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The Epidemic of COVID-19-Related Erectile Dysfunction: A Scoping Review and Health Care Perspective

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ABSTRACT

Introduction: COVID-19 infection is expected to be associated with an increased likelihood of erectile dysfunction (ED). Considering the high transmissibility of COVID-19, ED may be a concerning consequence for a large segment of the population.

Aims: To (1) summarize existing published evidence for the impact of COVID-19 on the prevalence, severity, treatment, and management of ED; and (2) identify health-related trends in the emerging literature and identify gaps in the existing research literature and make recommendations for future research needs in the area.

Methods: A scoping literature search was conducted on April 27, 2021. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (Preferred Reporting Items for Systematic Reviews and Meta-Analyses-ScR) checklist was followed. The literature search was performed in PubMed using the terms: COVID-19, erectile, sexual, and dysfunction. A total of 693 publications were screened for relevance. Studies were appraised for their level of evidence based on study design and the rigor of methodology.

Results: The evidence that COVID-19 infection causes or impacts ED is compelling. Four topics emerged regarding the nature of the association between COVID-19 and ED: (1) the biological impact of COVID-19 infection on ED; (2) the mental health impact of COVID-19 on ED; (3) the impact of COVID-19 on the management of ED and access to ED treatment; and (4) health disparities and the impact of COVID-19 on ED. Long-term and well-designed studies are needed to clarify the extent of the impact of COVID-19 on ED. The pandemic exposed several vulnerabilities within worldwide healthcare and social systems.

Conclusion: COVID-19 has a uniquely harmful impact on men's health and erectile function through biological, mental health, and healthcare access mechanisms. As the pandemic wanes, strategies to identify long-term effects and additional health care support may be needed to adequately mitigate the impact of COVID-19 on men's health. Hsieh T-C, Edwards NC, Bhattacharyya SK, et al. The Epidemic of COVID-19-Related Erectile Dysfunction: A Scoping Review and Health Care Perspective. Sex Med Rev 2022;10:286–310.

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Key Words: Erectile Dysfunction; COVID-19; Scoping Review; Biological; Mental Health; Men's Health

INTRODUCTION

The COVID-19 pandemic has had a devastating impact on the health and wellbeing of people across the world. The

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uniquely harmful impact of the virus on men's health is becoming more apparent and is more commonly being documented in the published medical literature.^{1–3} Men have been shown to

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Abbreviations: ACE2, angiotensin-converting enzyme 2; BMI, body mass index; ED, erectile dysfunction; FSFI, female sexual function index; IIEF, international index of erectile function; IL, interleukin; IQR, interquartile range; IS, intercourse satisfaction; NHANES, national health and nutrition examination survey; OS, overall satisfaction; PRISMA, preferred reporting items for systematic reviews and meta-analyses; PRISMA-ScR, preferred reporting items for systematic reviews and meta-analyses extension for scoping reviews; PTSD, post-traumatic stress disorder; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, sexual desire; TNF, tumor necrosis factor.

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have an increased risk of both developing the severe form of COVID-19 and dying from it.^{3,4} Biological (sex) and socio-cultural (gender) factors, compounded by socio-economic factors and ethnicity, have had a marked impact on the aftermath of COVID-19.^{2,3} Testosterone has been identified as a bivalent risk factor for poor prognosis (high/normal in younger; lower in elderly) in COVID-19.¹ It has been postulated that testosterone may facilitate SARS-CoV-2 entry in human cells and men may develop a blunted immune response against SARS-CoV-2, being exposed to less viral clearance and more viral shedding and systemic spread of the disease.¹ Low levels of serum testosterone observed in men, on the other hand, may predispose them to greater background systemic inflammation, cardiovascular and metabolic diseases, and immune system dysfunction from COVID-19 infection, hence potentially enhancing the longterm consequences of the virus.¹ Even men who have never contracted COVID-19 have had their lives severely affected by the pandemic both physically and emotionally as it has caused widespread disruption to normal existence, men's social world, preventative health and healthcare access, and the economy.²

One of the repercussions of COVID-19 is its impact on men's sexual health. COVID-19 infection is expected to be associated with an increased likelihood of erectile dysfunction (ED). Considering the high transmissibility of COVID-19, ED could be a concerning consequence for a large segment of the population.⁵ However, to our knowledge, the evidence for the association between COVID-19 and ED has not been collectively gathered, integrated, and appraised. The objectives of this study

were to conduct a scoping literature review to: (1) summarize existing published evidence for the impact of COVID-19 on the prevalence, severity, treatment, and management of ED; and (2) identify health-related trends in the emerging literature and identify gaps in the existing research literature and make recommendations for future research needs in the area.

MATERIALS AND METHODS

The approach for the literature review was a scoping review given the heterogenous nature of the body of literature describing the relationship between COVID-19 and ED.⁶ Scoping reviews are a relatively new approach to evidence synthesis.⁷ They can synthesize research evidence and categorize or group existing literature in a given field in terms of its nature, features, and volume.⁸ Researchers may conduct scoping reviews instead of traditional reviews when the purpose of the review is to identify knowledge gaps, scope a body of literature, clarify concepts, or to investigate research conduct.⁷ Scoping reviews may also be helpful precursors to traditional systematic reviews and can be used to confirm the relevance of inclusion criteria and potential questions.⁷ They deliberately cast a wider net to identify topics that are connected but not necessarily completely within the topic of interest in order to help better discern boundaries of relevant literature. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews (PRISMA-ScR) Checklist⁹ was followed and adhered to in conducting the scoping literature review.



Figure 1. PRISMA flow diagram of article selection.

The literature review used the PubMed search engine and was conducted on April 27, 2021 with the search terms "COVID-19", "erectile", "sexual", and "dysfunction". A total of 693 publications were obtained using the search strategy Studies were included if they provided information about the relationship between COVID-19 and ED or if they discussed patients' experience of care during COVID-19. All studies underwent a title and abstract screening, and potentially relevant citations were checked in a full-text screening. Reference lists of selected articles were also reviewed for additional possible sources of information (Figure 1). Data extracted included the journal citation, publication year, country of origin, study design, and a summary of the pertinent findings. Studies were appraised for their level of evidence based on study design and the rigor of methodology used, as well as the ability to prevent and/or control for biases to analyze cause and effect.

RESULTS

A total of 60 studies were selected for inclusion in the scoping review. Table 1 presents the characteristics of the included studies and a summary of their findings. Twenty-three studies (38.3%) were from the US, 10 were from Italy (16.7%), 6 were from China (10.0%), 5 were from Turkey (8.3%), 4 were from India (6.7%), 2 each were from Canada, Greece, and Brazil (3.3%), and 1 each were from Japan, Iran, the UK, the Netherlands, Egypt, Finland, and Portugal (1.7%) (note that one study was from the US and Iran). Twenty-five studies were narrative/literature reviews (41.7%), 12 were patient surveys (20.0%), 11 (18.3%) were expert commentaries/editorials, three were retrospective database evaluations (5.0%), two were urologist surveys (3.3.%), two were systematic reviews/meta-analyses (3.3%), and one each was a prospective cohort study, a retrospective chart review, a case series, a case report, and laboratory/pre-clinical research (1.7%).

Many of the studies identified in the literature review examined how COVID-19 may affect ED prevalence and severity either directly or indirectly through the extensive impact of the virus on men's genitourinary, cardiovascular, and nervous systems (n = 26; 43.3%). Another large grouping of studies addressed the mental and psychosocial aspects of COVID-19 and ED (n = 28; 46.7%). Twenty-two studies (36.7%) described how COVID-19 had affected patients' access to ED care and changes in ED management since the pandemic. Disparities in care and the effect of ED and COVID-19 on vulnerable populations was addressed in 18 studies (30.0%). The studies that contributed to each of these four groupings are also noted in Table 1.

DISCUSSION

Four topics emerged regarding the association between COVID-19 and ED: (1) the biological impact of COVID-19 infection on ED; (2) the mental health impact of COVID-19 on ED; (3) the impact of COVID-19 on the management of ED

and access to ED treatment; and (4) health disparities and the impact of COVID-19 on ED. Table 1 outlines the topics covered by each of the included studies and Figure 2 illustrates the interactions of the four emergent topics. The following summaries highlight the most significant findings that were revealed for each of the four topics.

Topic 1: Biological Impact of COVID-19 Infection on ED

Evidence that COVID-19 may biologically impact ED both in regard to the prevalence of ED (ie, the number of men with ED) and the severity of ED in men with existing ED is beginning to emerge. A retrospective chart review of 12 outpatient urology clinics across Turkey investigated whether there have been variations in the presentations of male patients with sexual and reproductive health problems during the COVID-19 pandemic.¹⁰ Andrological problems (ie, ED, premature ejaculation, Peyronie's disease, and priapism, varicocele, infertility, primary/ secondary hypogonadism, anejaculation, spermatocele, and undescended testicles) were detected in 721 of 4,955 male patients included in the study. Study findings showed that there was a significant increase in overall andrological diagnosis in these patients during the pandemic period compared with the pre-pandemic period (n = 293 [17%] vs n = 428 [13.2%], P < .001, respectively) (Figure 3). The number of patients diagnosed with ED during the pandemic was significantly higher during COVID-19 compared to the pre-COVID-19 pandemic period (n = 150 [8.7%] vs n = 214 [6.6%], P = .008) (Figure 3).¹⁰ The authors hypothesized that possible reasons for more frequent presentation to the outpatient urology clinics with ED may include relationship strain due to the "Stay Home" policies, job losses and economic problems, and increased anxiety and depression. Limitations of this study include its retrospective design, lack of randomization, differences in patient baseline characteristics between the comparison groups, and potential confounding from unknown and/or unmeasured variables.

An Italian online survey study by Sansone and colleagues (2021) compared the prevalence of ED among men with (n = 75) and without (n = 25) COVID-19 using 3:1 propensity score matching.¹¹ Study findings showed that the prevalence of ED as measured with the Sexual Health Inventory for Men was significantly higher in the COVID-19 group (28.0% vs 9.3%; P = .027). Logistic regression models confirmed a significant effect of COVID-19 on the development of ED, independently of other variables affecting erectile function, such as psychological status, age, and body mass index (BMI). Age, BMI, and psychological health scores failed to reach statistical significance; however, history of COVID-19 was highly significant, resulting in a 5.66 odds ratio (95% confidence interval: 1.50–24.01) of having ED.

The physiology relevant for penile erection may be affected by COVID-19 through vasculogenic, neurogenic, and endocrine mechanisms. A literature review of the possible mechanisms involved in the development of ED in COVID-19 survivors by

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Table 1. Characteristics of the included studies and a summary of the findings

		Study Design		Торіс				
Study	Country of Origin		Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities	
Lisco et al 2021 ¹	ltaly	Narrative Review	 Data support a role of T as a bivalent COVID-19risk factor for poor prognosis (high/normal in younger; lower in elderly) Testicular damage may be a harmful consequence of infection even if the patient was asymptomatic 	\checkmark				
Pijls et al 2020 ⁴	Netherlands	Systematic Review & Meta-Analysis	 Screened 11.550 titles and included 59 studies comprising 36,470 patients in the analyses Men had a higher risk for infection with COVID-19 than women (relative risk (RR) 1.08, 95% CI 1.03 –1.12) When infected, they also had a higher risk for severe COVID-19 disease (RR 1.18, 95% CI 1.10–1.27), a higher need for intensive care (RR 1.38, 95% CI 1.09 – 1.74) and a higher risk of death (RR 1.50, 95% CI 1.18 to 1.91) 	\checkmark				
Duran et al 2021 ¹⁰	Turkey	Multi-center retrospective chart review	 Andrological problems in 721 of 4,955 males During COVID-19, there was a significant increase in andrological diagnosis compared to pre-COVID-19 (n = 293 [17%] vs n = 428 [13.2%], P < .001, respectively) There was a significant increase in male reproductive or sexual health problems (n = 107 [6.2%] vs n = 149 [4.6%], P = .016 and n = 186 [10.8%] vs n = 279 [8.6%], P = .013, respectively) ED diagnosis was also significantly higher than pre-COVID-19 (n = 150 [8.7%] vs n = 214 [6.6%], P = .008) 	\checkmark				
Sansone et al 2021 ¹¹	Italy	Patient Survey	 100 subjects (25 COVID-positive; 75 COVID-negative) The prevalence of ED was significantly higher in the COVID+ group (28% vs 9.33%; P = .027) Logistic regression models confirmed a significant effect of COVID-19 on the development of ED, independently of other variables affecting erectile function, such as psychological status, age, and BMI [OR 5.66, 95% CI: 1.50-24.01] 	\checkmark				

(continued)

Table 1. Continued

				Торіс				
Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities	
			 Likewise, subjects with ED were more likely to have COVID-19, once corrected for age and BMI [OR 5.27, 95% CI: 1.49–20.09] 					
Jin et al 2020 ¹²	China	Narrative Review	 Endothelial cells with high levels of angiotensin-converting enzyme 2 expression are major participants and regulators of inflammatory reactions and coagulation Endothelial activation and dysfunction participate in COVID-19 pathogenesis by altering the integrity of vessel barrier, promoting pro-coagulative state, inducing endothelial inflammation, and even mediating leukocyte infiltration 	\checkmark				
Konstantinopoulos et al 2007 ¹³	Greece	Narrative Review	 Endothelial dysfunction is a pathological entity that multiply affects the health status ED is recognized as a condition that is strongly inter- related with endothelial dysfunction, being a vascular event itself 	\checkmark				
Fu et al 2020 ¹⁴	China	Laboratory (Pre- Clinical) Research	 High level of ACE2 expression in testis, cardiovascular and gastrointestinal system indicated that SARS-CoV-2 might not only attack the lungs, but also affect other organs, particularly the testes, thus it may severely damage male sexual development for younger male and lead to infertility in an adult male, if he contracted COVID-19 	\checkmark				
Zhang et al 2020 ¹⁵	Canada	Narrative Review	 The finding that SARS-CoV-2 and SARS-CoV use the ACE2 receptor for cell entry has important impli- cations for understanding SARS-CoV-2 transmissi- bility and pathogenesis SARS-CoV and likely SARS-CoV-2 lead to downre- gulation of the ACE2 receptor, but not ACE, through binding of the spike protein with ACE2. leading to viral entry and replication, as well as severe lung injury 	\checkmark				
Rajendran et al 2013 ¹⁶	Japan	Narrative Review	 Alterations of endothelial cells and the vasculature play a central role in the pathogenesis, as endothelial cells have the key function in maintenance of patent and functional capillaries 	\checkmark				
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Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
Shoar et al 2020 ¹⁷	USA & Iran	Case Report	 Presents the clinical course of 2 males with COVID- 19 who developed sexual dysfunction, as anorgas- mia, after COVID-10 Although no evidence of viral replication or inflam- matory involvement could be identified in these cases' urogenital organs, a lack of other known risk factors for anorgasmia points to the role of COVID- 19 as the contributing factor 	\checkmark			
Fraietta et al 2020 ¹⁸	Brazil	Narrative Review	 There is the theoretical possibility that testicular damage and subsequent infertility may result following COVID-19 infection Available data and study findings are recent, based on small sample sizes, and present conflicting information 	\checkmark			
Navarra et al 2020 ¹⁹	Italy	Narrative Review	 Testicular cells expressing both ACE2 and TMPRRS2 are rare, suggesting that the virus may not harm male gametes However, SARS-CoV-2 could indirectly compromise male gametes, testicular cells, and therefore fertility because the fever and the cytokine storm associated with COVID-19 induce a sperm DNA fragmentation and reduce the male reproductive 	\checkmark			
Vishvkarma & Rajender 2020 ²⁰	India	Systematic Literature Review	• The presence of ACE2 on almost all testicular cells and the report of a significant impact of previous SARS coronavirus on testes suggest that SARS- CoV-2 is highly likely to affect testicular tissue, semen parameters and male fertility	\checkmark			
Corona et al 2020 ²¹	ltaly	Literature Review	 Several molecular characteristics of the SARS-CoV-2 can justify the presence of virus within the testis and possible alterations of spermatogenesis and endocrine function. Orchitis has been reported as a possible complication of SARS-CoV infection, but similar findings have not been reported for SARS-CoV-2. Alternatively, the orchitis could be the result of a vasculitis as COVID-19 has been associated with abnormalities in coagulation and the segmental vascularization of the testis could account for an orchitis-like syndrome. 	\checkmark			

Table 1. Continued

				Торіс			
Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
			 Andrological consultation and evaluation of gonadal function including semen analysis should be sug- gested. 				
Jannini 2017 ²²	Italy	Narrative Review	 Sexual medicine can be used as a new tool to understand and manage non-communicable diseases and as a marker of systemic health Moreover, the multipronged application of systems medicine to pathophysiologic changes leading to sexual dysfunction might sustain the growth of a young science such as sexual medicine 	\checkmark	\checkmark		
Abbas et al 2020 ²³	Egypt	Expert Commentary	 COVID-19 harms the reproductive and sexual health of males through psychological, immunological, or systemic effects As a result of social isolation, some people become suffering from depressed mood, which disrupts chemicals in the brain that has a role in promoting libido in females and males. Acute cardiac injury leads to a decrease in blood supply to the genitalia, and this can end with impotence ICU use of thiazide-type diuretics, the aldosterone receptor blockers, the β-adrenergic receptor blockers, or ACE inhibitors to control blood pressure can cause ED Strokes have negative impacts on sexual function and desire, causing a significant decline in erection or ejaculation 	\checkmark	\checkmark		
Mao et al 2020 ²⁴	China	Case Series	 Among 214 patients with COVID-19, 36.4% had neurologic symptoms and were more common with severe infection (45.5%) Patients with more severe infection had greater neurologic manifestations such as acute cerebrovascular diseases (5 [5.7%] vs 1 [0.8%]), impaired consciousness (13 [14.8%] vs 3 [2.4%]), and skeletal muscle injury (17 [19.3%] vs 6 [4.8%]). 	\checkmark	\checkmark		

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Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
Beghi et al 2020 ²⁵	Italy	Narrative Review	 COVID-19 is an influenza virus with neurotropic potential, presents with neurological manifestations many individuals Postinfectious neurological complications are the result of the activation of immune mechanisms and can explain the insurgence of immune-mediated diseases 	\checkmark	\checkmark		
Thomas & Konstantinidis 2021 ²⁶	Greece	Narrative Review	 The pathophysiology of ED remains a labyrinth. Underlying mechanisms of ED may be vasculogenic, neurogenic, anatomical, hormonal, drug-induced and/or psychogenic Neurogenic ED consists of a large cohort of ED, accounting for about 10% to 19% of all cases 	\checkmark	\checkmark		
Wu et al 2020 ²⁷	China	Narrative Review	 Viral infections have detrimental impacts on neurological functions, and even to cause severe neurological damage Coronaviruses (CoV), especially SARS-CoV-2, exhibit neurotropic properties and may cause neurological diseases 	\checkmark	\checkmark		
Roychoudhury et al 2021 ²⁸	India	Narrative Review	 Preliminary findings so far suggest the possibility of both direct and indirect infection of SARS-CoV-2 in the reproductive system of males and possible impact on general health and well-being potentially leading to infertility Evidence indicates a possible long-term effect of the pathogenicity of SARS-CoV-2 infection on testicular tissue, which may further impact reproductive performance 	\checkmark	\checkmark		
Lipsky & Hung 2020 ³	USA	Narrative Review	 Plausible theories for why men respond differently to the SARS-CoV-2 infection include sex-related differences in angiotensin-converting enzyme 2 receptors, immune function, hormones, habits, and coinfection rates Data from the CDC demonstrate disparities among racial and ethnic minorities, with mortality rates for African American and Latino men exceeding those for White or Asian males 	\checkmark			\checkmark

Table 1. Continued

		Study Design		Торіс			
Study	Country of Origin		Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
			 Continuing to collect data disaggregated by sex can help us understand why men are more likely to expe- rience severe disease 				
Pennanen-lire et al 2021 ²⁹	Finland	Narrative Review	 COVID-19 affects sexual function with implications on overall health Increased awareness of health-care providers on sexual health implications related to the COVID-19 is needed Telemedicine has an imperative role in allowing con- tinued support at times of lockdown and preventing worsening of the sexual, mental, and physical health after the pandemic. 	\checkmark	\checkmark	\checkmark	
Riley et al 2020 ³⁰	USA	Expert Commentary	 The strain that the outbreak imposes on health systems will undoubtedly impact the sexual and reproductive health of individuals living in low- and middle-income countries (LMICs); however, sexual and reproductive health will also be affected by societal responses to the pandemic, such as local or national lockdowns that force health services to shut down if they are not deemed essential, as well as the consequences of physical distancing, travel restrictions and economic slowdowns 	\checkmark	\checkmark		\checkmark
White 2020 ²	UK	Narrative Review	 Men's vulnerability to COVID-19 demonstrates the biological and socio-cultural factors at play and we are all affected The emotional impact of the lockdown and the longer term emerging recession coupled with the complex grieving many will be experiencing will result in high mental health burden and increased rates of suicide in men There will be consequences of people being unable, or unwilling, to seek medical help Loss of school will mean for many of the most vulnerable the loss of critical services and a safe and nurturing environment increasing the risk of depression, self-harm, attempted suicide 	\checkmark	\checkmark	\checkmark	\checkmark
							(continued)

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Table	1.	Continued

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Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
Sansone et al 2020 ⁵	Italy	Narrative Review	 Endothelial dysfunction, subclinical hypogonadism, psychological distress and impaired pulmonary hemodynamics all contribute to the potential onset of ED COVID-19 might exacerbate cardiovascular conditions; therefore, further increasing the risk of ED Testicular function in COVID-19 requires careful investigation for the unclear association with testosterone deficiency and the possible consequences for reproductive health Confinement and the illness in itself are both causes of stress; while only a minority of individuals might be more vulnerable to psychological trauma, there is no doubt that most people would experience some degree of emotional distress following isolation, social distancing, loss of relatives and friends, difficulties in securing medications, as well as the obvious economic consequences of lockdown 	\checkmark	\checkmark	\checkmark	~
Sathyanarayana & Andrade 2020 ³¹	India	Narrative Review	 Lockdown, forced proximity, anxiety about work and finances, and other stresses could trigger or worsen psychiatric disorders Stress is itself is related with disturbances in sexual functioning, and so lockdown-related stressors can result in such disturbances even in persons who are psychiatrically stable 		\checkmark		
Paul et al 2020 ³²	Brazil	Expert Commentary	 Social distancing and quarantines have been necessary as public health strategies, they may contribute to psychological and mental problems Anxiety and depression may translate into higher rates of psychogenic sexual dysfunction 		\checkmark		
Banerjee & Rao 2020 ³³	India	Narrative Review	 Long-term psychosocial and occupational outcomes of health-care workers dealing with SARS patients showed a rise in ED, premature ejaculation (PME), lack of sexual satisfaction in partners, and height- ened performance anxiety. This contributed to the burnout, work stress, absenteeism, substance abuse, and depressive disorders. 		\checkmark		

Table 1. Continued

		Study Design		Торіс				
Study	Country of Origin		Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities	
			 Literature related to sexual health and current COVID-19 pandemic is still in their infancy 					
Li et al 2020 ³⁴	China	Patient Survey	 44% of participants reported a decrease in the number of sexual partners and about 37% of participants reported a decrease in sexual frequency Multiple regression analysis showed that age, partner relationship, and sexual desire were closely related to sexual frequency 		\checkmark			
McKay et al 2020 ³⁵	USA	Patient Survey	 Among 728 gay and bisexual men, many made significant changes to their sexual behavior and partner selection. Men engaged in new strategies to reduce their risks of infection from partners, and expressed high levels of concern about how HIV may affect COVID-19 risk, treatment, and recovery 		\checkmark			
Maretti et al 2020 ³⁶	ltaly	Narrative Review	 COVID-19 has dramatically affected the quality of life by changing inter-personal relationships, community life and obviously sexual health. 		\checkmark			
Karsiyakali et al 2020 ³⁷	Turkey	Patient Survey	 Based on the International Index of Erectile Function and Female Sexual Function Index (FSFI) forms, a decline in sexual functioning was observed during the COVID-19 pandemic period Living in a metropolitan area was associated with a decline in both sexual intercourse frequency and sex- ual desire during the COVID-19 pandemic 		\checkmark			
Fang et al 2020 ³⁸	China	Patient Survey	 8.4% and 8.5% subjects had deteriorated erectile function or ejaculation control ability by self-evaluation, whereas 31.9% and 17.9% subjects had decreased IIEF-5 scores or increased PEDT Subjects with deteriorated erectile function and decreased IIEF-5 scores had higher General Anxiety Disorder-7 (<i>P</i> < .001 and <i>P</i> < .001) and higher Patient Health Questionnaire-9 score (<i>P</i> < .001 and <i>P</i> = .002) after the epidemic, decreased frequency of sexual life (<i>P</i> < .001 and <i>P</i> < .001) and physical exercise (<i>P</i> = .009 and .007) after the epidemic 		\checkmark			
De Rose et al 2020 ³⁹	Italy	Patient Survey	 A higher proportion of health care workers had low sexual desire (65.3% vs 56.8%, P = .042) 		\checkmark			

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Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
			• Age, being female, being a health care worker, having children at home, living with the partner, and having low sexual satisfaction were predictors of low level of sexual desire				
Bulut et al 2021 ⁴⁰	Turkey	Patient Survey	 Both stress disorder and ED were seen at higher rates in healthcare professionals (<i>P</i> < .001). The median IIEF-5 scores of nurses, married subjects, and those working in the Diagnosed Patient Area, were found to be higher (<i>P</i> < .001, <i>P</i> = .014, <i>P</i> = .011 respectively) 		\checkmark		
Karagöz et al 2020 ⁴¹	Turkey	Patient Survey	 Sexual function scores (IIEF erectile function domain and total FSFI) were lower during pandemic (24.55 ± 5.79 and 24.87 ± 7.88, respectively) vs pre-pandemic period (26.59 ± 4.51 and 26.02 ± 6.22) (<i>P</i> = .001 and <i>P</i> = .027, respectively) The frequency of sexual intercourse decreased in men (<i>P</i> = .001) while sexual avoidance and solitary sexual approach behaviors (masturbation or watching sexual content videos, etc.) increased (<i>P</i> = .001) 		\checkmark		
Carvalho et al 2020 ⁴²	Portugal	Expert Commentary	 The time of COVID-19 has required healthcare and social systems, clinicians, and citizens to adjust to the digital era in a matter of days. There is little evidence on how professionals and patients appraise such tools and whether these are effective Psychological distress in this specific scenario must be accounted by sexual health professionals, given the strong comorbidity between emotional disorders and sexual dysfunction 		\checkmark	\checkmark	

(continued)

Table 1. Continued	
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						Topic	
Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
Ruprecht et al 2020 ⁴³	⁵ USA	Patient Survey	 Marginalized populations experienced significant disparities in COVID-19 exposure, susceptibility, and treatment access, as well as in psychosocial effects of the pandemic Notably, Black and Latinx populations reported significant difficulties accessing food and supplies (<i>P</i> = .002) Healthcare access disparities were also visible, with Black and Latinx respondents reporting significantly lower levels of access to a provider to see if COVID-19 testing would be appropriate (<i>P</i> = .013), medical services (<i>P</i> = .001), and use of telehealth for mental health services (<i>P</i> = .001) 		\checkmark	\checkmark	\checkmark
Purtle 2020 ⁴⁴	USA	Expert Commentary	 There are specific aspects of the COVID-19 pandemic that could cause it to have disproportionately adverse impacts on the mental health of racial/ethnic minorities as well as low-income populations Socially disadvantaged groups (eg, racial/ethnic minorities, people with low income) will experience more psychiatric morbidity related to the pandemic than advantaged groups. The origins of these disparities are structural in nature Historically produced arrangements of power and privilege provide socially advantaged groups with more resources to limit their exposure to, and cope with, stressors caused by disaster 		\checkmark	\checkmark	\checkmark
lbrahimi et al 2020 ⁴⁵	USA	Expert Commentary	 COVID-19 has unveiled the distressful reality of racial disparity in the US, with African Americans bearing a disproportionate burden of morbidity and mortality due to COVID-19 Systemic racism is the primary operator of mental health disparity, which disproportionately affects African American families at all levels of the social ecological model 		\checkmark	\checkmark	\checkmark

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Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
			 Programs tailored towards reducing the dispropor- tionate detrimental effects of COVID-19 on the men- tal health of African Americans need to be culturally appropriate and consider the nuances of systemic racism, discrimination, and other institutionalized biases 				
Burnett et al 2016 ⁴⁶	USA	Literature Review	 Some reports suggest a relatively greater trend in African-American men than other ethnic groups toward obtaining clinical management for sexual dysfunction and experiencing psychosocial effects from it, lending additional support for the possibly greater effect of this problem in African-American men 		\checkmark	\checkmark	\checkmark
Betron et al 2020 ⁴⁷	USA	Expert Commentary	 The global health community has tools to engage men and promote healthy masculinities, drawing on two decades of programs and research. To improve, we must gather evidence on both biological and social differences in men, including age and race, and tailor health strategies, accordingly. A strategic focus on gender in the COVID-19 response will be critical for mitigating the impacts of the pandemic, as well as for ensuring uptake of future treatments and vaccines. 		\checkmark	\checkmark	\checkmark
Tonyali et al 2020 ⁴⁸	Turkey	Narrative Review	 All elective surgeries for benign urological conditions such as urinary tract stone disease that not caused complicated obstruction, benign prostate enlarge- ment, infertility, incontinence and genitourinary pro- lapse, ED, undescended testis, vesico-ureteral reflux should be postponed till the lasting of Covid-19 outbreak 			\checkmark	
Cocci 2020 ⁴⁹	Italy	Expert Commentary	 Patients with Peyronie's disease, requesting a penile implant, and anyone who needs treatment for erectile dysfunction will not be able to access treatment. We are not in a position to currently criticize these historical moments, but certainly, as health managers, we also have a duty to think about these patients. 			\checkmark	

						Topic	
Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
Aboumohamed et al 2021 ⁵⁰	USA	Urologist Survey	 478 total urologic surgeries were canceled and categorized: 250 Level I, 130 Level II, 98 Level III (73 adult, 25 pediatric). Level IIIc involved renal cell carcinoma ≥T2b, high-grade bladder urothelial carcinoma, adrenal mass/cancer >6 cm, testicular cancer requiring radical orchiectomy, and penile cancer Surgeries for urologic reconstruction, non-complicated nephrolithiasis, erectile dysfunction, and urinary incontinence were considered Level I 			\checkmark	
Witherspoon et al 2020 ⁵¹	Canada	Urologist Survey	 Physical examination has a limited role in the evaluation and management of ED and, therefore, this condition lends itself well to virtual visits Including the partner (if applicable) in the virtual visit can help elucidate their overall treatment goals more easily 			\checkmark	
Vaduganathan et al 2020 ⁵²	USA	Retrospective Database Analysis	 The modest decline for most common long-term therapies after peak could represent reduced contact with prescribing clinicians, restricted access to phar- macies, pharmacist rationing, loss of insurance from unemployment, or replete supplies from early stock- piling. Steep declines for amoxicillin and azithromycin appeared out of proportion to expected seasonal declines and could represent fewer outpatient pre- scriptions for upper respiratory tract infection symp- toms. 			\checkmark	
Jeffery et al 2020 ⁵³	USA	Retrospective Database Analysis	 The decrease in ED visits ranged from 41.5% in Colorado to 63.5% in New York. The weeks with the most rapid rates of decrease in visits were in March 2020, which corresponded with national public health messaging about COVID-19. Hospital admission rates from the ED were stable until new COVID-19 case rates began to increase locally; the largest relative increase in admission rates was 149.0% in New York, followed by 51.7% in Massachusetts, 36.2% in Connecticut, 29.4% in Colorado, and 22.0% in North Carolina. 			\checkmark	

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Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
Hartnett et al 2020 ⁵⁴	USA	Retrospective Database Analysis	 During the early pandemic period, the total number of U.S. ED visits was 42% lower than during the same period a year earlier, with the largest declines in visits in persons aged ≤14 y, females, and the Northeast region. 			\checkmark	
Dooley et al 2020 ⁵⁵	USA	Literature Review	 Virtual visit utilizing audiovisual telecommunications is a very attractive approach for sexual medicine patients. Many patients with sexual medicine problems are no longer going to accept the antiquated method of healthcare involving making an appointment, visiting a brick-and-mortar facility, and the requirement of having a physical examination. The new normal will be communicating with patients by utilizing telemedicine. 			\checkmark	
Czeisler et al 2020 ⁵⁶	USA	Patient Survey	 By June 30, 2020, because of concerns about COVID-19, an estimated 41% of U.S. adults had delayed or avoided medical care including urgent or emergency care (12%) and routine care (32%) Avoidance of urgent or emergency care was more prevalent among unpaid caregivers for adults, persons with underlying medical conditions, Black adults, Hispanic adults, young adults, and persons with disabilities 			\checkmark	\checkmark
Papautsky et al 2020 ⁵⁷	USA	Patient Survey	 The top reported barrier to receiving health care was the fear of SARS-CoV-2 infection (126/374, 33.6%) Almost half (1227/2570, 47.7%) of the participants reported experiencing health care delays 			\checkmark	\checkmark
Klein et al 2010 ⁵⁸	USA	Narrative Review	 Disparity in urology care is apparent in urologic cancer screening, treatment choices, and survival, as well as in the arena of chronic kidney disease, transplant allocation, and transplant outcomes. Latino men also seem to be affected more often by erectile dysfunction than Caucasian counterparts. Disparities such as these have been identified as a problem in the delivery of health care in the US, and resources have been allocated to help allay the disparity. 			\checkmark	\checkmark

						Topic	
Study	Country of Origin	Study Design	Findings	Biological Impact	Mental Health Impact	Access to Care Impact	Health Disparities
Burnett et al 2020 ⁵⁹	USA	Narrative Review	 While federal and state mandates ensure access to treatment for women's breast health, female-factor infertility, and gender affirmation to ensure that these individuals do not experience a diminished QoL, there are no comparable mandates for men's sexual and reproductive health. The burden of ED necessitates a call to action to improve the accessibility of ED treatments. 			\checkmark	\checkmark
Shindel et al 2020 ⁶⁰	USA	Expert Commentary	 In many ways, sexual medicine is ideal for telemedi- cine. Sexual medicine care providers are a highly spe- cialized group of clinicians who are frequently based in metropolitan areas. Patients travel great distances to see us; telemedicine may increase our reach to patients who cannot otherwise access specialized care. 			\checkmark	\checkmark
Mmeje et al 2020 ⁶¹	USA	Expert Commentary	 The COVID-19 pandemic offers the United States the opportunity to reexamine SRH delivery to hard-to-reach and vulnerable populations such as youth. Providers can increase accessible SRH services by removing traditional barriers to care that youth routinely encounter. Virtual visits can also triage patients for in-person visits. 			\checkmark	\checkmark
Treadwell 2020 ⁶²	USA	Expert Commentary	 The coronavirus pandemic has amplified health disparities by race and gender, perhaps most notably among African American men Populations that have disproportionate rates of health conditions such as hypertension, diabetes mellitus, obesity, and cardiovascular disease are more susceptible to both contracting coronavirus and to adverse outcomes 				\checkmark
Mulukutla et al 2010 ⁶³	USA	Prospective Cohort Study	 Black race is independently associated with arterial endothelial dysfunction. Racial differences in CVD risk may be related, in part, to race-related differences in endothelial dysfunction. 				\checkmark
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				Biological Health	 Access to 	Health
Study	Country of Origin	Study Design	Findings	Impact Impac	t Care Impact	Disparities
Smith et al 2009 ⁶⁴	USA	Patient Survey	 Relative to white men, Hispanic (OR 1.05, 95% Cl 0.99, 1.12), Asian (OR 1.1, 95% Cl 1.02, 1.19), and other men (OR 1.13, 95% Cl 1.06, 1.1.21) had increased odds of moderate-severe ED, while black men were less likely to report moderate to severe ED (OR 0.86, 95% Cl 0.81, 0.92). Black (OR 0.54, 95% Cl 0.48, 0.61) and Asian men (OR 0.91, 95% Cl 0.80, 1.04) were less likely to have severe ED after adjustment for age, socioeconomic status, medical co-morbidities, and lifestyle characteristics. 			>

COVID-19 and Erectile Dysfunction Scoping Review

Sansone and colleagues (2021) found that endothelial dysfunction, subclinical hypogonadism, and impaired pulmonary hemodynamics all contribute to the potential onset of ED.⁶⁵

Vascular integrity is necessary for erectile function. Accumulating evidence suggests that SARS-COV-2 damages the vascular endothelium,¹² the layer of specialized cells lining the inner surfaces of blood vessels and spaces like the surface of the sinusoids of tissues like the corpus cavernosum of the penis.¹³ The endothelium expresses the protein angiotensin-converting enzyme 2 (ACE2), through which SARS-COV-2 can access host cells.^{14,15} The vascular endothelium regulates the vascular tone, coagulation, metabolism, and permeability of the vessels.¹³ Endothelial dysfunction results in abnormal regulation of blood pressure, response to inflammation, impairment of the sensitive balance between the vasoconstricting and vasodilating agents and stimuli, and coagulation disorders.^{13,16} Vascular damage associated with COVID-19 is likely to affect the fragile vascular bed of the penis, potentially resulting in impaired erectile function.⁵ The recognized relationship between vascular health and ED²² suggests an important knowledge gap that could be addressed with translational research to elucidate the penile vascular effects of COVID-19 and their relationship to ED.

ED that manifests during COVID-19 may be a signal for underlying cardiovascular disease and may provide opportunities for earlier assessment of vascular dysfunction. ED, as a surrogate marker of cardiovascular and/or pulmonary health, could become extremely valuable as a quick and inexpensive first-line assessment of the pulmonary and cardiovascular complications for COVID-19 survivors.⁶⁵ The study by Sansone and colleagues (2021) also measured the likelihood of having a self-reported history of COVID-19 following a diagnosis of ED. Logistic regression models adjusted for age and BMI showed a significant association between ED and COVID-19, with a 5.27 odds ratio [95% CI: 1.49–20.09]. Evidence coming from diagnostic procedures, such as penile color-doppler ultrasound and hypothalamic-pituitary-testicular axis evaluation, may aid in assessing the extent to which COVID-19 has been able to impair erectile, and finally vascular, function.⁶⁵

COVID-19 may also affect ED prevalence and severity through the indirect impact of the virus on men's cardiovascular system and through the indirect effects of treatments for COVID-19.⁶⁵ For example, in some cases, COVID-19 may cause acute cardiac injury, leading to a decrease in blood supply to genitalia.²³ Also, COVID-19 patients admitted to the ICU who are given thiazide-type diuretics, aldosterone receptor blockers, β -adrenergic receptor blockers, or ACE inhibitors to control blood pressure are believed to be at risk for ED.²³

It has been demonstrated that patients with COVID-19 commonly have neurologic manifestations.²⁴ Disorders of the central and peripheral nervous system are present in most COVID-19 patients, while stroke, ataxia, seizures, and depressed level of consciousness are more common in severely affected patients.²⁵ The neurological effects observed in some cases of COVID-19 may

Table 1. Continued



Figure 2. Four topics reflecting the multidimensional impacts of COVID-19 infection on ED.

also have negative impacts on ED.²³ Neurogenic ED consists of a large cohort of ED, accounting for about 10% to 19% of all cases.²⁶ Neurological effects can occur via direct infection injury (blood circulatory pathway and neuronal pathway), hypoxia injury, ACE2, and immune injury²⁷ The tremendous diversity in the etiological factors associated with neurogenic contributors to ED²⁶ combined with the multidimensional effects of COVID-19 demonstrate the importance of further exploring the impact of COVID-19 infections on the nervous system.²⁷

Finally, ED may be affected by COVID-19 through endocrine mechanisms. COVID-19 features a state of hyperinflammation promoted by the same inflammatory cytokines found to be associated with clinical progression of sexual dysfunction (tumor necrosis factor [TNF]- α , interleukin [IL]-6 and IL-1 β).⁵ Although COVID-19 has been shown to cause systemic inflammation predisposing the involvement of multiple organs, the extent of its effect on the urogenital system has not yet been adequately researched.¹⁷ It has been theorized that that testicular damage may result following COVID-19 infection.^{18,19,28} The ACE2 gene is a receptor of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) for COVID-19. High levels of ACE2 expression in testes indicate that SARS-CoV-2 might affect the testes, potentially affecting male sexual function.^{14,20} The effects on testicular tissue may harm

testosterone production which may, in turn, have an association with ED insofar as its endocrine pathophysiologic risk.⁶⁵ The more likely effect of testosterone deficiency resulting from COVID-19 infection is decreased sexual libido, and lesser risk on decreasing erection ability.⁶⁵

Endothelial damage by SARS-COV-2 tied to endothelial expression of ACE2 combined with testosterone's role in modulating endothelial function⁶⁶ and associated inflammatory effects could be a factor in the differential burden of COVID-19 observed in some men.⁵ Men at greatest risk for having serious complications secondary to COVID-19 are those traditionally at risk for ED: older adult, diabetic, men with cardiovascular disease, overweight/obesity, and with multiple comorbidities.²⁹ Furthermore, weight gain as a result of the pandemic could have compounding long range adverse effects on the risks for overweight and obesity, diabetes, hypertension, and cardiovascular disease, all of which are associated with ED.³¹

Topic 2: The Mental Health Impact of COVID-19 on ED

It is important to consider the role of added stress, anxiety, and physical health implications for men with ED amid the



Figure 3. Andrological diagnoses in male patients pre- and during COVID-19.

COVID-19 pandemic.²⁹ Increased rates of post-traumatic stress disorder (PTSD), depression, and anxiety are expected in the general population, and even more in COVID-19 survivors, following the pandemic.⁶⁵ Anxiety and depression are commonly seen in men with ED.³² Psychological and mental health issues may lead to ED or worsening ED. ED has been shown to be 1.3 –2.3 times more common in individuals with anxiety and depression.⁶⁷ Although the psychological effects such as depression, anxiety, posttraumatic stress, and sleep disturbances are being studied for COVID-19, literature evaluating the relationship between these psychological and mental consequences and ED is rather scarce.³³

Some evidence has shown that sexual behavior was altered during the pandemic, including a reduction in sexual desire and number of sexual partners during the lockdown.^{34,35} The COVID-19 outbreak has dramatically affected men's quality of life by changing inter-personal relationships, community life, and sexual health.³⁶ An Internet-based survey of 1,356 participants in Turkey in June 2020 evaluated sexual function in terms of sexual intercourse frequency and sexual desire during the COVID-19 pandemic using the International Index of Erectile Function (IIEF) and Female Sexual Function Index (FSFI) forms.³⁷ Study findings showed a decline in sexual function during the pandemic period (40.8% had decline in frequency of masturbation, and 31.5% had a decline in sexual desire), particularly among individuals living in metropolitan areas.³⁷

An online questionnaire administered to Chinese men (n = 612) during the pandemic (April-May 2020) found that 8.4% and 8.5% subjects reported deteriorated erectile function

or ejaculation control ability by self-evaluation, whereas 31.9% and 17.9% subjects showed decreased IIEF-5 scores or increased premature ejaculation diagnostic tool scores.³⁸ Subjects with deteriorated erectile function by self-evaluation and decreased IIEF-5 scores displayed higher General Anxiety Disorder-7 (P < .001 and P = .001) and higher Patient Health Questionnaire-9 score (P < .001 and P = .002) and decreased frequency of sexual life (P < .001 and P < .001) and physical exercise (P = .009 and .007).³⁸ Subjects with decreased frequency of sexual life had reduced income (P < .001), increased anxiety (P < .001) and depression (P < .001).³⁸

A study evaluating sexual activity and depression in a sample of hospital workers and their acquaintances (n = 544) during the COVID-19 lockdown in Italy analyzed responses to the IIEF-15, FSFI, and Beck Depression Inventory.³⁹ Levels of sexual satisfaction were measured with the IIEF-15 overall satisfaction (OS) and intercourse satisfaction (IS) domains. Low satisfaction levels were defined using an arbitrary cut-off score ≤ 12.5 in the sum of IIEF-IS and IIEF-OS domains. The sexual desire (SD) domain from the IIEF was also recorded and low sexual desire was defined using an arbitrary cut-off score of ≤ 5 . The median (interquartile range) IIEF-Erectile Function score was 10 (3, 11) and the IIEF-Orgasmic Function score was 3 (3, 5). The IIEF-Intercourse Satisfaction score was 5 (0, 7), IIEF-Overall Satisfaction score was 5 (4, 9), and the IIEF-Sexual Desire score was 4 (3, 5).³⁹ To our knowledge, there are no studies clearly defining a cut-off value for abnormal satisfaction domains for the IIEF-15. However, the IIEF validation study by Rosen et al (1997) tested it in a series of 111 men with sexual dysfunction and 109 age-matched, normal volunteer controls.⁶⁸ The authors found

that the mean OS scores were 8.6 for controls and 4.4 for patients, and the mean IS scores were 10.6 for controls and 5.5 for patients.⁶⁸ On average, controls scored 7.0 in the sexual desire domain and patients scored 6.3.

The frequency of ED among male healthcare professionals (n = 159) during COVID-19 was also evaluated using the Impact of Event Scale-Revised and the IIEF-5 and compared to a control group of 200 people.⁴⁰ Both stress disorder and ED were seen at higher rates in healthcare professionals (P < .001).⁴⁰ The median IIEF-5 scores of male nurses, married subjects, and those working with confirmed COVID-19 patients, were found to be worse (15 [5–24] for physicians vs 10 (5–23) for nurses, P < .001; 16 [5–24] for single vs 12 [5–24] for married, P = .014; 15 [6–24] for suspected patient area vs 11 [5–24] for diagnosed patient area, P = .011).⁴⁰

A Turkish study evaluating the effect of COVID-19 pandemic on couples' sexuality (n = 245) utilizing the IIEF-15 found that male sexual function scores (IIEF erectile function domain) during the pandemic (May 2020) were statistically significantly lower compared to the pre-pandemic period (pre-pandemic 26.59 ± 4.51 vs during pandemic 24.55 ± 5.79 ; *P* = .001).⁴¹

Parallels can be drawn between the psychological consequences of COVID-19 and those coming from similar disasters, such as the 9/11 attacks or earthquakes, and similar short- and long-term treatment strategies are, therefore, needed to provide adequate care.⁶⁵ Tailored psychological interventions may be helpful in supporting patients who develop ED either from the illness itself or as a consequence of the containment measures.⁶⁵

Topic 3: Impact of COVID-19 on the Management of ED and on Access to ED Treatment

Disruptions in elective and non-emergency medical care access and delivery were observed during COVID-19, particularly during periods of considerable community transmission of SARS-CoV-2.^{56,57} Many elective surgeries for benign urological conditions such as ED were postponed during the COVID-19 outbreak.^{48–50,69} One example summarizing shifts in men's urological care was published by the Canadian Urological Association.⁵¹ It noted the massive shift in only offering surgeries for emergencies and urgent oncology cases with management shifting to mostly virtual care for male sexual health conditions.⁵¹ Although not explicitly documented in the published medical literature, it is likely that the evaluation and treatment of ED was also postponed or delayed, potentially prolonging and possibly exacerbating ED problems.

The COVID-19 pandemic and related mitigation measures such as school closures and stay-at-home orders substantially affected patient healthcare- and medication-seeking patterns.⁵² ^{-54,56,57} Overall, an estimated 40.9% of US adults avoided medical care during the pandemic because of concerns about COVID-19.⁵⁶ Age, gender, sexual identity, education, and selfreported worry about general health were significantly associated with experiencing healthcare delays overall. $^{\rm 57}$

The COVID-19 pandemic exposed vulnerabilities within worldwide healthcare and social systems, some of them including services concerning sexual health.⁴² The need for improved healthcare access was a reality for countless citizens who had never experienced a crisis with such a dimension.⁴² COVID-19 required healthcare and social systems, clinicians, and citizens to adjust to the digital era in a matter of days.⁴² E-Health interventions; that is, the increased use of communication and information technologies for health (eg, short message service [SMS], email, video call, cell phone applications, etc.) have been brought to the center of discussion for improved access to healthcare in challenging situations.⁴² The World Health Organization followed by key professional societies such as the American Psychological Association deemed e-Health a priority target for the improvement of public and universal health.⁴²

The COVID-19 pandemic has accelerated the use of telemedicine and in many ways, sexual medicine healthcare is ideal for telemedicine. Sexual medicine healthcare providers are a highly specialized group of clinicians who are frequently based in metropolitan areas.⁶⁰ Patients travel great distances to see sexual medicine care providers and telemedicine may increase outreach to patients who cannot otherwise access specialized care.⁶⁰ The COVID-19 pandemic has offered healthcare professionals an opportunity to re-examine delivery of sexual health services to hard-to-reach and vulnerable populations.⁶¹ Providers can increase access to male sexual dysfunction treatment by removing traditional barriers to healthcare that these individuals routinely encounter.⁶¹ Rapid advances in telehealth have increased virtual (eg, phone or video) healthcare services and allowed access to confidential and private virtual care.⁶¹ Virtual visits can also triage patients for in-person visits required for services.⁶¹

Topic 4: Health Disparities and the Impact of COVID-19 on ED

The COVID-19 pandemic has magnified health disparities through loss of work and health insurance, having an impact on employee healthcare coverage and overall access to healthcare. In addition, the COVID-19 outbreak has amplified health disparities by race and gender in the US, perhaps most significantly for African American and Latino men.⁶² The strain that the outbreak imposed on already resource-constrained health systems undoubtedly disproportionately impacted the health of these individuals.³⁰ African American and Latino men reported significantly lower levels of access to a provider to see if COVID-19 testing would be appropriate (P = .013), lower utilization of medical services (P = .001), and less use of telehealth for mental health services (P = .001).⁴³ The disproportionate social disruption and losses from COVID-19 also contributed to a wide range of health and quality-of-life outcomes amongst these populations.44,45

Data regarding disparities in access to ED treatment are scarce. There is some evidence that there are disparities in sexual dysfunction outcomes following prostate cancer treatments in African-American men relative to ethnically different counterparts.⁴⁶ Disparities in urologic healthcare delivery and access; however, have been more thoroughly researched and documented in the published medical literature. These studies have demonstrated that there are apparent differences in urologic healthcare delivery and access among racial and ethnic groups in the US.⁵⁸ This has been shown in urologic cancer screening, treatment choices, and survival, as well as in the arena of chronic kidney disease, transplant allocation, and transplant outcomes.⁵⁸

Healthcare barriers that inhibit support for men seeking care for ED were already in existence before COVID-19,⁵⁹ and the disparities in access to all healthcare were exacerbated by the pandemic.⁵⁶ This further reinforces the need to ensure that these ED treatment barriers are not additionally amplified. A greater focus must be paid to health equity, including providing increased resources and supplies for affected groups, adapting to inequities in the existing environment, and ensuring adequate access to healthcare services to ameliorate the burden of COVID-19 on African American and Latino male respondents.⁴³

Aside from disparities in access to healthcare, other factors may also play a role in the differential impact of COVID-19 on particular subgroups of vulnerable populations. There is some evidence that Latino men may be affected more often by ED than Caucasian men in the US.⁵⁸ Evidence of racial differences in endothelial function has been known for over a decade; black race is independently associated with arterial endothelial function and this plays a role in overall cardiovascular risk.⁶³ A previous study found that the prevalence of ED among different racial and ethnic groups in the US is the result of complex phenomena and may be dependent upon the interplay of socioeconomic, demographic, medical, cultural, and lifestyle characteristics.⁶⁴

Pathways Forward

The COVID-19 pandemic has brought to light a remarkable awareness on many health and social issues, including ED and men's health.⁴² The four topics that emerged from the scoping review illustrate the far-reaching effects of COVID-19 on ED. Evidence that the COVID-19 pandemic may precipitate or worsen ED through biological and mental health effects is emerging and compelling. Preliminary evidence showed a significant association between ED and COVID-19, with a 5.27 odds ratio [95% CI: 1.49–20.09]. Multiple pathways and factors associated with ED and the significance of COVID-19 were identified in the published medical literature (Figure 4).



Figure 4. Pathways and factors associated with ED and the significance of COVID-19.

There is reason to suspect that impaired vascular function and ED might persist in COVID-19 survivors and even become a public health issue.⁶⁵ In patients recovered from COVID-19, ED evaluation and consultation may be important.²¹ Getting effective public health messages out to the population is vital and this current pandemic has demonstrated the need for more focused views on men's sexual health.^{2,3}

Studies with larger cohorts of subjects who were infected with COVID-19 are needed to evaluate the degree of impact on men's health.²¹ As data accumulate in administrative health databases, retrospective analyses may be conducted to better understand the patterns of interactions that men with ED had with the healthcare system through COVID-19 and to capture the extent of the impact of COVID-19 on pre-existing and emergent ED. Patient surveys such as the National Health and Nutrition Examination Survey and the National Ambulatory Medical Care Survey may be helpful in collecting patients' experiences with ED during and after COVID-19.

There are several limitations of this scoping review. Given the breadth of topics reviewed from the 693 peer-reviewed articles, we did not conduct a formal systematic review or meta-analysis. Moreover, given the paucity of primary data showing the relationship between COVID-19 infection and ED, many unanswered questions remain. In addition, publication bias may have affected the reported relationships and we were unable to assess the magnitude of publication bias given the limited studies. Finally, the generalizability of the findings may be limited given the significant variability in the underlying causes of and the varying healthcare systems, practices, and health infrastructure across the globe.

CONCLUSIONS

In conclusion, this scoping review of the literature showed emerging evidence that COVID-19 has a uniquely harmful impact on men's health and erectile function through biological, mental health, and healthcare access mechanisms. ED could be a concerning consequence for a large segment of the male population given the high transmissibility of COVID-19; therefore, long-term and well-designed studies are needed to clarify the extent of the impact of COVID-19 on ED. Men presenting with ED after COVID-19 infection may have underlying endothelial dysfunction and vasculature issues and hence pulmonary and cardiovascular complications from COVID-19. A strategic focus on gender in the COVID-19 response will be critical for mitigating the impacts of the pandemic.^{3,47} The pandemic exposed vulnerabilities within worldwide healthcare and social systems, some of them including services concerning sexual health.⁴² Telemedicine may be helpful in diagnosing and treating sexual medicine patients⁵⁵ and in ameliorating the burden of COVID-19 on vulnerable and marginalized populations.

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REFERENCES

- Lisco G, Giagulli VA, De Pergola G, et al. Covid-19 in man: a very dangerous affair. Endocr Metab Immune Disord Drug Targets. DOI: 10.2174/1871530321666210101123801. E-pub ahead of print.
- 2. White A. Men and COVID-19: the aftermath. Postgraduate Med 2020;132:18–27.
- Lipsky MS, Hung M. Men and COVID-19: a pathophysiologic review. Am J Mens Health 2020;14:1557988320954021.
- 4. Pijls BG, Jolani S, Atherley A, et al. Demographic risk factors for COVID-19 infection, severity, ICU admission and death: a meta-analysis of 59 studies. BMJ Open 2021;11:e044640.

- 5. Sansone A, Mollaioli D, Ciocca G, et al. Addressing male sexual and reproductive health in the wake of COVID-19 outbreak. J Endocrinol Invest 2021;44:223–231.
- Peters MD, Godfrey CM, Khalil H, et al. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc 2015;13:141–146.
- Munn Z, Peters MDJ, Stern C, et al. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol 2018;18:143.
- 8. Pham MT, Rajić A, Greig JD, et al. A scoping review of scoping reviews: advancing the approach and enhancing the consistency. Res Synth Methods 2014;5:371–385.
- 9. Tricco AC, Lillie E, Zarin W, et al. PRISMA extension for scoping reviews (prisma-scr): checklist and explanation. Ann Intern Med 2018;169:467–473.
- 10. Duran MB, Yildirim O, Kizilkan Y, et al. Variations in the number of patients presenting with andrological problems during the coronavirus disease 2019 pandemic and the possible reasons for these variations: a multicenter study. Sex Med 2021;9:100292.
- **11.** Sansone A, Mollaioli D, Ciocca G, et al. Mask up to keep it up: Preliminary evidence of the association between erectile dysfunction and COVID-19. Andrology 2021.
- Jin Y, Ji W, Yang H, et al. Endothelial activation and dysfunction in COVID-19: from basic mechanisms to potential therapeutic approaches. Signal Transduct Target Ther 2020;5:293.
- Konstantinopoulos A, Giannitsas K, Raptis S, Perimenis P. Endothelial dysfunction, erectile dysfunction and phosphodiesterase 5 inhibitors. An update of the current data and future perspectives. Drug Target Insights 2007;2:111–117.
- Fu J, Zhou B, Zhang L, et al. Expressions and significances of the angiotensin-converting enzyme 2 gene, the receptor of SARS-CoV-2 for COVID-19. Mol Biol Rep 2020;47:4383– 4392.
- **15.** Zhang H, Penninger JM, Li Y, et al. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. **Intensive Care Med 2020;46:586–590.**
- Rajendran P, Rengarajan T, Thangavel J, et al. The vascular endothelium and human diseases. Int J Biol Sci 2013;9:1057– 1069.
- Shoar S, Khavandi S, Tabibzadeh E, et al. A Late COVID-19 complication: male sexual dysfunction. Prehosp Disaster Med 2020;35:688–689.
- Fraietta R, Pasqualotto FF, Roque M, et al. SARS-COV-2 and male reproductive health. JBRA Assist Reprod 2020;24: 347–350.
- Navarra A, Albani E, Castellano S, et al. Coronavirus disease-19 infection: implications on male fertility and reproduction. Front Physiol 2020;11:574761.
- Vishvkarma R, Rajender S. Could SARS-CoV-2 affect male fertility? Andrologia 2020;52:e13712.

- Corona G, Baldi E, Isidori AM, et al. SARS-CoV-2 infection, male fertility and sperm cryopreservation: a position statement of the Italian Society of Andrology and Sexual Medicine (SIAMS) (Società Italiana di Andrologia e Medicina della Sessualità). J Endocrinol Invest 2020;43:1153–1157.
- 22. Jannini EA. SM = SM: the interface of systems medicine and sexual medicine for facing non-communicable diseases in a gender-dependent manner. Sex Med Rev 2017;5:349–364.
- 23. Abbas AM, Fathy SK, Khamees AA, et al. A focused review on the genital and sexual affection of COVID-19 patients. J Gynecol Obstet Hum Reprod 2020;49:101848.
- Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020;77:683–690.
- Beghi E, Feigin V, Caso V, et al. COVID-19 infection and neurological complications: present findings and future predictions. Neuroepidemiology 2020;54:364–369.
- 26. Thomas C, Konstantinidis C. Neurogenic erectile dysfunction. where do we stand? Medicines 2021;8:3.
- Wu Y, Xu X, Chen Z, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. Brain Behav Immun 2020;87:18–22.
- Roychoudhury S, Das A, Jha NK, et al. Viral pathogenesis of SARS-CoV-2 infection and male reproductive health. Open Biol 2021;11:200347.
- 29. Pennanen-lire C, Prereira-Lourenço M, Padoa A, et al. Sexual health implications of COVID-19 pandemic. Sex Med Rev 2021;9:3–14.
- **30.** Riley T, Sully E, Ahmed Z, et al. Estimates of the potential impact of the COVID-19 pandemic on sexual and reproductive health in low- and middle-income countries. **Int Perspect Sex Reprod Health 2020;46:73–76.**
- **31.** Sathyanarayana Rao TS, Andrade C. Sexual behavior in the days of COVID-19. J Psychosexual Health 2020;2:111–112.
- Paul GM, Nascimento BC, Afif-Abdo J, et al. The psychiatric impact of COVID-19 pandemic on sexual health. Braz J Psychiatry 2020.
- Banerjee D, Rao TSS. Sexuality, sexual well being, and intimacy during COVID-19 pandemic: an advocacy perspective. Indian J Psychiatry 2020;62:418–426.
- 34. Li W, Li G, Xin C, et al. Challenges in the practice of sexual medicine in the time of COVID-19 in China. J Sexual Med 2020;17:1225–1228.
- 35. McKay T, Henne J, Gonzales G, et al. The COVID-19 pandemic and sexual behavior among gay and bisexual men in the United States. **SSRN Electronic J** DOI: 10.1007/s13178-021-00625-3. E-pub ahead of print.
- **36.** Maretti C, Privitera S, Arcaniolo D, et al. COVID-19 pandemic and its implications on sexual life: recommendations from the Italian society of andrology. **Arch Ital Urol Androl 2020;92.**
- **37.** Karsiyakali N, Sahin Y, Ates HA, et al. Evaluation of the sexual functioning of individuals living in turkey during the covid-19 pandemic: an internet-based nationwide survey study. **Sex Med 2020;9:100279.**

- **38.** Fang D, Peng J, Liao S, et al. An online questionnaire survey on the sexual life and sexual function of Chinese adult men during the coronavirus disease 2019 epidemic. **Sex Med 2020;9:100293.**
- **39.** De Rose AF, Chierigo F, Ambrosini F, et al. Sexuality during COVID lockdown: a cross-sectional Italian study among hospital workers and their relatives. **Int J Impot Res 2021;33:131–136.**
- Bulut EC, Ertaş K, Bulut D, et al. The effect of COVID-19 epidemic on the sexual function of healthcare professionals. Andrologia 2021;53:e13971.
- Karagöz MA, Gül A, Borg C, et al. Influence of COVID-19 pandemic on sexuality: a cross-sectional study among couples in Turkey. Int J Impot Res DOI: 10.1038/s41443-020-00378-4. E-pub ahead of print.
- 42. Carvalho J, Pascoal PM. Challenges in the practice of sexual medicine in the time of COVID-19 in Portugal. J Sex Med 2020;17:1212–1215.
- **43.** Ruprecht MM, Wang X, Johnson AK, et al. Evidence of Social and Structural COVID-19 Disparities by Sexual Orientation, Gender Identity, and Race/Ethnicity in an Urban Environment. J Urban Health 2021;98:27–40.
- 44. Purtle J. COVID-19 and mental health equity in the United States. Soc Psychiatry Psychiatr Epidemiol 2020;55:969–971.
- Ibrahimi S, Yusuf KK, Dongarwar D, et al. COVID-19 devastation of african american families: impact on mental health and the consequence of systemic racism. Int J MCH AIDS 2020;9:390–393.
- **46.** Burnett AL. racial disparities in sexual dysfunction outcomes after prostate cancer treatment: myth or reality? J Racial Ethn Health Disparities 2016;3:154–159.
- 47. Betron M, Gottert A, Pulerwitz J, et al. Men and COVID-19: adding a gender lens. Glob Public Health 2020;15:1090–1092.
- **48.** Tonyali S, Haberal HB, Ergul R, et al. Management of patients who seek urologic care in Covid-19 pandemic era. **Urol J 2020;17:548–554.**
- **49.** Cocci A, Presicce F, Russo GI, et al. How sexual medicine is facing the outbreak of COVID-19: experience of Italian urological community and future perspectives. **Int J Impot Res 2020;32:480–482.**
- **50.** Aboumohamed A, Gottlieb J, DeMasi M, et al. Methodology for triage of urologic surgical cases in the setting of a pandemic. **BMC Surg 2021;21:116.**
- **51.** Witherspoon L, Fitzpatrick R, Patel P, et al. Clinical pearls to managing men's health conditions during the COVID-19 pandemic. **Can Urol Assoc J 2020;14:E161–EE66.**
- 52. Vaduganathan M, van Meijgaard J, et al. Prescription Fill Patterns for Commonly Used Drugs During the COVID-19 Pandemic in the United States. JAMA 2020;323:2524–2526.
- 53. Jeffery MM, D'Onofrio G, Paek H, et al. Trends in emergency department visits and hospital admissions in health care systems in 5 states in the first months of the COVID-19 Pandemic in the US. JAMA Int Med 2020;180:1328–1333.

- 54. Hartnett KP, Kite-Powell A, DeVies J, et al. Impact of the COVID-19 pandemic on emergency department visits - United States, January 1, 2019-May 30, 2020. MMWR Morb Mortal Wkly Rep 2020;69:699–704.
- 55. Dooley AB, Houssaye N, Baum N. Use of telemedicine for sexual medicine patients. Sex Med Rev 2020;8:507–517.
- Czeisler M, Marynak K, Clarke K, et al. Delay or avoidance of medical care because of COVID-19-related concerns - United States, June 2020. MMWR 2020;69:1250–1257.
- **57.** Papautsky EL, Rice D, Ghoneima H, et al. Characterizing healthcare delays and interruptions in the us during the covid-19 pandemic: data from an internet-based cross-sectional survey. J Med Internet Res 2021;23:e25446.
- 58. Klein JB, Nguyen CT, Saffore L, et al. Racial disparities in urologic health care. J Natl Med Assoc 2010;102:108–117.
- Burnett AL, Edwards NC, Barrett TM, et al. Addressing health-care system inequities in the management of erectile dysfunction: a call to action. Am J Mens Health 2020;14: 1557988320965078.
- **60.** Shindel AW, Rowen TS. Challenges in the practice of sexual medicine in the time of COVID-19 in the United States. J Sexual Med 2020;17:1216–1219.
- **61.** Mmeje OO, Coleman JS, Chang T. Unintended consequences of the COVID-19 pandemic on the sexual and reproductive health of youth. J Adolesc Health 2020;67:326–327.
- Treadwell HM. The pandemic, racism, and health disparities among African American men. Am J Mens Health 2020;14: 1557988320949379-79.
- **63.** Mulukutla SR, Venkitachalam L, Bambs C, et al. Black race is associated with digital artery endothelial dysfunction: results from the Heart SCORE study. **Eur Heart J 2010;31:2808–2815.**
- 64. Smith JF, Caan BJ, Sternfeld B, et al. Racial disparities in erectile dysfunction among participants in the California Men's Health Study. J Sex Med 2009;6:3433–3439.
- Sansone A, Mollaioli D, Ciocca G, et al. Addressing male sexual and reproductive health in the wake of COVID-19 outbreak. J Endocrinol Invest 2021;44:223–231.
- **66.** Isidori AM, Buvat J, Corona G, et al. A critical analysis of the role of testosterone in erectile function: from pathophysiology to treatment-a systematic review. **Eur Urol 2014;65:99–112.**
- **67.** Dunn KM, Croft PR, Hackett GI. Association of sexual problems with social, psychological, and physical problems in men and women: a cross sectional population survey. J Epidemiol Commun Health 1999;53:144–148.
- **68.** Rosen RC, Riley A, Wagner G, et al. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. **Urology 1997;49:822–830.**
- **69.** American College of Surgeons (ACS). COVID-19: guidance for triage of non-emergent surgical procedures. J Am Coll Surg 2020;231:490–496.