunctions (in male) • Lamotrigine: no data 	

Anxiolytics like Benzodiazepines (BZD)	<ul style="list-style-type: none"> Anorgasmia, decreased libido, ED Incidence- not known It can also cause sexual disinhibition (clonazepam) and increased sexual desire (lorazepam) Buspirone: Sexual dysfunctions is rare; reports of reversing Sexual dysfunctions¹³ 	<ul style="list-style-type: none"> May be secondary to sedation and excessive muscle relaxation Decreases plasma epinephrine concentrations l/t reduced anxiety, hence can improve sexual function anxiety
Opioids	<ul style="list-style-type: none"> High rates of sexual dysfunction ED, premature ejaculation, orgasmic dysfunction, and low libido PME after cessation of opioid use Illicit opioids, e.g, heroin: sexual dysfunctions in 34-85% of pts.¹⁴ OST-mainly decreased libido and orgasmic dysfunctions or ED -MMT: rate of sexual dysfunctions about 14-81%¹⁵ -BMT: rate of sexual dysfunctions about 36-83%¹⁶ Opioid antagonist therapy like naltrexone: Rate of sexual dysfunctions up to 90% (PME, ED, decrease in sexual desire)^{14,16}. Also has evidence of improvement in ED^{16,17} 	<ul style="list-style-type: none"> Decreases adrenal androgen (by inhibiting GnRH, and production of LH) Morphine administration suppresses LH release & reduces the levels of testosterone & estradiol, affecting testicular function Development of hypogonadism Effect on gonada-HP-axis through -rec. Improvement in ED may be due to inhibition of the inhibitory effect of endogenous opioid Endogenous opioid delays ejaculation when inhibited by NTx l/t PME¹⁷
Alcohol use	<ul style="list-style-type: none"> Small amount may l/t increased libido or improvement in erection Excessive consumption: affects all stages of the sexual cycle (decreased sexual desire in about 50%, ED in 16-59%, delayed ejaculation in 17-25%, and PME in 4-15%) 	<ul style="list-style-type: none"> Reducing anxiety and inducing vasodilation Decrease testosterone, increase estrogen, and polyneuropathy: affects penile nerves Central sedation may lead to transient ED
Tobacco use	<ul style="list-style-type: none"> ED 	<ul style="list-style-type: none"> Toxicity d/t elevated levels of CO, increased platelet aggregation, & atherosclerotic vessels may also play a role
MDMA (ecstasy)	<ul style="list-style-type: none"> Increased desire and satisfaction are more common Delayed orgasm and ED also reported 	<ul style="list-style-type: none"> Activation of dopaminergic system attributed to increased sexual desire & satisfaction Stimulation of the serotonergic system: has an inhibitory effect on erection and orgasm
Stimulants: amphet, MPH, etc	<ul style="list-style-type: none"> Increased libido Prolonged use may be associated with loss of desire & erection 	<ul style="list-style-type: none"> Raise plasma levels of NE and dopamine
Alpha & beta rec. antagonists (propranolol)	<ul style="list-style-type: none"> Impotence, decreased volume of ejaculate, and produce retrograde ejaculation, can also affect libido 	<ul style="list-style-type: none"> Diminish tonic sympathetic nervous outflow from vasomotor centers in the brain
Anticholinergic (benztropine)	<ul style="list-style-type: none"> ED 	<ul style="list-style-type: none"> Blockade of cholinergic receptors
Antihistaminic	<ul style="list-style-type: none"> Inhibitory effect on sexual function 	<ul style="list-style-type: none"> Anticholinergic activity & mild hypnotic agent
Hallucinogens (LSD, PCP, etc.)	<ul style="list-style-type: none"> May enhance sexual experience but can also affect sexual function adversely 	<ul style="list-style-type: none"> Enhanced sexual experience d/t psychotomimetic effect
Cannabis	<ul style="list-style-type: none"> May enhance sexual pleasure prolonged use may impair sexual function 	<ul style="list-style-type: none"> Altered state of consciousness Prolonged use decreases testosterone level

amphet.:amphetamine, Amtrp: amitriptyline, AP: Antipsychotics, BMT : Buprenorphine maintenance therapy, CBZ & Ox-CBZ: Carbamazepine, -: Oxcarbamazepine, Clomi: clomipramine, CO: carbon monoxide, CVDs: cardiovascular diseases, DE : Delayed ejaculation, Desi: desipramine, DM: diabetes mellitus, d/t- due to, ED: Erectle dysfunction, GnRH: Gonadotropin Gonadotropin-releasing hormone, HP: hypothalamic-pituitary, HTN: hypertension, Imi: imipramine, l/t: leading to, LH: Luteinizing hormone, Li: Lithium, LSD -: Lysergic acid diethylamide, MAOIs -Monoamine oxidase inhibitors, MDMA - 3,4-Methyl enedioxy methamphetamine, MHSDD: Male hypoactive sexual desire disorder, mians: mianserin, milnacpr: milnacipran, Mirtaz: Mirtazapine, MMT -: Methadone maintenance therapy, MPH: methylphenidate, NO: nitric oxide, Resp.: risperidone, nortryp: nortyptiline, NTx: naltrexone, NE: Norepinephrine, Olanz:olanzapine, Clzp:clozapine, OST: Opioid substitution therapy, palip: paliperidone, PCP -: Phencyclidine, , PME: Premature ejaculation, RCTs: Randomised control trials, rebex: reboxetine, SD: Sexual dysfunction,SGA - Second generation antipsychotics, SNRI: Serotonin and norepinephrine reuptake inhibitors, SSRIs: Selective serotonin reuptake inhibitors, TCAs: Tricyclic antidepressants, traz: trazodone

1.Smith, 2003	6.Peluso et al., 2013	10.Reichenpfader et al., 2014	14.Grover et al., 2014
2.Serretti and Chiesa, 2011	7.Aizenberg et al., 1995	11.Cleare et al., 2015	15.Nik Jaafar et al., 2013
3.Montalvo et al., 2013	8.Sadock et al., 2017	12.Wagner et al., 2018	16.Ramdurg et al., 2012
4.Raja, 1999	9.Montejo et al., 2018	13.Gitlin, 2003	17.Sathe et al., 2001
5.Dossenbach et al., 2006			

Table 5: Management of sexual dysfunctions with co-morbid psychiatric/medical illnesses

Co-morbid disorders	Common sexual disorders	Management
Physical Illness		
Cardio-vascular disorders Hypertension Atherosclerosis	ED is a common problem & heralds the onset of CVDs 5 -10yrs in advance.	<ul style="list-style-type: none"> • PDEIs (e.g., sildenafil, tadalafil) are preferred if BP>90/60mmhg. • Nitrated are contraindicated with PDEIs • Antihypertensives: Cardio selective beta blocker (metoprolol, atenolol, etc.) are preferred over non-selective beta blockers • Adequate control of glucose (if DM is co-morbid), lipids (hypo-lipidemic agents), and weight (lifestyle modifications).
Neurological diseases Traumatic brain & Spinal cord injury Multiple sclerosis Peripheral neuropathy Stroke	ED is a common problem. TBI: decreased desire d/t reduced gonadotropins Decreased genital sensation & painful penetration common with MS	<ul style="list-style-type: none"> • PDEIs are less effective • A vacuum tumescence device may be used • Intracavemous papaverine, phentolamine • Penile implant: however, associated with complications, results in poor response to other treatments • Testosterone supplements & lubricants • lubricants may be useful. • Early physical rehabilitation, nutritional support, addressing emotional & cognitive issues • For hyperprolactinemia (Rt. Cerebral damage): Dopamine agonist (ropinirole)
Endocrinological diseases DM Androgen deficiency Hyperprolactinemia Hypothyroidism	EDs are secondary to peripheral neuropathy. Body-image distortions. Decreased libido & EDs are common. Abnormal ejaculations are common	<ul style="list-style-type: none"> • PDEIs are useful • cognitive behavioural therapy • Interpersonal issues with the partner: couple therapy, family psychoeducation • Testosterone replacement therapy. • Tt: Dopamine agonist, surgical removal of the pituitary tumours • Emphasis on achieving euthyroid
Genito-urinary conditions Prostatitis, Peyronie's ds. Chronic renal failure	ED is common Depression is common, fear & anxiety related to worsening of medical condition with sexual activity	<ul style="list-style-type: none"> • Treat the underlying infection or inflammation • Can result in ED, painful penetration, & ejaculatory problems: PDEIs & other non-invasive treatment, surgery should be attempted if former Tt fail. • Continue coital activity as spontaneous remission is likely • Hormonal and metabolic abnormalities: correct the deficiency • CBT, relaxation exercises, antidepressants -if indicated

<p>Others: Metabolic syndrome</p>	<p>-</p>	<ul style="list-style-type: none"> • ED and decreased desire are common: • Lifestyle modifications (Mediterranean diet, Smoking cessation) • PDEIs for ED ; testosterone replacement therapy (TRT) & aromatase inhibitors (e.g., Letrozole) to correct hypogonadism. • Bariatric surgery for obese individuals not responding to medical and psychosocial treatments. • Intra-penile prosthesis
Psychiatric illness		
<p>Mood disorders (Depression, Bipolar Ds.)</p>	<p>Depression: Decreased libido</p>	<ul style="list-style-type: none"> • SSRIs, TCAs, & MAOIs, are detrimental to sexual functioning • Mgt.: decrease dose of antidepressants, drug holiday (for shorter-acting agents), • Cyproheptadine (4-12mg): 5HT_{2A} antagonist (1-2hrs before the act) & Nefazodone (5HT_{2A} antagonist) • Mianserin (5HT_{2A} & alpha-2 antagonist), • Buspirone (5HT_{1A} agonist) 15-60mg • Dopamine agonist: Bupropion • PDEIs: Sildenafil (25-50mg OD)
<p>Anxiety spectrum disorders (Generalized anxiety ds, social anxiety ds (SAD) PTSD, OCD, etc.)</p>	<p>Significantly affect all stages of the sexual cycle SAD (e.g., performance anxiety): ED & PME are widespread. PTSD: ED & PME are common.</p>	<ul style="list-style-type: none"> • Anxiolytics (e.g., clonazepam) used in PTSD can worsen sexual functioning • Mgt.: PDEIs, non-pharmacological intervention: psychodynamic psychotherapy, CBT/BT for performance anxiety and other anxiety Ds. • Psychotropic agents: buspirone & mirtazapine are preferable agents
<p>Schizophrenia and psychotic ds.</p>	<p>- Affects all stages of sexual functioning/d/t -decrease DA -anticholinergic & antiadrenergic effects</p>	<ul style="list-style-type: none"> • FGA>SGA (CLZ>RISP> OLZ & QUET) • General principles: switch to a lower dose, prefer SGA over FGA, couple/marital therapy for psychological issues • PDEIs are less effective
<p>Personality disorders</p>	<p>Borderline-narcissistic PD</p>	<ul style="list-style-type: none"> • Interpersonal therapy, DBT • PDEIs
<p>SUD (opioids, alcohol, MDMA, etc.)</p>	<p>Can affect all stages of the sexual cycle. Can l/t risky behaviour, including contracting HIV, STDs</p>	<ul style="list-style-type: none"> • Treat the underlying SUD • Use medications as highlighted above if symptoms do not get improved with abstinence of substance or when symptoms are severe
<p>Others: Eating disorders</p>	<p>Body-image distortion Negative self-evaluation, co-morbid depression</p>	<ul style="list-style-type: none"> • Psychoeducation about sexuality, systematic desensitization, etc.

CLZ: clozapine, DBT: dialectic behaviour therapy, FGA: first-generation antipsychotics (e.g., haloperidol, trifluoperazine), HIV/AIDS: human immunodeficiency virus/acquired immunodeficiency disorders, MAOI: monoamine oxidase inhibitors, MHPs: mental health professionals, OLZ: olanzapine, PDEIs: phosphodiesterase inhibitors, PTSD: posttraumatic stress disorders, QoL: quality of life, QUET: quetiapine, RISP: risperidone, SGA: generation antipsychotics, SSRIs: selective serotonin reuptake inhibitors, STDs: sexually transmitted disorders, TCAs: tri-cyclic antidepressants

Conclusion

Sexual dysfunctions are frequently seen with psychiatric as well as physical illnesses. Medications, both psychotropic, e.g., selective-serotonin-reuptake inhibitors, antipsychotics (first-generation>second-generation), and non-psychotropic, e.g., beta-blockers, thiazide diuretics, are equally implicated in sexual dysfunctions. Treating underlying co-morbid illnesses, reducing/discontinuing the offending drugs, including psychoactive substances, switching to an agent with less sexual adverse effects, and using medications (e.g., phosphodiesterase inhibitors), devices (prosthesis), and surgery (implants, correction of genito-urinary conditions) are the cornerstone of management. Better knowledge and understanding of sexual dysfunction among co-morbid psychiatric or physical illnesses, adequate assessment, and formulation of a comprehensive treatment plan are key to addressing these comorbidities.

Acknowledgment: None

Conflict of interest: None

References

- Abdelatti, S.I., Ismail, R.M., Hamed, R.A. (2020). Sexual dysfunctions in a sample of male psychiatric patients compared to medically ill patients. *Middle East Current Psychiatry*, 27, 12. [https://doi.org/ 10.1186/s43045-020-00022-3](https://doi.org/10.1186/s43045-020-00022-3)
- Abosetugn, A.E., Yehualashet, S.S. (2021). Estimate the burden of sexual dysfunction due to non-communicable diseases in Ethiopia: Systematic review and meta-analysis. *PLoS One* 16, e0258938. <https://doi.org/10.1371/journal.pone.0258938>
- Aizenberg, D., Zemishlany, Z., Dorfman-Etrog, P., Weizman, A. (1995). Sexual dysfunction in male schizophrenic patients. *J Clin Psychiatry*, 56, 137-141.
- Ajmal, A., Joffe, H., Nachtigall, L.B. (2014). Psychotropic-induced hyperprolactinemia: a clinical review. *Psychosomatics*, 55, 29-36. [https://doi.org/ 10.1016/j.psych.2013.08.008](https://doi.org/10.1016/j.psych.2013.08.008)
- al Khaja, K.A.J., Sequeira, R.P., al Damanhori, A.H.H., Mathur, V.S. (2003). Antihypertensive drug-associated sexual dysfunction: a prescription analysis-based study. *Pharmacoepidemiol Drug Saf*, 12, 203-212. <https://doi.org/10.1002/pds.814>
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.).
- Baggaley, M. (2008). Sexual dysfunction in schizophrenia: focus on recent evidence. *Hum Psychopharmacol*, 23, 201-209. [https://doi.org/ 10.1002/hup.924](https://doi.org/10.1002/hup.924)
- Basson, R., Gilks, T. (2018). Women's sexual dysfunction associated with psychiatric disorders and their treatment. *Womens Health (Lond)*, 14. <https://doi.org/10.1177/1745506518762664>
- Basson, R., Schultz, W.W. (2007). Sexual sequelae of general medical disorders. *Lancet*, 369, 409-424. [https://doi.org/10.1016/S0140-6736\(07\)60197-4](https://doi.org/10.1016/S0140-6736(07)60197-4)
- Bhasin, S., Enzlin, P., Coviello, A., Basson, R. (2007). Sexual dysfunction in men and women with endocrine disorders. *Lancet*, 369, 597-611. [https://doi.org/ 10.1016/S0140-6736\(07\)60280-3](https://doi.org/10.1016/S0140-6736(07)60280-3)
- Bitter, I., Basson, B.R., Dossenbach, M.R. (2005). Antipsychotic treatment and sexual functioning in first-time neuroleptic-treated schizophrenic patients. *Int Clin Psychopharmacol*, 20, 19-21. <https://doi.org/10.1097/00004850-200501000-00004>
- Bodinger, L., Hermesh, H., Aizenberg, D., Valevski, A., Marom, S., Shiloh, R., Gothelf, D., Zemishlany, Z., Weizman, A. (2002). Sexual function and behavior in social phobia. *J Clin Psychiatry*, 63, 874-879. <https://doi.org/10.4088/jcp.v63n1004>
- Burger, H.G., Papalia, M.A. (2006). A clinical update on female androgen insufficiency--testosterone testing and treatment in women presenting with low sexual desire. *Sex Health*, 3, 73-78. [https://doi.org/ 10.1071/sh05055](https://doi.org/10.1071/sh05055)
- Castellini, G., Lelli, L., Ricca, V., Maggi, M. (2016). Sexuality in eating disorders patients: etiological factors, sexual dysfunction and identity issues. A systematic review. *Horm Mol Biol Clin Investig*, 25, 71-90. <https://doi.org/10.1515/hmbci-2015-0055>
- Chung, E. (2019). Sexuality in Ageing Male: Review of Pathophysiology and Treatment Strategies for Various Male Sexual Dysfunctions. *Med Sci (Basel)*, 7, E98. <https://doi.org/10.3390/medsci7100098>
- Citrome, L. (2015). Brexpiprazole for schizophrenia and as adjunct for major depressive disorder: a systematic review of the efficacy and safety profile for this newly approved antipsychotic - what is the

- number needed to treat, number needed to harm and likelihood to be helped or harmed? *Int J Clin Pract*, 69, 978-997. <https://doi.org/10.1111/ijcp.12714>
- Citrome, L., Cucchiari, J., Sarma, K., Phillips, D., Silva, R., Tsuchiya, S., Loebel, A. (2012). Long-term safety and tolerability of lurasidone in schizophrenia: a 12-month, double-blind, active-controlled study. *Int Clin Psychopharmacol*, 27, 165-176. <https://doi.org/10.1097/YIC.0b013e32835281ef>
- Clayton, A., Ramamurthy, S. (2008). The impact of physical illness on sexual dysfunction. *Adv Psychosom Med*, 29, 70-88. <https://doi.org/10.1159/000126625>
- Clayton, A.H., Croft, H.A., Handiwala, L. (2014). Antidepressants and sexual dysfunction: mechanisms and clinical implications. *Postgrad Med*, 126, 91-99. <https://doi.org/10.3810/pgm.2014.03.2744>
- Cleare, A., Pariante, C.M., Young, A.H., Anderson, I.M., Christmas, D., Cowen, P.J. et al. (2015). Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2008 British Association for Psychopharmacology guidelines. *J Psychopharmacol*, 29, 459-525. <https://doi.org/10.1177/0269881115581093>
- Demirkiran, M., Sarica, Y., Uguz, S., Yerdelen, D., Aslan, K. (2006). Multiple sclerosis patients with and without sexual dysfunction: are there any differences? *Mult Scler*, 12, 209-214. <https://doi.org/10.1191/135248506ms1253oa>
- Figueira, I., Possidente, E., Marques, C., Hayes, K. (2001). Sexual dysfunction: a neglected complication of panic disorder and social phobia. *Arch Sex Behav*, 30, 369-377. <https://doi.org/10.1023/a:1010257214859>
- Ghormode, D., Gupta, P., Ratnani, D., Aneja, J. (2019). Evaluation of sexual dysfunction and quality of life in patients with severe mental illness: A cross-sectional study from a tertiary care center in Chhattisgarh. *Ind Psychiatry J*, 28, 75-81. https://doi.org/10.4103/ipj.ipj_16_19
- Gitlin, M. (2003). Sexual dysfunction with psychotropic drugs. *Expert Opin Pharmacother*, 4, 2259-2269. <https://doi.org/10.1517/14656566.4.12.2259>
- Grover, S., Mattoo, S.K., Pendharkar, S., Kandappan, V. (2014). Sexual dysfunction in patients with alcohol and opioid dependence. *Indian journal of psychological medicine*, 36, 355-365.
- Imprialos, K.P., Stavropoulos, K., Doumas, M., Tziomalos, K., Karagiannis, A., Athyros, V.G. (2018). Sexual Dysfunction, Cardiovascular Risk and Effects of Pharmacotherapy. *Curr Vasc Pharmacol*, 16, 130-142. <https://doi.org/10.2174/1570161115666170609101502>
- Johnson, S.D., Phelps, D.L., Cottler, L.B. (2004). The association of sexual dysfunction and substance use among a community epidemiological sample. *Arch Sex Behav*, 33, 55-63. <https://doi.org/10.1023/B:ASEB.0000007462.97961.5a>
- Kandeel, F.R., Koussa, V.K., Swerdloff, R.S. (2001). Male sexual function and its disorders: physiology, pathophysiology, clinical investigation, and treatment. *Endocr Rev*, 22, 342-388. <https://doi.org/10.1210/edrv.22.3.0430>
- Kennedy, S.H., Dickens, S.E., Eisfeld, B.S., Bagby, R.M. (1999). Sexual dysfunction before antidepressant therapy in major depression. *J Affect Disord*, 56, 201-208. [https://doi.org/10.1016/s0165-0327\(99\)00050-6](https://doi.org/10.1016/s0165-0327(99)00050-6)
- Khin, N.A., Kronstein, P.D., Yang, P., Ishida, E., Hung, H.M.J., Mathis, M.V. et al. (2015). Regulatory and scientific issues in studies to evaluate sexual dysfunction in antidepressant drug trials. *J Clin Psychiatry*, 76, 1060-1063. <https://doi.org/10.4088/JCP.14cs09700>
- Kok, E. (2004). Differences between male and female sexual functioning. *South African Family Practice*, 46, 12-15. <https://doi.org/10.1080/20786204.2004.10873065>
- Kotler, M., Cohen, H., Aizenberg, D., Matar, M., Loewenthal, U., Kaplan, Z. et al. (2000). Sexual dysfunction in male posttraumatic stress disorder patients. *Psychother Psychosom*, 69, 309-315. <https://doi.org/10.1159/000012413>
- Kovac, J.R., Labbate, C., Ramasamy, R., Tang, D., Lipshultz, L.I. (2015). Effects of cigarette smoking on erectile dysfunction. *Andrologia*, 47, 1087-1092. <https://doi.org/10.1111/and.12393>
- La Torre, A., Giupponi, G., Duffy, D.M., Pompili, M., Grözinger, M., Kapfhammer, H.P., Conca, A. (2014a). Sexual dysfunction related to psychotropic drugs: a critical review. Part III: mood stabilizers and anxiolytic drugs. *Pharmacopsychiatry*, 47, 1-6. <https://doi.org/10.1055/s-0033-1358683>
- La Torre, A., Giupponi, G., Duffy, D.M., Pompili, M., Grözinger, M., Kapfhammer, H.P., Conca, A. (2014b). Sexual dysfunction related to psychotropic drugs: a

- critical review. Part III: mood stabilizers and anxiolytic drugs. *Pharmacopsychiatry*, 47, 1-6. <https://doi.org/10.1055/s-0033-1358683>
- Laurent, S.M., Simons, A.D. (2009a). Sexual dysfunction in depression and anxiety: conceptualizing sexual dysfunction as part of an internalizing dimension. *Clin Psychol Rev*, 29, 573-585. <https://doi.org/10.1016/j.cpr.2009.06.007>
- Laurent, S.M., Simons, A.D. (2009b). Sexual dysfunction in depression and anxiety: conceptualizing sexual dysfunction as part of an internalizing dimension. *Clin Psychol Rev*, 29, 573-585. <https://doi.org/10.1016/j.cpr.2009.06.007>
- Lee, R.K., Chughtai, B., Te, A.E., Kaplan, S.A. (2012). Sexual function in men with metabolic syndrome. *Urol Clin North Am*, 39, 53-62. <https://doi.org/10.1016/j.ucl.2011.09.008>
- Lossius, M.I., Taubøll, E., Mowinckel, P., Mørkrid, L., Gjerstad, L. (2007). Reversible effects of antiepileptic drugs on reproductive endocrine function in men and women with epilepsy--a prospective randomized double-blind withdrawal study. *Epilepsia*, 48, 1875-1882. <https://doi.org/10.1111/j.1528-1167.2007.01147.x>
- Macdonald, S., Halliday, J., MacEWAN, T., Sharkey, V., Farrington, S., Wall, S. (2003). Nithsdale Schizophrenia Surveys 24: sexual dysfunction. Case-control study. *Br J Psychiatry*, 182, 50-56. <https://doi.org/10.1192/bjp.182.1.50>
- Malik, P. (2008). Sexual Dysfunction in Schizophrenia. *FOC*, 6, 234-238. <https://doi.org/10.1176/foc.6.2.foc234>
- McElrath, K. (2005). MDMA and sexual behavior: ecstasy users' perceptions about sexuality and sexual risk. *Subst Use Misuse*, 40, 1461-1477. <https://doi.org/10.1081/JA-200066814>
- McMahon, C.G. (2012). Dapoxetine: a new option in the medical management of premature ejaculation. *Ther Adv Urol*, 4, 233-251. <https://doi.org/10.1177/1756287212453866>
- Montalvo, I., Ortega, L., López, X., Solé, M., Monseny, R., Franch, J. et al. (2013). Changes in prolactin levels and sexual function in young psychotic patients after switching from long-acting injectable risperidone to paliperidone palmitate. *Int Clin Psychopharmacol*, 28, 46-49. <https://doi.org/10.1097/YIC.0b013e32835ba832>
- Monteiro, W.O., Noshirvani, H.F., Marks, I.M., Lelliott, P.T. (1987). Anorgasmia from clomipramine in obsessive-compulsive disorder. A controlled trial. *Br J Psychiatry*, 151, 107-112. <https://doi.org/10.1192/bjp.151.1.107>
- Montejo, A.L., Montejó, L., Baldwin, D.S. (2018). The impact of severe mental disorders and psychotropic medications on sexual health and its implications for clinical management. *World Psychiatry*, 17, 3-11. <https://doi.org/10.1002/wps.20509>
- Mynderse, L.A., Monga, M. (2002). Oral therapy for Peyronie's disease. *Int J Impot Res*, 14, 340-344. <https://doi.org/10.1038/sj.ijir.3900869>
- Nasrallah, H.A., Earley, W., Cutler, A.J., Wang, Y., Lu, K., Laszlovszky, I. et al. (2017). The safety and tolerability of cariprazine in long-term treatment of schizophrenia: a post hoc pooled analysis. *BMC Psychiatry*, 17, 305. <https://doi.org/10.1186/s12888-017-1459-z>
- Nik Jaafar, N.R., Mislan, N., Abdul Aziz, S., Baharudin, A., Ibrahim, N., Midin, M. et al. (2013). Risk factors of erectile dysfunction in patients receiving methadone maintenance therapy. *J Sex Med*, 10, 2069-2076. <https://doi.org/10.1111/jsm.12105>
- Nordvig, A.S., Goldberg, D.J., Huey, E.D., Miller, B.L. (2019). The cognitive aspects of sexual intimacy in dementia patients: a neurophysiological review. *Neurocase*, 25, 66-74. <https://doi.org/10.1080/13554794.2019.1603311>
- Palha, A.P., Esteves, M. (2008). Drugs of abuse and sexual functioning. *Adv Psychosom Med*, 29, 131-149. <https://doi.org/10.1159/000126628>
- Peluso, M.J., Lewis, S.W., Barnes, T.R.E., Jones, P.B. (2013). Non-neurological and metabolic side effects in the Cost Utility of the Latest Antipsychotics in Schizophrenia Randomised Controlled Trial (CUtLASS-1). *Schizophr Res*, 144, 80-86. <https://doi.org/10.1016/j.schres.2012.12.008>
- Pizzol, D., Xiao, T., Yang, L., Demurtas, J., McDermott, D., Garolla, A. et al. (2021). Prevalence of erectile dysfunction in patients with chronic kidney disease: a systematic review and meta-analysis. *Int J Impot Res*, 33, 508-515. <https://doi.org/10.1038/s41443-020-0295-8>
- Polland, A., Davis, M., Zeymo, A., Venkatesan, K. (2018). Comparison of correlated comorbidities in male and female sexual dysfunction: findings from the third national survey of sexual attitudes and lifestyles (Natsal-3). *The journal of sexual medicine*, 15, 678-686.
- Raja, M. (1999). Risperidone-induced absence of ejaculation. *Int Clin Psychopharmacol*, 14, 317-319.

- Ramdurg, S., Ambekar, A., Lal, R. (2012). Sexual Dysfunction among Male Patients Receiving Buprenorphine and Naltrexone Maintenance Therapy for Opioid Dependence. *The Journal of Sexual Medicine*, 9, 3198-3204. <https://doi.org/10.1111/j.1743-6109.2011.02219.x>
- Rees, P.M., Fowler, C.J., Maas, C.P. (2007). Sexual function in men and women with neurological disorders. *Lancet*, 369, 512-525. [https://doi.org/10.1016/S0140-6736\(07\)60238-4](https://doi.org/10.1016/S0140-6736(07)60238-4)
- Reffellmann, T., Kloner, R.A. (2006). Sexual function in hypertensive patients receiving treatment. *Vasc Health Risk Manag*, 2, 447-455. <https://doi.org/10.2147/vhrm.2006.2.4.447>
- Reichenpfader, U., Gartlehner, G., Morgan, L.C., Greenblatt, A., Nussbaumer, B., Hansen, R.A. et al. (2014). Sexual dysfunction associated with second-generation antidepressants in patients with major depressive disorder: results from a systematic review with network meta-analysis. *Drug Saf*, 37, 19-31. <https://doi.org/10.1007/s40264-013-0129-4>
- Rowland, D.L., Oosterhouse, L.B., Kneusel, J.A., Hevesi, K. (2021). Comorbidities Among Sexual Problems in Men: Results From an Internet Convenience Sample. *Sex Med*, 9, 100416. <https://doi.org/10.1016/j.esxm.2021.100416>
- Sadock, B.J., Sadock, V.A., Ruiz, P. (2017). *Kaplan & Sadock's Comprehensive Textbook Of Psychiatry, Tenth Edition*. ed. Wolters Kluwer, Lippincott Williams & Wilkins, Philadelphia, United States.
- Sathe, R.S., Komisaruk, B.R., Ladas, A.K., Godbole, S.V. (2001). Naltrexone-Induced Augmentation of Sexual Response in Men. *Archives of Medical Research*, 32, 221-226. [https://doi.org/10.1016/S0188-4409\(01\)00279-X](https://doi.org/10.1016/S0188-4409(01)00279-X)
- Serretti, A., Chiesa, A. (2011). Sexual side effects of pharmacological treatment of psychiatric diseases. *Clin Pharmacol Ther*, 89, 142-147. <https://doi.org/10.1038/clpt.2010.70>
- Shiferaw, W.S., Akalu, T.Y., Aynalem, Y.A. (2020). Prevalence of Erectile Dysfunction in Patients with Diabetes Mellitus and Its Association with Body Mass Index and Glycated Hemoglobin in Africa: A Systematic Review and Metaanalysis. *Int J Endocrinol*, 5148370. <https://doi.org/10.1155/2020/5148370>
- Smith, S. (2003). Effects of antipsychotics on sexual and endocrine function in women: implications for clinical practice. *J Clin Psychopharmacol*, 23, S27-32. <https://doi.org/10.1097/01.jcp.0000084035.22282.31>
- Smith, S.M., O'Keane, V., Murray, R. (2002). Sexual dysfunction in patients taking conventional antipsychotic medication. *Br J Psychiatry*, 181, 49-55. <https://doi.org/10.1192/bjp.181.1.49>
- Solursh, L.P., Solursh, D.S. (2011). Male erectile disorders in Vietnam combat veterans with chronic posttraumatic stress disorder. *Int J Adolesc Med Health*, 7, 119-124. <https://doi.org/10.1515/IJAMH.1994.7.2.119>
- Soykan, A., Boztas, H., Kutlay, S., Ince, E., Nergizoglu, G., Dileköz, A.Y. et al. (2005). Do sexual dysfunctions get better during dialysis? Results of a six-month prospective follow-up study from Turkey. *Int J Impot Res*, 17, 359-363. <https://doi.org/10.1038/sj.ijir.3901324>
- Torre, A.L., Giupponi, G., Duffy, D., Conca, A. (2013). Sexual Dysfunction Related to Psychotropic Drugs: A Critical Review - Part I: Antidepressants. *Pharmacopsychiatry*, 46, 191-199. <https://doi.org/10.1055/s-0033-1345205>
- Vaishnav, M., Gupta, S., Vaishnav, P. (2022). Psychiatric intervention pre- and post-bariatric surgery. *Indian Journal of Psychiatry* 64, S473. https://doi.org/10.4103/indianjpsychiatry.indianjpsychiatry_1_22
- Wagner, G., Schultes, M.T., Titscher, V., Teufer, B., Klerings, I., Gartlehner, G. (2018). Efficacy and safety of levomilnacipran, vilazodone and vortioxetine compared with other second-generation antidepressants for major depressive disorder in adults: A systematic review and network meta-analysis. *J Affect Disord*, 228, 1-12. <https://doi.org/10.1016/j.jad.2017.11.056>
- Waldinger, M.D. (2015). Chapter 27- Psychiatric disorders and sexual dysfunction, in: Vodusek, D.B., Boller, F. (Eds.), *Handbook of Clinical Neurology, Neurology of Sexual and Bladder Disorders*. Elsevier, pp. 469-489. <https://doi.org/10.1016/B978-0-444-63247-0.00027-4>
- Wylie, K., Kenney, G. (2010). Sexual dysfunction and the ageing male. *Maturitas*, 65, 23-27. <https://doi.org/10.1016/j.maturitas.2009.10.018>
- Zemishlany, Z., Aizenberg, D., Weizman, A. (2001). Subjective effects of MDMA ('Ecstasy') on human sexual function. *European Psychiatry*, 16, 127-130.
- Zemishlany, Z., Weizman, A. (2008). The impact of mental illness on sexual dysfunction. *Adv Psychosom Med*, 29, 89-106. <https://doi.org/10.1159/000126626>