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REVIEW

Sexual Health in COPD: A Systematic Review and **Meta-Analysis**

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Abstract: COPD has a profound impact on the lives of patients and their partners, but the influence on physical, psychological and social aspects of sexual health has not been reviewed systematically. Searches for studies of the impact of COPD on sexual health were conducted independently by two authors in the databases of PubMed, PsycINFO, Embases, CINAHL, Web of Science, Scopus and The Cochrane Library. English-language quantitative and qualitative studies assessing one or more aspects of sexual health in patients diagnosed with COPD were narratively reviewed and, when possible, subjected to meta-analytic evaluation. A total of 31 studies, including 4 qualitative, were included. Twelve studies assessing erectile dysfunction with the International Index of Erectile Function were subjected to meta-analysis. The pooled prevalence of erectile dysfunction was 74% (95% CI: 68-80%) in a total of 1187 patients with COPD, compared with 56% (37-73%) in 224 age-matched, non-COPD controls. The sexual health outcomes assessed in the remaining studies varied considerably, compromising the comparability of the results. None of the qualitative studies had sexual health as their primary focus. Compared with non-COPD individuals, erectile dysfunction appears to be more prevalent among patients with COPD, but more studies including non-COPD controls are needed to confirm this finding. In addition, the impact of COPD on other physical, psychological and social aspects of sexual health remains unclear due to the lack of comparable assessment methods and study designs.

Keywords: sexual problems, chronic obstructive pulmonary disease, psychosocial aspects, gender, quality of life, systematic review

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease, typically diagnosed relatively late in life.¹ Physical symptoms include breathlessness, cough and excessive sputum production, often accompanied by fatigue, low levels of exercise capacity and psychological symptoms of anxiety and depression.² Hence, the illness has persistent, profound effects on the lives of the patients and their caregivers, including negative impacts on intimate relationships and sexuality.^{3,4}

According to the World Health Organization (WHO), sexual health can be described as "a state of physical, emotional, mental and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction or infirmity".⁵ While, historically, sexual health has been relatively overlooked as a contributing factor to constructs of life satisfaction and quality of life (QoL),⁶ in recent years, attention has been drawn to aspects of sexual health as strong predictors and correlates of general subjective well-being.^{7,8}

Sexual health has been explored widely in somatic diseases such as breast-, colorectal- and testicular cancers, demonstrating *direct* effects of disease and treatment on hormone regulatory processes, reproductive organs and sexual function.⁹⁻¹¹ In COPD, on the other hand, changes in sexual health appears to be more *indirectly* linked to disease symptoms through fear of breathlessness on exertion as well as reductions in functional level and exercise capacity.¹² but the evidence base on sexual health in COPD is limited. The few existing literature reviews in the area are either nonsystematic¹³ or focused narrowly on the treatment of physiological deficits such as erectile dysfunction.¹⁴ Vincent and Singh's narrative review¹³ emphasises the relevance of addressing physical, emotional, relational, social and spiritual factors when assessing the impact of COPD on sexuality, which leads them to advocate for a multidisciplinary approach in future sexual healthcare in COPD. Yet, they build their argumentation mostly on studies of chronic illness or geriatric populations in general, lacking potentially specific aspects of the COPD population. Moreover, the narrative review does not reflect critically on the heterogeneity in the measurement of sexual health aspects. In contrast, the review and meta-analyses by Levack and colleagues¹⁴ applies a systematic and stringent operationalisation and its treatment leaves little insight into 1) other organic factors of sexual health, eg, ejaculation-, orgasmic and pain-related issues, 2) the impact on other biopsychosocial factors of sexual health, which can only partly be explained by organic factors, and 3) the impact of COPD sexual health in female patients. To our knowledge, there have been no later attempts to summarise the empirical literature in the area, and an up-to-date, systematic overview of the literature is therefore warranted.

On this background, the present systematic review aimed to evaluate the impact of COPD on sexual health and to explore the relationship between sexual health and relevant biological, psychological and social variables in this group. Furthermore, we assessed the methodological quality of existing studies with the purpose of critically evaluating the current state of the evidence in the area and identifying implications for clinical practice and future research needs.

Methods

Prior to the data collection, the review protocol was registered with PROSPERO, The National Institute for Health Research (Reg. ID: CRD42020145161). The methods and results are documented according to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Checklist.¹⁵

Search Strategy and Study Selection

Literature searches were performed for the period from database inception to January 2021 in the electronic databases of PubMed, PsycINFO, Embases, CINAHL, Web of Science, Scopus and the Cochrane Library, using keywords related to sexual health (sexual OR sexuality OR romantic OR romance OR intimacy OR psychosexual) in combination with keywords related to COPD ("chronic obstructive pulmonary disease" OR "COPD" OR "chronic obstructive lung disease" OR emphysema OR "chronic bronchitis" OR "chronic obstructive respiratory disease" OR "chronic obstructive airway disease"). Relevant additional terms were applied for the individual databases when relevant, eg, using MeSH terms in PubMed and Emtree terms in Embase. Moreover, chain searches were performed by screening the reference lists of included studies. With the purpose of identifying potentially missed studies, supplementary searches were performed using Google Scholar. A trained university librarian was involved in the development of the search strategy and monitored the search procedures.

Inclusion/Exclusion Criteria

English-language quantitative and qualitative studies were included if they explored aspects of sexual health in patients diagnosed with COPD. If the same study included several different measures of the same variable (eg, an established scale and a non-validated scale), the more well-established and most frequently used scale was selected. Studies were excluded if data from patients with COPD were pooled with data from other populations or chronic conditions. Intervention studies were included if they reported relevant baseline data, but excluded if they reported only change scores from pre- to post-intervention. Abstracts were included if they provided sufficient data.

Study Selection and Data Extraction

All study screening and selection procedures were performed using the Covidence software (© 2019, v1254 1df2c3cf). Two researchers (IFV and YF) performed the literature search independently. After the elimination of duplicates, the same researchers independently screened all titles and abstracts and excluded ineligible studies. In the second screening round, full-texts of all remaining references were obtained and read in full by both researchers, and they independently

excluded all ineligible studies and stated inclusion reasons. Relevant data were extracted from the included studies by IFV and cross-checked by YF. Authors of eligible studies were contacted via email to obtain missing data.

Assessment of Methodological Quality

The methodological quality of the included quantitative studies was assessed using the Appraisal tool for Cross-Sectional Studies (AXIS),¹⁶ and the Critical Appraisal Skills Programme (CASP) was applied for the methodological assessment of qualitative studies as recommended by the GRADE Working Group.¹⁷ Two researchers (IFV and YF or SRR and YF) rated the methodological quality of the included studies separately and resolved conflicts when relevant.

Data Synthesis and Analysis

To enable between-study comparisons, the included studies were grouped according to the specific sexual health instrument used. A random effects meta-analysis was conducted for each group. The impact of COPD on sexual health outcomes was explored by combining the inverse variance weighted mean results for the included studies, thereby taking the precision of each study into consideration. When available for \geq 5 studies, demographic, biological, psychological or social variables were explored with meta-regression as possible moderators of sexual health. All analyses were performed using Comprehensive Meta-Analysis, version 3, and various formulas in Microsoft Excel.

Qualitative studies were planned to be subjected to a qualitative data synthesis in accordance with the guidelines of Timulak. 18

Results

The study selection process is summarised in the PRISMA flow diagram shown in Figure 1. The initial search yielded 844 unique references out of which 147 articles were read in full during the second screening round. Initially, 23 studies were included, and the supplementary searches yielded an additional 8 eligible studies, resulting in a total of 27 quantitative and 4 qualitative studies published between 1977 and 2021.

Study Characteristics

The characteristics of the included studies are listed in Table 1, and an overview of the instruments used to measure sexual health outcomes in the included studies can be found in Table 2. An overview of AXIS and CASP study quality ratings can be found in <u>Supplementary Materials</u>, <u>Tables S1</u> and <u>S2</u>. Twelve studies had sufficient and comparable data for conducting a meta-analysis, ie, had all used the International Index of Erectile Function (IIEF) to measure erectile dysfunction (ED). The instruments used in the remaining studies were too heterogeneous to allow for meta-analytical evaluation.

Erectile Dysfunction

See Table 2, section A for an overview of studies reporting outcomes on erectile dysfunction. The pooled prevalence of ED in 12 studies of a total of 1187 patients with COPD was 74% (95% CI: 68–80%). The results appeared heterogeneous (Q=60.5, p<0.001), with the I^2 of 81.8% suggesting that a considerable proportion of the variance can be explained by true differences in prevalence across samples. The 95% prediction interval indicates that 95% of similar future studies will yield prevalences between 46.7% and 90.5%. As seen in Table 3, when attempting to explore the possible sources of heterogeneity with meta-regression, mean age of the sample was associated with increased prevalence of ED, whereas higher mean sample FEV¹ (%) was associated with lower prevalence. The results for the remaining moderators did not reach statistical significance. As only four studies^{25,31,41,44} examined erectile dysfunction in an age-matched non-COPD control group, comparative analysis was considered exploratory. The pooled prevalence in a total of 224 controls was 56% (95% CI: 37–73%). While the prevalence is smaller in controls, as seen when comparing the confidence intervals, the difference between patients with COPD and controls does not reach statistical significance in the available data.

The remainder of studies exploring erectile dysfunction applied other assessment methods, including nocturnal tumescence monitoring and diagnosis codes, and data from these studies could therefore not be included in the metaanalysis.



Figure I PRISMA flow diagram of the study selection process.

Notes: Adapted from: Liberati A, Altman D, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Journal of Clinical Epidemiology*. 2009;62(10)e1-e34.⁷⁴ Creative Commons.

Sexual Function and Satisfaction

See Table 2, section B for an overview of studies reporting outcomes on sexual function and satisfaction. Across studies, limitations in sexual function and satisfaction were reported by 48–82% and was associated with reduced quality of life, more anxiety and depression symptoms and female gender. Limitations were more common in COPD, compared to healthy samples and other patient populations, eg, heart failure patients.

Illness Impact on Sexual Health

See Table 2, section C for an overview of studies reporting outcomes on the impact of illness on sexual health. Patients with COPD tended to report greater impact of illness on sexual health compared with patients with heart failure, whereas the impact of asthma and COPD on sexual health were generally more comparable.

Table	I	Study	Characteristics
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Author	Year	Country	Study Design	Study Groups (n) ^a	COPD Sar	nple Chara	cteristics		Main Findings
				A	Mean Age (Yrs ^b)	Gender (% Female)	Lung Function (Mean FEVI % Predicted ^b)	Partner Status (% Living with Partner ^b)	
(I) Agle & Baum ¹⁹	1977	US	Psychiatric interviews with longitudinal follow-up (qualitative)	I) COPD patients referred to PR (n=23)	NR	NR	NR	NR	Decreased libido and ability to erect was reported by 19 patients and was attributed to shortness of breath and easy fatigability, but was not reported to be directly related to measured physiologic impairment.
(2) Fletcher & Martin ²⁰	1982	US	Prospective study	I) COPD outpatients (n=20)	56.0	0	NR	85	6 Patients failed to attain an average of one full erection per night. 7 participants had ceased sexual activity while 13 continued sexual activity at 16% of the pre-COPD sexual activity level. Patients reported interest in engaging in sexual intercourse to be 25% of pre-COPD level.
(3) Sturesson & Bränholm ²¹	2000	Sweden	Cross-sectional study	 COPD patients receiving LTOT (n=28) COPD patients referred to PR (n=91) Non-COPD control group (n=150) 	LTOT: 70.0 PR: 68.0	LTOT: 71 PR: 45	NR	NR	62% of the healthy reference group reported being satisfied with their sex life, which was significantly lower in the COPD rehabilitation sample (35%) and the COPD LTOT sample (26%).
(4) Ibáñez et al. ⁴	2001	Spain	Cross-sectional (interview- based with quantitative coding)	I) COPD patients receiving LTOT (n=49)	68.0	0	Mean FEVI mL= 681.3	100	67.3% of the COPD patients showed some type of sexual problem, out of which 18% manifested as lack of desire, 42% as impotence, and 40% as a combination. No differences in age or lung obstruction were found between patients who did versus did not report sexual impairment.
(5) O'Neill ²²	2002	US	Cross-sectional interview study (qualitative)	I) COPD patients referred to PR (=21)	67.0	100	NR	57	Patients' perceived consequences of COPD included loss of intimacy, inability to have sexual relations with their partners and stigmatisation.

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Table I (Continued).

Author	Year	Country	Study Design	Study Groups (n) ^a	COPD Sa	mple Chara	cteristics		Main Findings	
					Mean Age (Yrs ^b)	Gender (% Female)	Lung Function (Mean FEVI % Predicted ^b)	Partner Status (% Living with Partner ^b)		
(6) Svartberg et al. ²³	2004	Norway	RCT (only baseline data extracted)	I) COPD outpatients (n=29)	66.1	0	42.0	NR	IIEF-5 average score at baseline= 14.2 Sexual quality of life average at baseline=2.3	
(7) Köseoglu et al. ²⁴	2005	Turkey	Cross-sectional study	I) COPD outpatients (n=53)	63.4	0	NR	100	ED ratio=75.5%. Low levels of all IIEF domains were associated with longer COPD duration. Low levels of all IIEF domains, except sexual desire, were associated decrease more sever COPD.	
(8) Karadag et al. ²⁵	2007	Turkey	Cross-sectional study	I) COPD outpatients (n=95)	63.5	0	44.3	100	ED ratio in COPD=87% (controls=83%). Moderate/ severe ED ratio in COPD=57% (controls=20%). Systemic inflammation (TNF- α) level was higher in patients with moderate/severe compared with mild/moderate ED.	
(9) Kaptein et al. ²⁶	2008	The Netherlands	Cross-sectional study	 COPD outpatients (n=25) Non-COPD control group (n=300) Asthma outpatients (n=30) 	57.0	40	58.4	100	Compared with non-COPD controls, male COPD patients reported significantly poorer scores on eight out of nine subscales measuring intimate physical contact, while female COPD patients reported significantly poorer scores on one out of nine subscales. General levels of sexual impairment in asthma was comparable, but male patients reported less impairment compared to female.	
(10) Thomsen & Jensen ²⁷	2009	Denmark	Cross-sectional interview study (qualitative)	 COPD patients after lung transplantation (n=10) 	Range 50–69	50	NR	40	Patients' mentioned resumption of sex life as an important factor for returning to an ordinary life after lung transplantation. Their desire to have sex was still present although problematic due to reduced breathing capacity and partner's fear that something would go wrong.	

(11) Collins et al. ²⁸	2012	US	Cross-sectional study	I) COPD outpatients (n=90)	69.0	0	46.0	NR	74% had at least one sexual dysfunction, out of these 72% reported erectile dysfunction. Testosterone levels, significant depressive symptoms and presence of a partner were independently associated with ED after controlling for active smoking, comorbidity, obstructive severity, dyspnea, and medications that could cause ED.
(12) Hansen et al. ²⁹	2012	Denmark	Cross-sectional study	 Severe COPD patients (n=39) Heart failure patients (n=22) 	66.0	46	NR	NR	A larger proportion of COPD patients reported troublesome dyspnea during sexual activity compared to HF patients (44% versus 5%), and that dyspnea was a limiting factor for sexual activity (56% versus 27%).
(13) Uzaslan et al. ³⁰	2012	Various, Middle East	Cross-sectional epidemiological study	 Patients with a COPD diagnosis from the general population (n=1392) 	NR	24.4	NR	NR	37.5% reported 'some' or 'a lot' of limitation with sexual intercourse.
(14) Kahraman et al. ³¹	2013	Turkey	Cross-sectional study	 COPD outpatients (n=70) Non-COPD control group (n=68) 	63.34	0	60.6	NR	ED ratio in COPD=78.6% (controls=55.8%). ED was associated with lower levels of lung function in COPD sample, but not in controls. ED was associated with lower levels of oxygen saturation and higher age in COPD sample and controls.
(15) Mulhall et al. ³²	2013	US	Cross-sectional postal survey	I) COPD outpatients (n=493)	NR	NR	NR	NR	Limitations in sexual activity were reported by 48% of the COPD patients who knew about their diagnosis, compared to 23% of the COPD who did not know.
(16) Panos et al. ³³	2013	US	Cross-sectional focus group study (qualitative)	I) COPD outpatients (n=42)	64.6	0	NR	47	Sexual activity was prohibited or severely impeded and related to marital separation for some individuals.
(17) Theander et al. ³⁴	2014	Sweden	Cross-sectional study	 Patients with a COPD diagnosis from primary health care registries (n=437) Patients with a chronic heart failure diagnosis from primary care registries (n=388) 	70.44	54	NR	62	42% of the COPD sample reported problems with sexual interest or activity, compared to 33% in the chronic heart failure sample.

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Author	Year	Country	Intry Study Design	Study Groups (n) ^a	COPD Sar	nple Chara	cteristics		Main Findings
					Mean Age (Yrs ^b)	Gender (% Female)	Lung Function (Mean FEVI % Predicted ^b)	Partner Status (% Living with Partner ^b)	
(18) Abd- Elsalam et al. ³⁵	2015	Egypt	Cross-sectional study	 COPD outpatients (n=86) Non-COPD control group (n=86) 	30 yrs: 14.0% 31–40 yrs: 41.9% 41–50 yrs: 37.1% 51 yrs: 7.0%	100	NR	100	Compared with controls, COPD patients scored significantly lower on the sexual function domains of desire, arousal, orgasm and sexual satisfaction, and scored higher on the pain domain.
(19) Marques et al. ³⁶	2015	Portugal	RCT (only baseline data extracted)	I) COPD patients referred to PR (n=42)	67.4	33	70.5	76	Mean scores on a domain scale measuring sexual relationships was 3.5.
(20) Shen et al. ³⁷	2015	Taiwan	Retrospective cohort study	 Patients with a COPD diagnosis from the general population (n=29,042) Non-COPD control group from the general population (n=28,886) 	61.0	0	NR	NR	After adjusting for age and comorbidity, COPD patients had an adjusted hazard ratio of 1.52 (95% CI 1.30–1.79) for ED in COPD, compared with non-COPD patients.
(21) Lauretti et al. ³⁸	2016	ltaly	Cross-sectional study	I) COPD patients referred to PR (n=66)	62.4	0	NR	NR	ED ratio=83.3%. ED was associated with higher age more severe COPD.
(22) Turan et al. ³⁹	2016	Turkey	Cross-sectional study	I) COPD outpatients (n=93)	61.4	0	Mean FEVI L=1.71	NR	ED ratio=67.7%. ED was associated with higher age, more pack-years of smoking, more dyspnea and lower levels of arterial blood gases, physical activity QoL.
(23) Dias et al. ⁴⁰	2017	Portugal	Cross-sectional study	I) COPD outpatients (n=67)	Median=65	0	48.0	79	ED ratio=87% Higher CAT scores independently associated with presence of ED (odds ratio=1.123).

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(24) Hasan et al. ⁴¹	2017	Egypt	Cross-sectional study	I) COPD outpatients (n=30)	NR	0	NR	NR	ED ratio=76% versus 23% in healthy controls. ED was associated with lower levels of lung function and oxygen saturation and physical activity and longer COPD duration.
(25) Anjum et al. ⁴²	2018	Pakistan	Cross-sectional study	I) COPD outpatients (n=336)	60.2	0	NR	NR	ED ratio=67.3%. Presence of ED was associated with lower levels of income and active smoking status.
(26) Sinoj et al. ⁴³	2018	India	Cross-sectional study	I) COPD outpatients (n=87)	54.1	0	71.5	100	ED ratio=42.5%. Presence of ED was associated with lower levels of lung function, higher levels of sexual impairment and poorer marital quality.
(27) Kawshty et al. ⁴⁴	2019	Egypt	Cross-sectional study	 COPD outpatients (n=100) Non-COPD control group (n=96) 	61.5	0	50.0	NR	ED ratio in COPD=78% versus (controls=58.3%). Presence of ED was associated with more severe COPD. Significant, independent predictors of ED were exercise capacity, testosterone level and lung function.
(28) Oh & Yoo ⁴⁵	2019	Korea	Longitudinal cohort study	I) Patients with COPD diagnosis from a hospital-based cohort (n=185)	65.4	0	59.9	NR	Erectile function in total sample improved in the first year after baseline and then deteriorated. Older age, lower economic status and poorer subjective health status affected the progression of erectile function.
(29) Macêdo et al. ⁴⁶	2020	Brazil	Cross-sectional study	I) COPD outpatients (n=52)	71.1	54	44.3	61	Sexual function was classified as 'poor/absent' in 82%. Poor/absent sexual function was more frequent among female patients and was associated with lower levels of QoL and higher levels of anxiety and depression.
(30) Zysman et al. ⁴⁷	2020	France	Cross-sectional survey	I) Patients with self- reported COPD (n=751)	61.0	51	FEV1% pred ≤30=23.0	62	68% Reported 'low/absent' sexual appetite, 60% reported 'low/absent' sexual desire, 60% of male participants reported erectile dysfunction. Low/absent sexual appetite or desire was associated with higher levels of anxiety and depression.
(31) Kamal et al. ⁴⁸	2021	Egypt	Cross-sectional study	I) COPD outpatients (n=100)	56.3	0	NR	NR	ED ratio in COPD=71% Mean levels of erectile function were significantly higher in controls, compared to COPD. Higher levels erectile function were associated with higher levels of testosterone.

Notes: ^aNon-COPD control samples are age- and gender-matched; ^bUnless reported otherwise. Abbreviations: COPD, chronic obstructive pulmonary disease; ED, erectile dysfunction; FEV1, forced expiratory volume in the first second; IIEF, International Index of Erectile Function; NR, not reported; PR, pulmonary rehabilitation; RCT, randomised controlled trial.

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Outcome	Measurement Instrument	Sexual health Outcome	Subdomains	Number of Items	Total Score Range	Interpretation	Applied in Which Studies
A) Erectile dysfunction	International Index of Erectile Function-5Presence and severity of erectile dysfunction		Erectile function	5	5–25	Cutoff score for presence of erectile dysfunction = 21 Higher scores indicating higher levels of erectile function	[23,25,31,39– 42,44,45,48]
	International Index of Erectile Function – full scale ⁵⁰	Erectile function and satisfaction	Erectile function; orgasmic function; sexual desire; intercourse satisfaction; overall satisfaction	15	4–55	Higher scores indicating higher levels of erectile function	[24,38,43]
	Tumescence monitor ^{51–53}	Erectile function measured by circumferential change of the penis during sleep	Erection	1	Yes/no	-	[20]
-	Diagnosis codes	Erectile dysfunction (ICD-9-CM codes 302.72, 607.84)	-	1	Yes/no	-	[37]

Table 2 Overview of Instruments Applied to Measure Sexual Health in the Included Studies

B) Sexual function and satisfaction	Respiratory Experiences with Sexuality Profile (RESP) ⁵⁴	Impact of respiratory symptoms on sexuality	"During sexual activity I experience breathing difficulties"; "Because of my breathing difficulties I am not capable to be as sexually active as I would like to be"; "I talk with my partner about the consequences that my breathing difficulties have on our sexual activity"; "I talk with my physician about the consequences that my breathing difficulties have on my sexual activity"	4	Items are not summed but reflect the responses of individual items: I: 'Often' 2: 'Frequently' 3: 'Sometimes' 4: 'Never'	Items I and 2: 'Often' is negative and 'never' is positive Items 3 and 4: 'Often' is positive and 'never' is negative	[26,29,40]
	Male Sexual Quotient (MSQ) ⁵⁵	Male sexual function and satisfaction	Desire; confidence; foreplay quality; partner satisfaction; erection quality; ejaculatory control; ability to achieve orgasm; intercourse satisfaction	10	0-100	Higher scores indicating higher levels of sexual function and satisfaction	[46]
	Female Sexual Quotient (FSQ) ⁵⁶	Female sexual function and satisfaction	Not reported	10	0-100	Higher scores indicating higher levels of sexual function and satisfaction	[46]
	Modified Global Study of Sexual Attitudes and Behaviors (GSSAB) Questionnaire ⁵⁷	Subjective sexual well-being	Emotional satisfaction with sexual relationships; Physical satisfaction with sexual relationships; Satisfaction with sexual function; Importance of sex in overall life	NR	NR	NR	[28]
	Arizona Sexual Experience Scale (ASEX) ⁵⁸	Sexual function and satisfaction	Drive; arousal; penile erection/vaginal lubrication; ability to reach orgasm; satisfaction from orgasm	5	5–30	Higher scores indicating lower levels of sexual function and satisfaction	[47]
	Female Sexual Function Index (FSFI) ⁵⁹	Female sexual function and satisfaction	Desire; arousal; lubrication, orgasm, satisfaction, pain	19	2–36	Higher scores indicating higher levels of sexual function and satisfaction	[35]
	Single item from the Memorial Symptom Assessment Scale ⁶⁰	"Problems with sexual interest or activity"	-	I	Yes/no	-	[34]

(Continued)

Table 2 (Continued).

Outcome	Measurement Instrument	Sexual health Outcome	Subdomains	Number of Items	Total Score Range	Interpretation	Applied in Which Studies
	ltems formulated by authors (non- validated)	Satisfaction with sexuality Sexual quality of life (not specified) Limitations in sexual activity	-	1	1–6 0–6 Yes/no	Higher score = higher satisfaction Higher score = higher quality-	[21,23,32]
C) Illness impact on sexual health	Intimate Physical Contacts Scale (IPCS) ⁶¹	Illness impact on intimate physical contacts	Physical problems influencing sexual desire; frequency of excitement; frequency of intimacy; appreciation of intimacy; appreciation of excitement; low self-esteem interfering with sexuality; low esteem for partner interfering with sexuality; general assessment of partner; general sexual satisfaction	9	NR	Individual interpretation for each item	[26]
	Psychosocial Adjustment to Illness Scale (PAIS) Sexual relationships subdomain ⁶²	Illness sexual functioning or	The scale is a subscale of the PAIS	6	0–18	Higher scores indicating higher levels of illness impact on sexual functioning or relationships	[36]
-	Relationship and Sexuality scale [NR]	Illness and treatment impact on sexuality and relationships	Sexual function; sexual frequency; sexual fear	10	0–36	Higher scores indicating higher levels of dysfunction	[43]
	Coded from semi- structured interviews (non-validated)	Illness impact on sexuality	Impotence; lack of desire	2	Yes/no	-	[4]
	Items formulated by authors (non- validated)	Impact of COPD on sexual intercourse	-	1	NR	NR	[30]

Abbreviations: COPD, chronic obstructive pulonary disease; NR, not reported.

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<0.001

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Moderator Variable	K ^a	Slope (95% CI) ^b	þc	
Mean age of sample (years)	11	0.095 (0.028–0.162)	0.005	
Mean BMI in sample	6	-0.057 (-0.322-0.208)	0.673	
Mean pack-years in sample	5	0.035 (-0.033-0.102)	0.314	
COPD duration (months)	6	0.006 (-0.005-0.017)	0.277	
Mean sample PaO ₂	6	-0.022 (-0.052-0.008)	0.147	
Mean sample PaCO ₂	6	0.055 (-0.048-0.159)	0.296	

Table 3 Exploratory Meta-Regression: Moderators of the Pooled Prevalence of Erectile Dysfunction in Samples of COPD Patients

Notes: ^aNumber of studies in the analysis; ^bMixed effects regression, unrestricted maximum likelihood, calculated for $K \ge 5$; ^cStatistically significant values <0.05 are presented in bold.

-0.015 (-0.088--0.031)

0.450 (-0.305-1.205)

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In the qualitative studies, sexual impairment was attributed to shortness of breath and easy fatigability. Moreover, qualitative data pointed to the perceived impact of COPD on relational factors, including loss of intimacy, stigmatisation and partner's fear that something would go wrong. Nevertheless, patients described that their desire to have sex was still present.

Discussion

Mean sample FEVI (%)

IIEF-5 vs IIEF (referent)

The present study systematically reviewed existing studies of sexual health in COPD, applying the term 'sexual health' as an umbrella term for aspects of sexuality instead of focusing solely on specific sexual functions, eg, erectile dysfunction. A total of 27 quantitative studies and 4 qualitative studies was included. Studies were generally heterogeneous in terms of recruitment settings, measurement instruments as well as study designs.

Despite overall heterogeneity, the majority of the included quantitative studies focused on biological deficits related to sexual function, such as erectile dysfunction (ED), in male patients with COPD. Due to large variation in measurement instruments applied across the included quantitative studies, it was only possible to calculate a quantitative, summarised estimate of COPD impact on the outcome of ED as assessed with the International Index of Erectile Dysfunction (IIEF).

Erectile Dysfunction

Meta-analysis results showed that three out of four patients with COPD met the criteria for a diagnosis of ED, which represented a higher – albeit not statistically significant – proportion than in age-matched, non-COPD control samples. The lack of statistical significance of this finding may be due to lack of power, with only 224 participants being included in the pooled control sample. In a recently published meta-analysis, Luo et al⁶³ directly compared the risk of developing ED in patients with COPD and non-COPD, age-matched controls. They found that the risk of developing moderate or severe ED was significantly higher in COPD, compared to the age-matched general population. However, the risk was not increased for ED in general.

ED results in the present study were heterogeneous, and exploratory analyses showed that higher mean age was associated with increased prevalence of ED. This trend was similar in an umbrella meta-analysis of the global prevalence of ED, eg, prevalences of ~25% at age 30–39 and ~80 at age 60–69.⁶⁴ Furthermore, results of the present study showed that better lung function was associated with lower ED prevalence. There may be numerous explanatory factors for this finding. For example, the vast majority of patients with COPD are current or former smokers, and higher levels of both past and current cigarette smoking have been shown to be associated with increased ED risk in the general population.⁶⁴ However, results of the moderating effects of smoking, body mass index (BMI), COPD duration, partial pressure of oxygen (PaO₂), and partial pressure of carbon dioxide (PaCO₂) did not reach statistical significance. This could, however, be caused by power issues, and should therefore be interpreted with caution.

Sexual Function and Satisfaction

In the present review, studies that applied instruments assessing sexual function and satisfaction generally reported low levels of function and satisfaction among patients with COPD. Sexual function and satisfaction was shown to be associated with higher levels of anxiety and depression.^{46,47} However, the causality of this association is unclear, since psychological symptoms could be both a reason and a consequence of poor sexual function.⁶⁵ Poor sexual function was more frequently reported among women, which can generally not be explained by gender differences in psychological symptoms. However, since the majority of studies of sexual health in COPD focus on sexual function among male patients, it is not possible to draw reliable conclusions on gender difference based on existing data, and more studies applying non-gender specific assessment instruments are needed.

Illness Impact on Sexual Health

In the present review, a number of the included studies applied measurement instruments that directly assess illness impact on sexual health. The included studies indicated that sexual health of patients with COPD is compromised by respiratory symptoms to a similar extent as in patients with asthma, whereas the impact of respiratory symptoms on sexual health is more profound in patients with COPD, compared to patients with heart failure. Whether or not these results can be explained by differences in respiratory symptoms across different patient groups is currently not clear, and more research is needed to confirm the disease-specific mechanisms of sexual health in COPD.

The included qualitative studies emphasised the influence of relational factors for understanding the impact of COPD on sexual health, where loss of intimacy, patients' perceived inability to have sexual relations with their partners and partners' fear of patients' breathing problems during sexual activities, was highlighted. It is highly relevant to consider relational factors, eg, dyadic coping,⁶⁶ in order to understand interactions, activities and cognitions related to sexuality and sexual health. In studies of cancer populations, aspects of sexual health can be both a predictor and outcome of dyadic coping, ⁶⁷ In a study of dyadic coping in COPD,⁶⁸ patients as well as partners reported low levels of satisfaction with dyadic coping, compared to a norm group. According to the authors, this finding can be linked with the limited sexual activity in couples with one partner suffering from COPD. A longitudinal study of dyadic coping in COPD⁶⁹ concludes that, as the illness progresses, it is important that both partners communicate about stress and provide appropriate practical and emotional support to maintain quality of life. However, neither studies explore the role of sexual health in dyadic coping, which should be a priority in future studies, as dyadic coping with COPD may differ from coping with malignant diseases or diseases with different illness and treatment trajectories.

Methodological Quality

With regard to the methodological quality of the included studies, the systematic quality ratings of the present review generally point to four areas with potential for improvement in future studies: First, the majority of included studies failed to describe their approach to sample size justification. While sample size justification is less commonly performed and reported in observational studies, compared to RCTs, a systematic consideration of the number of participants required to estimate prevalence levels in a given population is important with the purpose of increasing the precision of estimates, and sample size justification should therefore be described in future studies. Second, only few of the included studies systematically addressed and categorised non-responders, which compromises the external validity of the study results. Future studies should therefore pay careful attention to the systematic registration and characterisation of non-responders. Third, and related to the second point, concerns about non-response bias was raised due to limited response rates, and a lack of description of reasons for non-response, in the majority of studies. Fourth, the majority of included studies failed to report study limitations, which challenges the reader's interpretation and applicability of study results. Concerning the included qualitative studies, the methodological quality of three out of four included studies was relatively high. It should be noted, however, that is it questionable whether the remaining study¹⁹ could be classified as a qualitative study at all.

Strengths and Limitations

The present review is the first attempt to systematically review and summarise existing quantitative and qualitative studies on sexual health in COPD. Among its strengths are the adherence to existing systematic guidelines for preregistration, literature search and methodological quality rating, with two reviewers performing procedures independently with the purpose of reducing the risk of bias in selection and reporting. While meta-analysis has been performed to obtain a more precise prevalence estimate, the review also takes a broader approach to sexual health. Historically, studies of erectile dysfunction have dominated the field, and the present study is the first systematic attempt to set a more comprehensive agenda for exploring sexual health in COPD.

A number of limitations of the present review should also be mentioned. First, meta-analytic evaluation and qualitative result syntheses of the including studies could not be performed for all outcomes due to heterogeneity in study objectives and measurement instruments across studies. Limiting the scope to one primary outcome in future systematic reviews may result in a more homogenous evidence base, but might also result in an oversimplified approach to sexual health. Second, the tools applied for methodological quality ratings of quantitative and qualitative studies, respectively, are not developed congruently, and does therefore assess diverse aspects of methodological quality (eg, AXIS focus more extensively on reporting, compared to CASP that focus relatively more on study design). The development of congruent quality rating systems for cross-sectional quantitative and qualitative studies could be relevant for future research. Third, while the present study aimed to evaluate the impact of COPD on sexual health and to explore the relationship between sexual health and relevant biological, psychological and social variables in patients with COPD, treatment methods to improve sexual health in this group was not within the scope. When sufficient knowledge on the prevalence and underlying mechanisms of sexual health in COPD has been obtained, studies developing and testing treatment approaches are needed. Fourth, studies included in the present review were conducted in various settings, ie, outpatient (K=9), rehabilitation (K=3), transplantation/long-term oxygen treatment (K=4) or epidemiological (K=3), resulting in relatively diverse samples. The considerable heterogeneity in outcomes and study design within study settings makes direct comparison of study results across settings difficult and greater uniformity in settings, outcomes and designs are warranted in future studies. And fifth, a vast number of the included studies were performed in Eastern, Middle Eastern or North African regions of the world, eg, Egypt,^{35,41,44,48} India,⁴³ Korea,⁴⁵ Taiwan,³⁷ Turkey,^{24,25,31,39} Pakistan,⁴² mixed.³⁰ Sexual norms in these areas may differ from Western and Nordic regions, thereby questioning the cultural generalisability of the present results.

Clinical Implications

Based on results from the meta-analysis of the present study, the majority of male patients with COPD suffer from comorbid ED, potentially influencing their sexual health, partnership and quality of life. Meanwhile, studies on communication needs in COPD indicate that in more than 60% of the patients with COPD, sexual issues have not been addressed in healthcare consultations, despite a patient-reported need for information.⁷⁰ Apparently, patients are increasingly motivated to achieve information about sexual and relational issues during the first five years after their COPD diagnosis, and especially male patients lack information on these issues.⁷⁰ This highlights the need for a systematic approach to sexual health screening, which should be initiated shortly after diagnosis and maintained throughout the illness trajectory as age increases and lung function decreases. Since most studies of sexual health in COPD have focused on ED, results are currently more robust for this outcome, compared to outcomes of general sexual function, sexual satisfaction and illness impact on sexual health. However, this points to the current state of the evidence in the area, and not necessarily to which outcomes of sexual health have most impact on patients' health status and quality of life. When screening for comorbid diagnosis of ED, clinicians should be careful not to overlook other important factors of sexual health by applying existing, validated questionnaires (see Table 2) – especially when it comes to female patients.

Nonetheless, interpersonal barriers, social stigma and myths about sexuality, eg, "older people with chronic illness automatically looses interest in sex", can hinder the initiation of screening and communication about sexual health.⁷¹ If designed properly, counselling guidelines for the clinician⁷¹ and informational leaflets or other types of patient material

can serve as tools to support communication about sexual issues, as long as they do not end up being used "mechanically" or as a substitute to a clinical conversation.⁷² When sexual or relational issues have been identified in the clinic, relevant management of such issues is needed. Research about medical treatment of ED is limited,¹⁴ and most likely, sexual health management in COPD demands a holistic, rehabilitative approach, preferably including the partner when there is one. Such an approach could be composed by relevant components, eg, medical management, lifestyle and behaviour change interventions, psychological and psychosexual counselling, and/or dyadic coping interventions.^{66,68,73}

Conclusions

The results of the present study indicate that COPD has a negative impact on sexual health. The majority of included studies focus on organic deficits in male patients, ie, erectile dysfunction (ED), and it is estimated that three out of four patients with COPD are living with erectile dysfunction, which is a larger proportion than in age-matched, non-COPD individuals. However, while sexual health cannot be reduced to organic deficits such as erectile dysfunction, included studies exploring physical, psychological and social aspects of sexual health are limited in number and apply heterogeneous outcomes measures and design, which challenges the comparability of their results. Also, there are currently very few qualitative studies of sexual health in COPD, and none of them has sexual health as the primary study focus. Moreover, the field appears to be dominated by methodological challenges, especially concerning sample size justification, analysis of non-responders and dropouts, and authors' considered relatively poor, compared to sexual health research in other patient populations, eg, cancer. In the future, studies should consider 1) including non-COPD control groups with the purpose of exploring COPD-specificity of results; 2) applying existing, validated measures of sexual health that are applicable in both genders; 3) not limiting outcomes to organic deficits, such as erectile dysfunction; and 4) exploring the subjective experience of COPD impact on sexual health in patients and partners with the purpose of identifying COPD-specific areas that may have been overlooked so far.

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