General

Mental Health in Non-Oncologic Urology Patients

Danyon Anderson[1a], Devesh Kumar[1b], Divya Divya[2], Jose L. Zepeda[1], Abrahim N. Razzak[1], Jamal Hasoon[3], Omar Viswanath[4], Alan D. Kaye[5], Ivan Urits[6]

[1] School of Medicine, Medical College of Wisconsin, [2] School of Medicine, University of Missouri- Kansas City, [3] Department of Anesthesia, Critical Care, and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, [4] Department of Anesthesia, Critical Care, and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School; Valley Anesthesiology and Pain Consultants, Envision Physician Services; Department of Anesthesiology, University of Arizona College of Medicine Phoenix; Department of Anesthesiology, Creighton University School of Medicine, [5] Department of Anesthesiology, Louisiana State University Health Shreveport, [6] SouthCoast Health

Keywords: Mental Health, Urology, Erectile Dysfunction, Urinary Incontinence, Depression, Anxiety, Quality of Life, Sexual Health, Infertility

https://doi.org/10.52965/001c.38352

Health Psychology Research

Vol. 10, Issue 3, 2022

This article is a literature review of mental health concerns in non-oncologic urology patients. Pathologies represented in this review include Peyronie's Disease (PD), erectile dysfunction (ED), urinary incontinence and urinary tract infections (UTI), infertility, benign prostatic hyperplasia (BPH), kidney stones, and urinary retention. While there has been great interventional focus as of late for urogenitary malignancies (i.e. prostate cancer awareness with the Movember campaign), literature studies and intervention focused on non-oncologic urology patients has been limited. As such, we conducted a review on urology patients with non-oncologic pathologies as an effort to increase clinician awareness of mental health concerns among such patients, increase the comfort level for clinician communication on socially sensitive topics surrounding pathologies, and review ongoing interventions conducted within these pathologies. We outlined different ongoing Mental Health Illness (MHI) needs and treatments for various pathologies. Patients with non-cancerous urologic pathologies had lower quality of life and higher incidence of MHI than the general population. As such, in line with the American Urological Association recommendations, psychological and social support from peers, therapists, and healthcare providers further prove to be crucial for some subpopulations. The review also yielded pathology specific interventions such as group therapy for ED patients. Given the higher incidence of MHI in the patient population after the Covid-19 pandemic, MHI awareness in the sphere of non-oncologic urology treatment continues to be crucial when creating a collaborative treatment platform for patients.

INTRODUCTION

Over the past several years, efforts have been made to address mental health concerns in healthcare. Numerous studies have found a strong correlation of mental health illness (MHI) being directly correlated with the onset of debilitating or restricting conditions that affect one's way of living. Initiatives such as Bell Let's Talk in January in Canada, National Suicide Prevention Week in September in the US, Mental Health Awareness Week in May in the UK have been effective at raising awareness on a topic that is often rejected due to negative stigma (i.e. mental health). More specific to urology, the Movember campaign has made the public cognizant of prostate and testicular cancer since 2003.[1] Now with the COVID-19 pandemic, these initiatives are crucial to address the mental health epidemic.[2] A recent meta-analysis found that one in four adults are experience significant distress due to the pandemic.[3]

a **Corresponding author:**
Danyon Anderson
Medical College of Wisconsin
Medical School
8701 W Watertown Plank Rd
Milwaukee, WI 53226
Phone: (719)-310-2831
djanderson@mcw.edu

b Danyon Anderson & Devesh Kumar Made Equal Contributions and Share First Authorship

Conservative measures (i.e. self-reported surveys) suggest that the lifetime prevalence of major depressive disorder (MDD) is 17% and of generalized anxiety disorder is 6%.[1] A recent study in late 2021 found global point prevalence of MDD between 2001-2020 to be as high as 35% (95% CI: 0.30-0.38).[4] There is limited literature focusing on MHI related to urological conditions. Previous work on MHI and urology conditions has been centered around urological malignancies. This analysis aims to address MHI in non-oncological urology patients in an attempt to increase awareness amongst clinicians, improve comfort levels when discussing MHI with patients and educating urologists to make referrals for psychiatric evaluation for patients at risk.

PEYRONIE'S DISEASE

Peyronie's disease (PD) is a condition that affects 0.5% of men.[5] Although, a population-based study concluded that there is a significant difference between the definitive and probable cases of PD, indicating that the true prevalence of PD is underestimated. This may be due to patients being hesitant to share such information with their physician to avoid shame and embarrassment.[6] PD occurs when a fibrous plaque on the tunica albuginea results in an alteration of the penis anatomy and causes curvature, pain, and sexual dysfunction.[6] The physical effects are undoubtedly debilitating; however, psychological consequences associated with this condition must also be considered. The psychological impact of PD is an understudied effort, but scant literature on the topic recognizes one main point that depression and relationship distress is prevalent in this cohort.[7] Using self-reported measures, a study conducted by Gelbard, et al. found that 77% of men experienced psychological effects due to PD.[8] Despite improvement in PD and post treatment, 48% of those still declared that they ruminate about their condition frequently.[8] Another study, Smith, et al. focused on the prevalence of emotional and relationship difficulties and found that 81% of men in the study had emotional manifestations and 54% reported that their relationship issues were due to PD.[9] The psychological and social impact of PD is becoming increasingly prevalent. PD is often viewed as a rare, stable disease with no significant effect on health, however, it becomes a larger societal issue if we take into consideration the depressive and emotional impact of PD.[7] The Journal of Sexual Medicine demonstrated in their study that 48% of men with PD have clinical depression requiring medical intervention and this depression stayed consistent even years after this diagnosis.[10] This alludes to the difficulty in coping with their condition and the necessity of mental health screening in those afflicted. Aside from just depression, a Swedish study with a 3.5 million cohort found that men with PD had increased risk of substance use disorders, anxiety disorders, self-injurious behaviors, and other psychiatric illnesses.[11]

Current treatment options for PD include medical management with fibrosis reducing agents such as pentoxifylline or collagenase clostridium histolyticum injections or surgical management.[6] However, surgical outcomes seem to be a more definitive treatment and aid in rebuilding a man's psychosocial health.[12] Nonetheless, there are many men that are not satisfied even after surgical correction. This was due to resultant shortening of the penis, negative self-perception about their bodies, and changes in attitude about sexuality.[13] Currently, there is limited to no medical treatments targeting the psychological impact associated with PD.

ERECTILE DYSFUNCTION

Erectile dysfunction (ED), also known as impotence, is defined by the inability to achieve or maintain an erection when desired. ED is increasingly prevalence with age which aligns with the frequency of sexual activity decreases with age. According to the Massachusetts Male Aging Study, approximately 40% affected by the age of 40 and 70% of men are affected by the age of 70. High prevalence with older ages has been supported by many studies.[14-18] Decreased libido is also associated amongst the older population and men may have a loss of libido secondary to ED. However, most men who complain of ED don't complain of a loss of sexual desire.[19]

The pathophysiology of ED has not been fully elucidated, but it is thought to be multifactorial with a possible involvement of vasogenic, neurologic, hormonal, cavernous, veno-occlusive, psychogenic and/or pharmacogenic factors.[20-22]

Normal erectile physiology requires blood flow from the hypogastric arterial system into the corpus spongiosum. This leads to an increase in pressure, preventing a venous outflow from the emissary veins, leading to an achievement and maintenance of a penile erection. Nitric oxide functions by promoting the generation of cyclic guanosine monophosphate which in turn facilitates the relaxation of the intracavernosal trabeculae and acts as a vasodilator.[19, 23] This mechanism is thought to play a role in the pathogenesis of ED as phosphodiesterase-5 inhibitors such as sildenafil are effective at improving erectile response to sexual stimulus. Other regulatory mechanism implicated include cyclic adenosine monophosphate, gap junctions and ionic channels which lead to a disturbance of the smooth muscle contraction and relaxation.[24]

As ED is multifactorial with a large vasogenic involvement, there are many known risk factors. Current knowledge has shown a strong association between ED and cardiovascular disease and risk factor. This link is particularly strong among men above 50 years of age. There is still a large cohort of younger patients with a long duration of ED but do not seem to have cardiac abnormalities.[25] There is a need for more research to be conducted on the link between cardiovascular disease amongst younger ED patients. Other risk factors associated with ED include hypertension, diabetes mellitus, tobacco use, hyperlipidemia, hypogonadism, lower urinary tract symptoms, metabolic syndrome, and depression.[26,27]

Besides quality of life and physical health, sexual dysfunction is associated with psychological health as well. With an inability to perform or achieve/maintain an erection, there is a myriad of mental health concerns that affect

men with ED. After adjusting for age, comorbidity, use of erectile aids, and a lack of a positive prostate cancer screening, a large cohort study by Korfage et al., consisting of 3800 patients, found that men with ED have a significantly lower MH rates on a 36-item short form than men without ED.[28]This study also found that MHI related to ED is associated with a potential mediator "satisfaction with sex life", but not with mediator "importance attached to sex life".[28]

Depression is often seen in men with ED. In a Malaysian study, significantly higher proportion of men with ED had depression compared to men without ED.[29] Another study in Japan showed that odds ratio of the association of ED and depression was 2.02.[30] Prior studies have shown a strong link of depression and ED amongst older patients and the link between depression and younger patients had not been studied until 2021. Calzo, et al. found that after adjusting for a prior history of depression, antidepressant use was associated with a greater than three times the odds of moderate to severe ED in young, sexually active men.[31] This risk is highest amongst those taking selective serotonin uptake inhibitors (SSRIs).[31] Anxiety and tranquilizer use was also associated with greater odds of moderate to severe ED as well.[31] The American Urological Association now recommends that all men who present with ED undergo an evaluation for potential psychological factors, such as anxiety and depression.[32]

Currently, the pharmaceutical and behavioral therapies are understudied for the mental health concerns related to erectile dysfunction. As ED is a common symptom of depression, psychotherapy and anti-depressive use should be considered. Of note, the most effective antidepressants of the SSRI class promote erectile dysfunction and decreased libido.[33] A metanalysis in 2007 found that group therapy might be beneficial.[34] There is sparse literature regarding therapies to treat the MHI associated with ED but there are some experimental methods in development and one plant-based pharmaceutical therapy, Yohimbine, with limited data, efficacy, and availability.[35]

INCONTINENCE/URINARY TRACT INFECTION

Urinary incontinence is the involuntary leakage of urine in both males and females. Urinary incontinence can occur at any point in life, but it is greatly associated with increased age. Although it is more prevalent with increasing patients age, it is not part of the normal aging process. Instead, it is attributed to several different etiologies, all with an uncharacterized pathophysiology with known ranges in severity. Urinary incontinence can be categorized as urge urinary incontinence, stress urinary incontinence, and mixed urinary incontinence. Men have a higher prevalence of urge urinary incontinence, and females have a higher prevalence of stress urinary incontinence.[36] Urinary incontinence is more prevalent with increasing age, with a reported range from 9%-50% in patients age 50 and above.[37] However, there is considerable underreporting due to a lack of knowledge that the disease is not part of the normal aging process, embarrassment of the condition, and anxiety from the condition. Also, the emotional toll is an added factor that patients who suffer from urinary incontinence must be acknowledged when seeking care. Women also have an increased prevalence of urinary incontinence with greater prevalence at an increased age. It is estimated that worldwide there are 2.3 billion individuals affected by one of the types of urinary incontinence, and this is believed to increase as our world's aging population increases.[38]

There is no clear pathophysiology to explain all forms of urinary incontinence, but it is associated with a weakening pelvic floor and overall frailty. It is hypothesized that a plausible cause of urinary incontinence is based on abnormalities in serotonin levels, which gives some insight into the associations between urinary incontinence and depression.[39] Urinary incontinence can sometimes be confused with overactive bladder, but both diagnoses are separate and can coexist within a patient and worsen the associated morbidities of the conditions. While there are contributing factors to the onset and progression of urinary incontinence, such as BMI, anxiety, diabetes mellites, and other medical conditions, age is the most noteworthy factor associated with the condition and its progression.[39,40] While not part of the ordinary aging course, the condition does tend to get worse and more prevalent as patients age.[41]

Diagnosis of urinary incontinence is often not considered with how it affects the patient's mental health and overall well-being. With causes of urinary incontinence often being benign, it is vital for clinicians not to overlook the impact the condition has on patients. Studies have found associations between urinary incontinence and higher odds of depressive symptoms.[38,41] The condition becomes harder for the patient's emotion if it is combined with an overactive bladder which may worsen the deleterious impact of urinary incontinence. It was found that in patients who have overactive bladders, there is a higher association with increased anxiety, depression, loneliness, sexual dysfunction, and sleep disturbances relative to controls.[37,42] These findings were amplified in patients who also suffered from incontinence.

Disease burden greatly impacts a patient's mental wellbeing. The overall mental wellbeing of patients suffering from incontinence can progressively worsens if psychological factors are not addressed appropriately as the patient ages or condition worsens. Depression is a highly associated condition with urinary incontinence. The manifestation of depression in patients is known to be multifactorial, but prior studies have shown clear associations with disease progression and worsening mental health outcomes.[37, 39] Urinary incontinence, especially in men, has been found to be an embarrassing and taboo condition that is often underdiagnosed and underreported due to a multitude of factors associated with both patients and clinicians. Initially, the condition can be embarrassing to a patient, which can lead to insecure feelings about their physical health and leaving them prone to underreporting due to embarrassment or increased anxiety about their physical health. As the condition worsens, patients suffer in many facets of their life. Sleep quality has been shown to worsen due to the worsening severity of urinary incontinence.[39] Urinary tract infections may become more prevalent in pa-

tients with severe urinary incontinence.[39] Self-esteem and relationships may become harder to maintain due to the burden of the condition and difficulty finding appropriate accommodations for the patient in social settings.[39-41] This then leads to changes in behavior and potentially self-isolation to accommodate the condition.[43] This multitude of differences and difficulty in daily tasks is believed to contribute to worsening symptoms of depression and anxiety for patients. There are also associations with sexual dysfunction in patients with incontinence for both men and women, thus potentially worsening the social isolation and difficulty in relationships that patients may experience.[42] Both men and women were found to have increased difficulty reaching orgasms with worsening urinary incontinence, higher rates of erectile dysfunction in men, and decreased sexual satisfaction in women.[42] One study did find an adaptation for some patients in which those who reported urinary incontinence for less than 4 years were associated with poorer sexual health than those who had the condition for greater than 4 years.[42] This showed some ability to adapt to the illness in some patients, which has given some insight into sustainable and low side effect therapies addressing the mental health aspect of urinary incontinence.

There are many therapies available for urinary incontinence, but few notable therapies that encompass the mental health and impact on the patient's social life. One well studied first-line treatment for incontinence and its effect on mental health is cognitive behavioral therapy and pelvic floor muscle exercises with lifestyle modification.[44] Cognitive behavioral treatment allows patients to become aware of their condition and analyze their known beliefs and fears about their condition. This allows them to directly address inappropriate behaviors that are associated with their voiding.[44] The goal is to increase a patient's independence in performing emotional control and coping strategies to help control their bladder and create an outline of adherence. To help urinary incontinence, other comorbidities may need to be addressed in conjunction with cognitive behavior therapy, such as weight loss, diet changes, smoking cessation, and physical therapy.[44] Unfortunately, while there are some pharmacological treatments to treat certain aspects of incontinence there fails to be a pharmacological treatment that helps patients address the social and mental health impacts that incontinence has on a patients' wellbeing.

INFERTILITY

Infertility is the inability to conceive after 12 months of frequent unprotected intercourse.[45] This can be due to female or male concerns. The male to female distribution of causes is not well-defined.[45] However, men make up a significant percent of the infertile population. This appears to be an overlooked concern when considering the impact this can have on men sexually and psychosocially. Universally, masculinity is often tied to fertility. For many men, especially in certain cultures, being able to produce children is a direct indication of one's manhood and virility.[46] Evidently, when that ability is stripped away, it can have a profound impact. In a series of interviews, it was found that men tended to struggle with expressing their feelings about their infertility. Because they were unable to fulfill their roles sexually, they felt failure. Many often use denial as a coping mechanism and therefore did not seek medical treatment.[47] This loop can be problematic and encourages the need to recognize psychosocial impact urological conditions may have on men. Smith, et al. conducted a study that found that infertility due to a male factor is linked to a lower quality of life.[47,48] When men believed that they were solely responsible for the infertility, they had less sexual enjoyment and more feelings of failure.[47,48] A study from Taiwan with 13,317 infertile patients highlighted the total prevalence of mental disorders of 12.41%.[49] The average time from diagnosis of infertility to the onset of mental illness was 1.67 years, indicating a strong argument for a direct correlation.[49] Many factors played a role in the onset of mental illness, for example, income, occupation, treatment methods, hospital level.[49] While the diagnosis of infertility itself is heartbreaking, the journey through fertility treatment can be a grueling process as well. Two studies examined in the Human Fertility journal displayed significant distress in couples undergoing treatment for fertility. This was based on multiple factors as well, such as relationship dynamics, self-esteem, mental health, and attitude towards masculinity.[50] It is no surprise that mental illness is very prevalent with the diagnosis of infertility, and requesting support is particularly challenging for men. There are many in-person and online support groups for those going through similar struggles, but since asking for help is traditionally seen as a feminine trait, men are often neglected in these settings.[51] Many men even report that they feel that these groups are geared towards women.[51] A population-based analysis of urology male infertility specialists, conducted by Nangia, et al., demonstrated the following that male fertility specialists are very scarce, men do not participate in support networks as much, and mental health providers who specialize in infertility are practically non-existent.[47,52] These statistics prompt the need for more resources and better counseling availability for men battling with such issues. It is important to recognize that there are differences in generally how men and women cope and react to health concerns. This emphasizes the importance of health and fertility counselor, whose primary focus should be identifying those disparities to guide both parties to limit distress within the individual as well as in the relationship.[53]

BENIGN PROSTATIC HYPERPLASIA

Benign prostatic hyperplasia (BPH) is a condition that is characterized by a proliferation of stromal and glandular cells in the prostate gland, hence only affecting men. A majority of men as they age eventually acquire this condition. Based on medical records, 80% of men over 70 years old get BPH.[54] This can be an asymptomatic condition, or it can cause lower urinary tract issues.[54] While the symptoms of this condition may not be particularly severe, it can lead to lower quality of life and overall well-being. A

survey study published in the Journal of Clinical Nursing highlights the significantly lower quality of life and psychological well-being in patients with BPH.[55] The symptoms caused by the conditions as well the consequent anxiety and depression played the largest role in determining quality of life.[55] In fact, a retrospective study conducted in South Korea correlated increased rates of suicide amongst men with BPH.[56] The suicide rate of people with BPH was 97.3 per 100,000, compared in 61.6 in non-BPH patient.[56] This is a 1.58 times higher risk in patients with BPH.[56] There are treatments available for BPH and while some can help alleviate some of the emotional burden by treating the symptoms, treatments can also be associated with their own set of emotional consequences. For example, a meta-analysis published in the Journal of Clinical Psychopharmacology illustrates that finasteride, a well-known treatment for BPH, may be associated with causing mental health issues, such as depression, anxiety, and even increased suicidal ideation.[57] To investigate this further, a study done on rats found that repeated and long-term administration of finasteride increased immobility and lack of motivation, implying depression-like behavior. It also decreased overall cognitive function.[58] The exact neural mechanism is not well-defined; however, it is important to note that a treatment that is meant to help a condition can end up causing harm in other ways.

BPH is an emotionally draining condition and some treatment modalities can substantially improve overall well-being. Prostatic surgery is one such treatment option. A survey showed a significant improvement in quality of life three months after undergoing prostate surgery. It revealed that men felt like they had better physical and social function and a lot less limitations than they had previously due to emotional issues, pain, and health perceptions caused by the condition.[59] When considering treatment for BPH, it is important to weigh the risk and benefits as an aftereffect of the surgery in terms of mental health, as well as physical health.

KIDNEY STONES

Kidney stones are a prevalent disease with a higher incidence with increasing age in males and females. The disease can present as an acute emergency that can develop into an infection and lead to other medical complications or an asymptomatic condition than can later manifest. Symptoms of kidney stones include flank pain, nausea, urinary urgency, difficulty urinating, and penile or testicular pain.[60] The stones originate from calcium stone formations in the kidney medullary interstitium. To confirm the diagnosis, patients undergo imaging to assess the location and cause of the obstruction, which can be done through a CT of the abdomen.[60] Treatment can usually be passive or surgical. However, the uncertainty of the condition has been shown to affect patients' mental health and lead to increased anxiety about the unknowns of the formation of other stones.

In general, the health-related quality of life in patients suffering from kidney stones was found to be worse when compared to the general population and patients with kidney stones were more likely to suffer from depression relative to the general population.[61] Treatment for kidney stones is often a complex, multifaceted approach that requires multiple hospital visits from the patients.[62] These treatment modalities can worsen the patients' health-related quality of life. Given the complexity of the treatment, the American Urological Association has put in their guidelines that treatment decisions should incorporate the patients' preferences.[62] Effects of kidney stones are different within each patient in terms of variability with aggressivity, acuity, and symptomology.[63] No current metric allows clinicians to use this variability to best tailor treatment to a specific method. The relationship between kidney stones and worsened mental health and quality of life is strengthened by studies that have shown promise in using the Wisconsin Stone Quality of Life questionnaire in capturing various symptoms and challenges associated with kidney stones.[63] This metric is useful in relating the disease to the patients' health-related quality of life and may help clinicians make treatment decisions that help improve the quality of life of patients suffering from kidney stones. The interventions used to treat kidney stones tend to significantly impact the patients' quality of life and can negatively impact their mental health and social security. A significant stressor for patients is that there is no clear end to their disease, which further exacerbates fear of the unknown.[62] Factors that significantly alter the quality of life in patients with kidney stones are concerns about their overall health, pain, anxiety about the course of the disease, sleep disruption, and disruption of disease inability to socialize and travel.[62]Based on these findings it is important for clinicians to adapt treatment approaches for kidney stones to involve the patient to a greater degree and if possible to incorporate impacts on mental health and quality of life into treatment decisions.

URINARY RETENTION

Urinary retention is a condition that can stem from many causes and lead to potential delirium in patients.[64] Urinary retention may arise from obstructions, prostatic hyperplasia in males, aging, diabetes mellitus, neurologic disorders, medications, distortion of ureters, and functional causes such as damage to the detrusor muscle. Urinary retention can more commonly lead to UTIs or, if severe enough, renal impairment due to the high pressure. If left untreated, urinary retention may lead to increased fear of damaging vital organs in patients who may be unsure of their disease. Treatment is typically done by catheterization.

Delirium from urinary retention is poorly documented in the literature but can have deleterious effects on a patient's well-being and care. The proposed mechanism of urinary retention delirium is increased catecholamine production due to increased bladder tension leading to increased sympathetic tones.[64,65] While urinary retention is not reported to cause immediate mental health changes in patients, it is important for clinicians to immediately evaluate the poten-

tial of urinary retention causing delirium or a neurologic deterioration in an acute setting.

CONCLUSION

From the review of the diverse set of GU pathologies we also understand that there is great difference in MHI needs depending on the pathology. For Peyronie's Disease, we recognized that its rarity alongside the physically debilitating symptoms cause a higher incidence of MHI amongst this subpopulation and there is no available treatment noted for MHI associated with this disease. Given the greater number of erectile dysfunction cases, MHI treatment has been studied for this population ranging from group therapy to plant based medications. It is also recognized that depression and anxiety symptoms are also elevated within this sub-population and the American Urological Association highly recommends psychiatric referral in case. As for infertility especially in men, societal pressures can be very heavy and the establishment of support networks of care would be higher priority for those patients. While it is also recognized that there is lower quality of life for all benign prostatic hyperplasia, kidney stone, and urinary retention patients, a careful coordination on what treatment plan to move forward oftentimes acts as a component for the mental health of those patients. As such, in line with previous recommendations, psychological support from peers, therapists, and healthcare providers further prove to be crucial for those subpopulations.

To provide greater psychosocial support for patients undergoing non-oncologic GU treatment, incorporating mental health metrics into patient care, careful coordination with psychiatrists and psychologists for psychotherapy and psychopharmacology, alongside MHI considerations of operative vs nonoperative treatment by urologists will all act as significant variables of care for non-oncologic GU patients.

REFERENCES

1. Volkert J, Schulz H, Härter M, Wlodarczyk O, Andreas S. The prevalence of mental disorders in older people in Western countries – a meta-analysis. *Ageing Research Reviews*. 2013;12(1):339-353. doi:10.1016/j.arr.2012.09.004

2. Hisham IN, Townsend G, Gillard S, Debnath B, Sin J. COVID-19: the perfect vector for a mental health epidemic. *BJPsych Bull*. 2021;45(6):332-338. doi:10.1192/bjb.2020.60

3. Cooke JE, Eirich R, Racine N, Madigan S. Prevalence of posttraumatic and general psychological stress during COVID-19: A rapid review and meta-analysis. *Psychiatry Research*. 2020;292:113347. doi:10.1016/j.psychres.2020.113347

4. Shorey S, Ng ED, Wong CHJ. Global prevalence of depression and elevated depressive symptoms among adolescents: A systematic review and meta-analysis. *British J Clinic Psychol*. 2022;61(2):287-305. doi:10.1111/bjc.12333

5. Stuntz M, Perlaky A, des Vignes F, Kyriakides T, Glass D. The Prevalence of Peyronie's Disease in the United States: A Population-Based Study. *PLoS ONE*. 2016;11(2):e0150157. doi:10.1371/journal.pone.0150157

6. Brand WO. Peyronie's Disease: Diagnosis and medical management. In: Post T, ed. *UpToDate*. UpToDate; 2022. Accessed May 28, 2022. http://www.uptodate.com

7. Terrier JE, Nelson CJ. Psychological aspects of Peyronie's disease. *Transl Androl Urol*. 2016;5(3):290-295. doi:10.21037/tau.2016.05.14

8. Gelbard MK, Dorey F, James K. The natural history of Peyronie's disease. *J Urol*. 1990;144(6):1376-1379. doi:10.1016/s0022-5347(17)39746-x

9. Smith JF, Walsh TJ, Conti SL, Turek P, Lue T. Risk factors for emotional and relationship problems in Peyronie's disease. *J Sex Med*. 2008;5(9):2179-2184. doi:10.1111/j.1743-6109.2008.00949.x

10. Nelson CJ, Diblasio C, Kendirci M, Hellstrom W, Guhring P, Mulhall JP. The Chronology of Depression and Distress in Men with Peyronie's Disease. *The Journal of Sexual Medicine*. 2008;5(8):1985-1990. doi:10.1111/j.1743-6109.2008.00895.x

11. Kuja-Halkola R, Henningsohn L, D'Onofrio BM, et al. Mental Disorders in Peyronie's Disease: A Swedish Cohort Study of 3.5 Million Men. *Journal of Urology*. 2021;205(3):864-870. doi:10.1097/ju.0000000000001426

12. Zachalski W, Krajka K, Matuszewski M. Evaluation of the Treatment of Congenital Penile Curvature Including Psychosexual Assessment. *The Journal of Sexual Medicine*. 2015;12(8):1828-1835. doi:10.1111/jsm.12933

13. Soave A, Laurich S, Dahlem R, et al. Negative Self-Perception and Self-Attitude of Sexuality Is a Risk Factor for Patient Dissatisfaction Following Penile Surgery with Small Intestinal Submucosa Grafting for the Treatment of Severe Peyronie's Disease. *Journal of Clinical Medicine*. 2019;8(8):1121. doi:10.3390/jcm8081121

14. Ferrini MG, Gonzalez-Cadavid NF, Rajfer J. Aging related erectile dysfunction—potential mechanism to halt or delay its onset. *Transl Androl Urol*. 2017;6(1):20-27. doi:10.21037/tau.2016.11.18

15. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and Its Medical and Psychosocial Correlates: Results of the Massachusetts Male Aging Study. *Journal of Urology*. 1994;151(1):54-61. doi:10.1016/s0022-5347(17)34871-1

16. Araujo AB, Mohr BA, McKinlay JB. Changes in Sexual Function in Middle-Aged and Older Men: Longitudinal Data from the Massachusetts Male Aging Study. *J Am Geriatr Soc*. 2004;52(9):1502-1509. doi:10.1111/j.0002-8614.2004.52413.x

17. Laumann EO, Paik A, Rosen RC. Sexual Dysfunction in the United States. *JAMA*. 1999;281(6):537. doi:10.1001/jama.281.6.537

18. Bacon CG, Mittleman MA, Kawachi I, Giovannucci E, Glasser DB, Rimm EB. Sexual Function in Men Older Than 50 Years of Age: Results from the Health Professionals Follow-up Study. *Ann Intern Med*. 2003;139(3):161. doi:10.7326/0003-4819-139-3-200308050-00005

19. Raymond CR, Khera M. Epidemiology and etiologies of male sexual dysfunction. In: Post T, ed. *UpToDate*. UpToDate; 2022. Accessed June 5, 2022. http://www.uptodate.com

20. Krane RJ, Goldstein I, de Tejada IS. Impotence. *N Engl J Med*. 1989;321(24):1648-1659. doi:10.1056/nejm198912143212406

21. Karacan I, Williams R, Thornby J, Salis P. Sleep-related penile tumescence as a function of age. *American Journal of Psychiatry*. 1975;132(9):932-937. doi:10.1176/ajp.132.9.932

22. Melehan KL, Hoyos CM, Hamilton GS, et al. Randomized Trial of CPAP and Vardenafil on Erectile and Arterial Function in Men With Obstructive Sleep Apnea and Erectile Dysfunction. *The Journal of Clinical Endocrinology & Metabolism*. 2018;103(4):1601-1611. doi:10.1210/jc.2017-02389

23. Kedia GT, Ückert S, Tsikas D, Becker AJ, Kuczyk MA, Bannowsky A. The Use of Vasoactive Drugs in the Treatment of Male Erectile Dysfunction: Current Concepts. *Journal of Clinical Medicine*. 2020;9(9):2987. doi:10.3390/jcm9092987

24. Melman R. Pathophysiology of Erectile Dysfunction. *Mol Urol*. 1999;3(2):87-102.

25. Kaiser DR, Billups K, Mason C, Wetterling R, Lundberg JL, Bank AJ. Impaired brachial artery endothelium-dependent and -independent vasodilation in men with erectile dysfunction and no other clinical cardiovascular disease. *J Am Coll Cardiol*. 2004;43(2):179-184. doi:10.1016/j.jacc.2003.07.042

26. DeLay KJ, Haney N, Hellstrom WJ. Modifying Risk Factors in the Management of Erectile Dysfunction: A Review. *World J Mens Health*. 2016;34(2):89-100. doi:10.5534/wjmh.2016.34.2.89

27. Tan HM, Tong SF, Ho CCK. Men's Health: Sexual Dysfunction, Physical, and Psychological Health—Is There a Link? *The Journal of Sexual Medicine*. 2012;9(3):663-671. doi:10.1111/j.1743-6109.2011.02582.x

28. Korfage IJ, Pluijm S, Roobol M, Dohle GR, Schröder FH, Essink-Bot ML. Erectile Dysfunction and Mental Health in a General Population of Older Men. *The Journal of Sexual Medicine*. 2009;6(2):505-512. doi:10.1111/j.1743-6109.2008.01111.x

29. Low WY, Khoo EM, Tan HM, Hew FL, Teoh SH. Depression, hormonal status and erectile dysfunction in the aging male: results from a community study in Malaysia. *The Journal of Men's Health & Gender*. 2006;3(3):263-270. doi:10.1016/j.jmhg.2006.02.007

30. Sugimori H, Yoshida K, Tanaka T, et al. Relationships between Erectile Dysfunction, Depression, and Anxiety in Japanese Subjects. *The Journal of Sexual Medicine*. 2005;2(3):390-396. doi:10.1111/j.1743-6109.2005.20354.x

31. Calzo JP, Austin SB, Charlton BM, et al. Erectile Dysfunction in a Sample of Sexually Active Young Adult Men from a U.S. Cohort: Demographic, Metabolic and Mental Health Correlates. *Journal of Urology*. 2021;205(2):539-544. doi:10.1097/ju.0000000000001367

32. Liu Q, Zhang Y, Wang J, et al. Erectile Dysfunction and Depression: A Systematic Review and Meta-Analysis. *The Journal of Sexual Medicine*. 2018;15(8):1073-1082. doi:10.1016/j.jsxm.2018.05.016

33. Herman JB, Brotman AW, Pollack MH, Falk WE, Biederman J, Rosenbaum JF. Fluoxetine-induced sexual dysfunction. *J Clin Psychiatry*. 1990;51(1):25-27.

34. Melnik T, Soares B, Nasello AG. Psychosocial interventions for erectile dysfunction. *Cochrane Database of Systematic Reviews*. 2007;2010(1). doi:10.1002/14651858.cd004825.pub2

35. Riley AJ, Goodman RE, Kellett JM, Orr R. Double Blind Trial of Yohimbine Hydrochloride in the Treatment of Erection Inadequacy. *Sexual and Marital Therapy*. 1989;4(1):17-26. doi:10.1080/02674658908407870

36. Coyne KS, Kvasz M, Ireland AM, Milsom I, Kopp ZS, Chapple CR. Urinary Incontinence and its Relationship to Mental Health and Health-Related Quality of Life in Men and Women in Sweden, the United Kingdom, and the United States. *European Urology*. 2012;61(1):88-95. doi:10.1016/j.eururo.2011.07.049

37. Stickley A, Santini ZI, Koyanagi A. Urinary incontinence, mental health and loneliness among community-dwelling older adults in Ireland. *BMC Urol*. 2017;17(1):29. doi:10.1186/s12894-017-0214-6

38. Choi EPH, Lam CLK, Chin WY. Mental health of Chinese primary care patients with lower urinary tract symptoms. *Psychology, Health & Medicine*. 2016;21(1):113-127. doi:10.1080/13548506.2015.1032309

39. Lee H yeon, Rhee Y, Choi KS. Urinary incontinence and the association with depression, stress, and self-esteem in older Korean Women. *Sci Rep*. 2021;11(1):9054. doi:10.1038/s41598-021-88740-4

40. Stewart W, van Rooyen J, Cundiff G, et al. Prevalence and burden of overactive bladder in the United States. *World J Urol*. 2003;20(6):327-336. doi:10.1007/s00345-002-0301-4

41. Coyne KS, Wein A, Nicholson S, Kvasz M, Chen CI, Milsom I. Comorbidities and personal burden of urgency urinary incontinence: a systematic review. *Int J Clin Pract*. 2013;67(10):1015-1033. doi:10.1111/ijcp.12164

42. Lee DM, Tetley J, Pendleton N. Urinary incontinence and sexual health in a population sample of older people. *BJU Int*. 2018;122(2):300-308. doi:10.1111/bju.14177

43. Abrams P, Smith AP, Cotterill N. The impact of urinary incontinence on health-related quality of life (HRQoL) in a real-world population of women aged 45-60 years: results from a survey in France, Germany, the UK and the USA. *BJU Int*. 2015;115(1):143-152. doi:10.1111/bju.12852

44. Steenstrup B, Lopes F, Cornu JN, Gilliaux M. Cognitive-behavioral therapy and urge urinary incontinence in women. A systematic review. *Int Urogynecol J*. 2022;33(5):1091-1101. doi:10.1007/s00192-021-04989-3

45. Anawalt DB. Causes of Male infertility. In: Post T, ed. *UpToDate*. UpToDate; 2022. Accessed May 28, 2022. http://www.uptodate.com

46. Evans J. 'They are called Imperfect men': Male Infertility and Sexual Health in Early Modern England. *Soc Hist Med*. 2016;29(2):311-332. doi:10.1093/shm/hku073

47. Petok WD. Infertility counseling (or the lack thereof) of the forgotten male partner. *Fertility and Sterility*. 2015;104(2):260-266. doi:10.1016/j.fertnstert.2015.04.040

48. Smith JF, Walsh TJ, Shindel AW, et al. Sexual, marital, and social impact of a man's perceived infertility diagnosis. *J Sex Med*. 2009;6(9):2505-2515. doi:10.1111/j.1743-6109.2009.01383.x

49. Wang JY, Chen JD, Huang CC, et al. Investigation of time-dependent risk of mental disorders after infertility diagnosis, through survival analysis and data mining: a nationwide cohort study. *The European Journal of Contraception & Reproductive Health Care*. 2018;23(3):218-226. doi:10.1080/13625187.2018.1450972

50. Dooley M, Dineen T, Sarma K, Nolan A. The psychological impact of infertility and fertility treatment on the male partner. *Human Fertility*. 2014;17(3):203-209. doi:10.3109/14647273.2014.942390

51. Miner SA, Daumler D, Chan P, Gupta A, Lo K, Zelkowitz P. Masculinity, Mental Health, and Desire for Social Support Among Male Cancer and Infertility Patients. *Am J Mens Health*. 2019;13(1):155798831882039. doi:10.1177/1557988318820396

52. Nangia AK, Likosky DS, Wang D. Distribution of male infertility specialists in relation to the male population and assisted reproductive technology centers in the United States. *Fertility and Sterility*. 2010;94(2):599-609. doi:10.1016/j.fertnstert.2009.02.012

53. Peterson B, Boivin J, Norré J, Smith C, Thorn P, Wischmann T. An introduction to infertility counseling: a guide for mental health and medical professionals. *J Assist Reprod Genet*. 2012;29(3):243-248. doi:10.1007/s10815-011-9701-y

54. McVary KT. Epidemiology and pathophysiology of benign prostatic hyperplasia. In: Post T, ed. *UpToDate*. UpToDate; 2022. Accessed May 28, 2022. http://www.uptodate.com

55. Pinto JDO, He HG, Chan SWC, Toh PC, Esuvaranathan K, Wang W. Health-related quality of life and psychological well-being in patients with benign prostatic hyperplasia. *J Clin Nurs*. 2015;24(3-4):511-522. doi:10.1111/jocn.12636

56. Lee SU, Lee SH, So AH, et al. Association between benign prostatic hyperplasia and suicide in South Korea: A nationwide retrospective cohort study. *PLoS ONE*. 2022;17(3):e0265060. doi:10.1371/journal.pone.0265060

57. Pompili M, Magistri C, Maddalena S, Mellini C, Persechino S, Baldessarini RJ. Risk of Depression Associated With Finasteride Treatment. *J Clin Psychopharmacol*. 2021;41(3):304-309. doi:10.1097/jcp.0000000000001379

58. Sasibhushana RB, Shankaranarayana Rao BS, Srikumar BN. Repeated finasteride administration induces depression-like behavior in adult male rats. *Behavioural Brain Research*. 2019;365:185-189. doi:10.1016/j.bbr.2019.03.006

59. Erkoc M, Otunctemur A, Besiroglu H, Altunrende F. Evaluation of quality of life in patients undergoing surgery for benign prostatic hyperplasia. *The Aging Male*. 2018;21(4):238-242. doi:10.1080/13685538.2018.1433654

60. Evan AP, Worcester EM, Coe FL, Williams J Jr, Lingeman JE. Mechanisms of human kidney stone formation. *Urolithiasis*. 2015;43(S1):19-32. doi:10.1007/s00240-014-0701-0

61. Raja A, Hekmati Z, Joshi HB. How Do Urinary Calculi Influence Health-Related Quality of Life and Patient Treatment Preference: A Systematic Review. *Journal of Endourology*. 2016;30(7):727-743. doi:10.1089/end.2016.0110

62. Raja A, Wood F, Joshi HB. The impact of urinary stone disease and their treatment on patients' quality of life: a qualitative study. *Urolithiasis*. 2020;48(3):227-234. doi:10.1007/s00240-019-01142-0

63. Penniston KL, Nakada SY. Development of an Instrument to Assess the Health Related Quality of Life of Kidney Stone Formers. *Journal of Urology*. 2013;189(3):921-930. doi:10.1016/j.juro.2012.08.247

64. Thelmo FL, Tzarnas S, Rosal NR, Kramer M, Walters L. Cystocerebral Syndrome: An Updated Review and a New Proposed Mechanism for an Often Forgotten Cause of Delirium. *Cureus*. Published online October 19, 2020. doi:10.7759/cureus.11034

65. Waardenburg IE. Delirium caused by urinary retention in elderly people: A case report and literature review on the "cystocerebral syndrome." *J Am Geriatr Soc*. 2008;56(12):2371-2372. doi:10.1111/j.1532-5415.2008.02035.x