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The Incidence of Sexual Dysfunction in Patients With Irritable Bowel Syndrome



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ABSTRACT

Introduction: Several studies have suggested that patients with irritable bowel syndrome (IBS) frequently have symptoms of sexual dysfunction.

Aim: The current study aims to map the current knowledge about the burden of sexual dysfunction in patients with IBS.

Methods: A literature review was conducted on PubMed and EMBASE using the following search terms or combinations thereof: irritable bowel syndrome; functional colonic disease; sexual function; sexual health; sexual behavior; sexual dysfunction; dyspareunia; erectile dysfunction; quality of life; and questionnaire.

Main Outcome Measure: Sexual dysfunction.

Results: 1,273 texts were found, 331 duplicates were removed, and 844 texts were excluded because they did not meet the inclusion criteria, leaving 98 full text articles. These were examined and it was found that 41 fulfilled the criteria. 4 questionnaires were found; Irritable Bowel Syndrome Quality of Life (IBS-QOL) questionnaire, the Irritable Bowel Syndrome — Quality of Life (IBSQOL) questionnaire, the Irritable Bowel Syndrome-36 question (IBS-36) questionnaire, and the Arizona Sexual Experience Scale. Subscores for sexual relations in IBS-QOL ranged from 37.7–100 (11.9) for patients with IBS and 82.2–100 (6.6) for controls. The IBSQOL and IBS-36 subscores for sexual relations ranged from 49.7–90.5 (9) to 3.9–5.4 (0.8) with no healthy controls for comparison. After interventions were implemented, there was an improvement in subscores (the IBS-QOL mean changed to 10.5%, IBSQOL mean changed to 3.8%, and the IBS-36 mean changed to 40%). The study using Arizona Sexual Experience Scale showed that 51% of patients with IBS had sexual dysfunction and also scored lower on the IBSQOL questionnaire.

Conclusion: The information about sexual dysfunction in patients with IBS is sparse and emerges primarily from quality of life questionnaires. It seems as though patients with IBS have more sexual problems compared to controls, but further investigation regarding the extent and type of sexual dysfunction is needed. Sørensen J, Schantz Laursen B, Drewes AM, et al. The Incidence of Sexual Dysfunction in Patients With Irritable Bowel Syndrome. Sex Med 2019;7:371–383.

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Key Words: Irritable Bowel Syndrome (IBS); Sexual Dysfunction; Diarrhea; Flatulence; Soiling

INTRODUCTION

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder with a prevalence of 12–15% in Europe

and North America.¹ Patients experience abdominal pain, bloating, and changes in stool habits. It is further divided into subtypes, such as constipation dominant, diarrhea dominant, or

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mixed type. The recommendation for diagnosing IBS is to make use of the Rome IV criteria.²

Quality of life (QOL) in patients with IBS has been shown to be as low as the QOL measured in patients with diabetes mellitus or end-stage renal disease.³ However, the disease does not only have a negative impact on the general health-related QOL, but also more specifically on sexual dysfunction. Hence, symptoms of bloating, flatulence, soiling, and abdominal pain can impact sexual life, and previous studies have shown significant sexual dysfunction in patients suffering from IBS when compared to healthy controls.^{4–6}

In recent years, there has been more focus on sexual dysfunction in patients suffering from inflammatory bowel disease. The Studies have shown not only a higher occurrence of sexual dysfunction, but also of sexual dysfunction independent of disease severity. With a major overlap in symptoms between IBS and inflammatory bowel disease, it could be speculated that sexual dysfunction is also problematic for patients with IBS. 9,10

Even though patients with IBS have symptoms that can lead to sexual problems, no systematic reviews have targeted sexual dysfunction in IBS. Knowledge in this field is of clinical relevance to health care professionals in order to improve QOL in this patient group. Therefore, we conducted a systematic review with the primary objective of synthesizing existing knowledge regarding sexual dysfunction among patients suffering from IBS.

In general, sexuality and sexual functioning have been demonstrated to be important for well-being and QOL. In a Danish population study, 90% stated that their sexuality was important, very important, or extremely important for their well-being. Furthermore, sexuality and intimacy can provide means for coping and developing survivorship skills for people living with a life-threatening or chronic disease, as sexual and intimate encounters can serve as a refuge in an otherwise chaotic and turbulent situation. ¹¹

METHODS

A systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Systematic searches in the PubMed and EMBASE databases were undertaken in November 2018. The search strategy used consisted of the following terms: "functional colonic disease," "irritable bowel syndrome," and "quality of life," both in Mesh terms and text words. They were combined using AND in conjunction with the terms "surveys and questionnaires" (both in Mesh terms and text words) and then again combined using AND in conjunction with the terms "sexual dysfunction" (Mesh), "sexual behavior" (Mesh), "sexual health" (Mesh), "sexual" (text word) OR "erectile dysfunction" (text word), and "dyspareunia" (text word). We excluded the following terms: "sex offences" (Mesh), "sexual abuse" (text words), "sexual violence" (text words), and "cancer" (Mesh term and text word).

Inclusion Criteria

The studies included in the review meet the following inclusion criteria:

- Peer reviewed articles. The articles showed a broad variety of different types of studies, including observational and prospective studies, but also intervention studies with some randomized trials. A few articles were either validating a new questionnaire or conducted a linguistic validation of an already validated questionnaire.
- Use of validated questionnaires with 1 or more questions about sexual life. All information regarding sexual dysfunction was accepted (dyspareunia, erectile dysfunction, lack/loss of interest, etc.).
- Questionnaires with values indicating the level of sexual functioning.
- 4. Diagnosis of IBS using the Manning, Rome I, II, III, or IV criteria. 13
- 5. Publications in English.

Exclusion Criteria

- 1. Other diseases or illnesses that could explain the sexual dysfunction, including earlier sexual abuse or violence.
- 2. Age younger than 18 years and older than 90 years.
- 3. Studies with <10 participants.

Data Collection and Analysis

The initial screening of the articles was performed by reading the titles and abstracts. If IBS and QOL or any form of sexual relations were mentioned, the articles were assessed more thoroughly looking for specific data on sexual relations. If none was identified, then the articles were excluded. All articles that met the inclusion criteria went through a full text analysis.

RESULTS

Initially, 1,273 records relevant to the research terms were found in the selected databases (see Figure 1). Of these, 331 articles were duplicated and, thus, removed, leaving 942 publications. After the first screening, 844 articles were excluded because they did not meet the inclusion criteria. 98 potentially eligible studies were identified. After examining the full texts, 41 articles were excluded. 7 articles did not use the Manning or Rome criteria when diagnosing IBS, and another 2 analyzed functional bowel diseases and not solely IBS. 11 articles did not give precise information on the subscore for sexual relations in the questionnaire. One article was excluded due to the inclusion of children in the cohort. 5 studies only reported changes in the subscore for sexual relations from baseline to after the intervention. 2 studies were excluded as the same cohort was used in other articles that had already been included. The majority (13) of studies was excluded either due to the lack of information

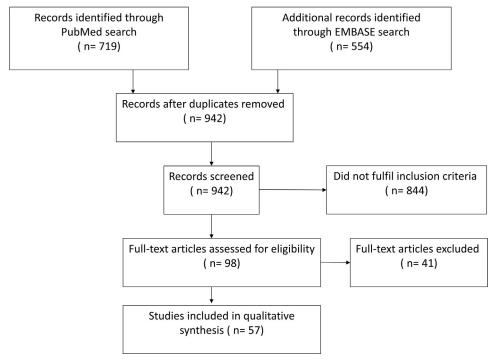


Figure 1. Flow diagram for database search.

regarding the questionnaire in use or due to the use of a questionnaire that had not been validated. The final search resulted in the inclusion of 57 studies.

Questionnaires

In the final search we identified 4 questionnaires with information on sexual relations among patients suffering from IBS. Information primarily came from 2 questionnaires: the Irritable Bowel Syndrome Quality of Life (IBS-QOL)¹⁴ questionnaire and the Irritable Bowel Syndrome — Quality of Life (IBSQOL) questionnaire.¹⁵ A description of these, in addition to the Irritable Bowel Syndrome-36 question (IBS-36)¹⁶ and the Arizona Sexual Experience Scale (ASEX),¹⁷ is provided in Table 1. Only 1 study had sexual dysfunction as a measuring end point. All other studies contained information on sexual relations from a QOL questionnaire.

IBS-QOL Questionnaire

Of the 57 included studies, 39 studies that make use of the IBS-QOL questionnaire were included. The results of 35 of the studies can be seen in Table 2. 14,18-49 The questionnaire has 2 items regarding sexual function, with the following text: "Because of my bowel problems, sexual activity is difficult for me" and "My bowel problems reduce my sexual desire." The minimum score is 0, whereas the maximum score is 100, with a higher score indicating higher QOL/less sexual problems. Subscores for sexual relations ranged from 37.7-100 (SD 11.9) for patients with IBS. Only 5 studies reported information for healthy controls with subscores ranging from 82.2-100

(SD 6.6). 14 papers described intervention studies with subscores after intervention of 41.0–100 (SD 12.2). Overall, there was an improvement in subscores after an intervention (mean change of 10.5%).

In total, the subscores for sexual relations vary greatly from one study to another, and only a few studies include healthy controls. In 4 of 5 studies, there were higher scores among healthy controls indicating less sexual problems, whereas the fifth study found no difference in scores between healthy controls and patients with IBS.

Four studies do not include specific data on sexual life but only correlations with other symptoms, and they are, therefore, not included in Table 2 but are described here. Ringel et al⁵⁰ looked at QOL and found no difference between patients complaining of bloating and nonbloating, with a sexual life score of 73.4 and 79.8, respectively. Balboa et al⁵¹ show that patients diagnosed with IBS and with upper digestive symptoms had a lower score for sexual relations. The same could not be found for the symptoms of heartburn or clinical functional dyspepsia. Jafari et al⁵² looked at the correlation between the IBS-specific symptom burden and sexual relations and found that a lower IBS-QOL sexual relation score correlates with a higher IBS symptom burden. Finally, Le Nevé et al⁵³ found no significant difference in the scores for sexual relations between patients with IBS with low or high intensity gastrointestinal symptoms.

IBSQOL Questionnaire

We found 17 studies using the IBSQOL questionnaire, with 15 studies providing specific scores for sexual relations (see

Table 1. Questionnaire overview

Instrument	Author and year	Description	Score
IBS-QOL	Patrick et al, 1998	Disease-specific HRQOL questionnaire including 34 items, measuring 8 dimensions of health, including 2 questions regarding sexual relations	5-point Likert response scale ranging from 1 ("not at all") to 5 ("extremely/a great deal"). A summed total score is transformed into 0–100 range scale (low score indicating low QOL)
IBSQOL	Hahn et al, 1997	Disease-specific HRQOL questionnaire including 30 items, measuring 9 dimensions of health, including 3 questions regarding sexual relations	5- or 6-graded scale. A summed total score is transformed into a 0–100 range scale (low score indicating low QOL)
IBS-36	Groll et al, 2002	Disease-specific HRQOL questionnaire including 36 items, measuring 8 dimensions of health, including 2 questions regarding sexual relations	7-point Likert scale where 0 = "never" and 6 = "always," yielding a score between 0 and 216 (high score indicating low QOL)
ASEX	McGahuey et al, 2000	Specific questionnaire for quantification of sexual dysfunction in psychiatric patients measuring 5 core elements (drive, arousal, vaginal lubrication, ability to reach orgasm, and satisfaction from orgasm)	6-point Likert scale, ranging from 5–30, with a higher score indicating a greater level of sexual dysfunction. A total ASEX score of >19, any 1 item with a score of >5, or any 3 items with a score of >4 would indicate sexual dysfunction.

ASEX = Arizona Sexual Experience Scale; HRQOL = health related quality of life; IBS-36 = Irritable Bowel Syndrome-36 question; IBS-QOL = Irritable Bowel Syndrome Quality of Life questionnaire; IBSQOL = Irritable Bowel Syndrome — Quality of Life questionnaire.

Table 3). ^{15,54–66} The questionnaire contains 3 items regarding sexual function, asking about interference related to sexual activity, avoidance of sexual activity, and lowered satisfaction levels. The minimum score is 0 and the maximum is 100, with a higher score indicating higher QOL/less sexual problems. Subscores for sexual relations ranged from 49.7–90.5 (SD 9.5). Only 1 study included controls exhibiting other gastrointestinal diseases, ¹⁵ and indicates higher subscores for sexual relations than patients with IBS corresponding to better QOL in the sexual domain. None of the studies included healthy controls and it is, therefore, not possible to conclude whether or not patients with IBS have more or less sexual problems than healthy controls.

7 studies had interventions with subscores ranging from 55.2–82 (SD 8.6). 11 of the 14 articles show improvement in subscores after an intervention, corresponding to an increase in QOL in the sexual domain. 2 studies report no change after an intervention and 1 study shows a lower score after intervention.

2 studies do not include specific data on sexual relations, but look at correlations to other factors. Böhn et al⁶⁷ looks at the correlation between avoiding specific food items and QOL, and found no significant correlation between sexual relations and food items reported to result in gastrointestinal symptoms. One study only includes data on sexual relations in correlation with low or high frequency symptoms. In general, it was found that a low intensity frequency pattern gave a higher sexual relation score than a high intensity frequency pattern.⁶⁸

IBS-36 and ASEX

Only 1 study uses the QOL questionnaire IBS-36 (see Table 4).⁶⁹ The IBS-36 questionnaire contains 2 items

that read: "Did your bowel condition interfere with having sexual relations?" and "Did your bowel symptoms interfere with your desire to have sexual relations with your partner?" The minimum score is 0 and the maximum score is 12, with higher scores indicating more sexual problems. The study does not make use of healthy controls for comparison. There was an improvement in sexual relations subscores and thereby an increase in QOL in the sexual domain after the intervention for all 3 groups in the study (with a mean change of 40%).

Eugenio et al⁶² conducted the only study addressing sexual dysfunction more specifically through the use of ASEX. The aim was to compare demographics and clinical factors in women with IBS with or without sexual dysfunction using both ASEX and IBSQOL. The results are reproduced in Table 5. The cohort was divided into 2 groups depending on whether or not sexual dysfunction was reported according to the ASEX questionnaire. 51% of the cohort with IBS had sexual dysfunction. They also show that patients with sexual dysfunction have significantly lower sexual relations scores in the IBSQOL, indicating that IBS negatively impacts sexual relations. In order to evaluate the quality of the studies we used Jadad Score. The Jadad Scores for the included studies are shown in Tables 6–9.

DISCUSSION

In this systematic review, a search was done through PubMed and EMBASE for information regarding sexual dysfunction in patients with IBS. We chose these 2 databases as they include research papers from all medical and psychological disciplines. Of the 57 papers included, 56 measured health-related QOL and

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Study	No of patients	Female	% Female	Age (mean)	Healthy controls		% with IBS-D/Mixed type	Score before intervention	Score before intervention (healthy controls)		Intervention type	Score after intervention (patients)
Abbasnezhad, 2016	44	28	63.6	37.5		34.1	65.9	69.4		б то	Vitamin D	85.1
/ 1524511621144, 2016	41	29	70.7	38.3		34.1	65.9	68.4		б то	Placebo	79.5
Abel, 2018	809	527	65.1	46.4				64.0		26 wk	Placebo	78.0
,	808	537	66.5	44.8				64.0		26 wk	Elux 75	78.0
	806	538	66.7	45.0				64.0		26 wk	Elux100	78.0
Ahmed, 2011	40	32	80.0		77.0	37.5	62.5	67.5	93.7			
Begtrup, 2013	67	51	76.1	31.6		20.9	79.1	78.2		6 то	Probiotics	82.4
	64	46	71.9	29.4		17.2	82.8	72.5		б то	Placebo	79.6
Boltin, 2015	15	11	73.3	38.9		20.0	80.0	73.2			GAI	73.2
	19	15	78.9	53.1		36.8	63.2	75.0		8 wk	Control	82.9
Canon, 2017	240			22.6				84.5				
		0						90.4				
Cash, 2017	2579	1759	68.2	46.4				65.2			Rifaximin open label	
	328	222	67.7	47.9				69.7			Rifaximin dbl blind	
	308	219	71.1	45.6				69.4			Placebo	
Cha, 2012	25	13	52.0	37.9				88.0		8 wk	Probiotics	93.5
	25	11	44.0	40.3				92.4		8 wk	Placebo	97.0
Cho, 2011	124	61	49.2	45.8	91.0	24.2	75.8	89.3				
Choi, 2011	45	17	37.8	40.2		22.2	77.8	86.6		4 wk	S.boulardii	92.9
	45	20	44.4	40.6		13.3	86.7	85.0		4 wk	Placebo	86.9
De Gucht, 2015	123	108	87.8	32.4				70.3				
Drisko, 2006	20	15	75.0					73.1		3-4 wk	Diet	79.6
Drossman, 2009	1966	1632	83.0	40.4				60.2				
El-Salhy, 2010	143	136	95.1	32		32.9	67.1	76.0		3 mo	Info, diet, excercise, probiotika	87.0
Frändemark, 2018	370	307	83.0	35.0 (median)		9.7	90.3	57.8				
Gholamrezaei, 2011	141	115	81.6	30.8		32.6	67.4	62.1				
Graham, 2010	113	113	100.0	48.5	224.0			64.8	82.8			
Huang, 2007	61	36	59.0	33.4	70.0			37.7	99.3	4 wk		41.0
Jang, 2014	39	39	100.0	21.9		53.8	46.2	98.1		24 wk	Cognitive therapy	100.0
	37	37	100.0	21.2		45.9	54.1	99.3		24 wk	Control	98.7
Kang, 2011	89	16	18.0	28.1		12.4	87.6	92.4		9 wk	Lifestyle modification	95.9
Kim, 2010	81	81	100.0	46.2				86.9		4 wk	Tegaserod	87.5
Kopczynska, 2018	87	69	79.3	39.2	56.0	41.2	58.8	76.4	99.8			

(continued)

Table 2. Continued

Study	No of patients	Female	% Female	Age (mean)	Healthy controls		% with IBS-D/Mixed type	Score before intervention	Score before intervention (healthy controls)	Duration of intervention	Intervention type	Score after intervention (patients)
Lauche, 2015	44	40	90.9	53.9		27.1	72.9	76.1		3 wk	CarO	77.1
	41							76.5		3 wk	OlivH	76.3
	41							80.2		3 wk	OlivC	85.8
Lee, 2008	159	144	63.6	39.4				69.0				
	261	228	63.6	40.7				73.4				
Park, 2006	103	74	71.8	38.3		46.0	54.0	87.1				
Park, 2009	664	367	55.3	43.0		25.3	74.7	86.7				
Patrick, 1998	155	138	89.0	39.0				73.5				
Remes-Troche, 2015	47	44	93.6	42.0	49.0	53.0	47.0	85.0				97.0
Schmulson, 2007	63	63	100.0	42.6		51.0	49.0	76.6				
	63	63	100.0	42.5		51.0	49.0	71.8				
Sherwin, 2016	101	79	78.2	42.0				66.8				
Singh, 2015	54	47		45.4		100		73.9				
	56	51		42.8			100	74.6				
	121	85		41.3			100	68.8				
Tana, 2009	26	13	50.0	21.9	26.0	42.3	57.7	100.0	100.0			
ten Berg, 2006	169	105	62.1	50.2				83.0				
Voci, 2009	144	144	100.0	32.5		7.0	93.0	52.4				
Zhu, 2015	227			44.68				83.1				
		94						82.3				
	133	0						83.7				

Some studies have several groups included in the study; each are listed in the table above.

CarO = caraway oil poultice; GAI = guided affective imagery; IBS-QOL = Irritable Bowel Syndrome Quality of Life questionnaire; OlivC = non-heated olive oil poultice; OlivH = hot olive oil poultice; S. boulardii = Saccharomyces boulardii.

 Table 3. IBSQOL Questionnaire

Study	No of patients	Female	% Female	Age (mean)	Healthy controls	% with IBS-C	% with IBS-D/Mixed type	Score before intervention (patients)	Score before intervention (controls)	Duration of intervention	Intervention type	Score after intervention
Amouretti, 2006	253	192	75.9	47.6				79.5				
Amouretti, 2000	61	122	0.0	48.5				90.5				
Bjorkman, 2015	405	405	72.7	43.1				58.0				
bjorkman, 2015	152	0	0.0	40.1				69.0				
Chassany, 1998	227	J	0.0	10.1				65.0				
Cremonini, 2012	705	177	100.0	45.9				51.8		2 wk	Alosetron 0.5 mg	
Cicinomin, 2012	,05	175	100.0	46.6				52.7		2 wk	Alosetron 1.0 mg once	
		177	100.0	47.7				55.9		2 wk	Alosetron 1.0 mg twice a day	
		176	100.0	46.6				53.9		2 wk	Placebo	
Euenio, 2012	86	86	100.0	38.7				69.7			Non-sexual dysfunction	
	89	89	100.0	46.2				69.7			Sexual dysfunction	
Hahn, 1997	248				37.0			64.9	90,0			
Johannesson, 2015	39	32	82.1	45.0		28.2	71.8	60.0		12 wk	Physical activity	60
Lindfors, 2012	45	35	77.8	40		15.6	84.4	49.7		1 y	Hypnotherapy	61.3
	45	36	0.08	41		15.6	84.4	54.7		3 mo	Control	55.2
Lindfors, 2013	83	65	78.3	42.0		15.7	84.3	55.1		12 wk	Hypnotherapy	60.9
Ringstrøm, 2007	218	151	69.3	42.0		20.2	79.8	74.0				
Ringstrøm, 2009	72	117	162.5	38		21.7	78.3	58.0		6 то	IBS-school	75
	71	117	164.8	38		21.7	78.3	58.0		6 то	Guidebook	67
Ringstrøm, 2012	40	33	82.5	36.0	0.0	27.5	72.5	50.0		12 mo	Long group IBS-School	67
	40	37	92.5	38.0	0.0	17.5	82.5	58.0		12 mo	Short group IBS school	54
Simrén, 2009	37	37	100.0	42		13.0	87.0	67.0			Active	75
	37	37	100.0	44		16.0	84.0	67.0			Control	67
Watson, 2001	317			45.3				64.0		12 wk	Placebo	69
	309			46.5				70.0		12 wk	Alo001	82
	323			45.6				63.0		12 wk	Placebo	68
	324			46.5				69.0		12 wk	Alo002	80
Williams, 2006	98	0	0.0					75.7			Healthcare seekers	
	239	239	100.0					72.2			Healthcare seekers	

 $Alo001 = alosetron \ hydrochloride (U.S. clinical trial study S3BA001); Alo002 = alosetron \ hydrochloride (U.S. clinical trial study S3BA3002); IBS = irritable bowel syndrome; IBSQOL = Irritable Bowel Syndrome — Quality of Life questionnaire.$

 Table 4. IBS-36 questionnaire

Study	No of patients	Female	% Female	Age (mean)	Healthy controls	% with IBS-C	% with IBS-D/Mixed type	Score before intervention	Score before intervention (healthy controls)	Duration of intervention	Intervention type	Score after intervention (patients)
Wilson, 2013	15	10	66.7	49.1				5.4		6 wk	SBI 10 g	3.2
	16	8	50.0	44.9				4.3		бwk	SBI 5 g	2.9
	14	10	71.4	47.8				3.9		бwk	Placebo	2.0

IBS-36 = Irritable Bowel Syndrome-36 question; SBI = serum-derived bovine immunoglobulin/protein isolate.

Table 5. ASEX questionnaire

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Study	No of	Female	% Female	Age (mean)	Healthy controls	% with IBS-C	% with IBS-D/Mixed type	Score before intervention	IBSQOL - subscore sexual relations	ASEX sexual dvsfunction	
Jiuuy	patients	remale	70 i erriale	(ineall)	COLLLOS	70 WILIT ID3-C	rhhc	intervention	SEXUAL LEIGHIOLIS	uysiuriction	
Eugenio, 2012	86	86	100	38.7		23	77	11.9	69.7	No dysfunction	
	89	89	100	46.2		28	72	20.6	69.7	Dysfunction	

ASEX = Arizona Sexual Experience Scale.

Table 6. Jadad score for studies using IBS-QOL.

Jadad score	Randomization	Double blind	Withdrawals/dropout	Total points
Abbasnezhad, 2016	2	2	1	5
Abel, 2018	1	2	0	3
Ahmed, 2011	0	0	0	0
Begtrup, 2013	2	2	1	5
Boltin, 2015	2	0	0	2
Canon, 2017	0	0	1	1
Cash, 2017	2	2	0	4
Cha, 2012	2	2	1	5
Cho, 2011	0	0	1	1
Choi, 2011	2	2	1	5
De Gucht, 2015	0	0	0	0
Drisko, 2006	0	0	1	1
Drossman, 2009	0	0	0	0
El-Salhy, 2010	0	0	1	1
Frändemark, 2018	0	0	1	1
Gholamrezaei, 2011	0	0	0	0
Graham, 2010	0	0	1	1
Huang, 2007	0	0	1	1
Jang, 2014	2	0	1	3
Kang, 2011	0	0	1	1
Kim, 2010	0	0	0	0
Kopczynska, 2018	0	0	0	0
Lauche, 2015	2	0	1	3
Lee, 2008	0	0	0	0
Park, 2006	0	0	0	0
Park, 2009	0	0	1	1
Patrick, 1998	0	0	0	0
Remes-Troche, 2015	0	0	0	0
Schmulson, 2007	0	0	0	0
Sherwin, 2016	0	0	0	0
Singh, 2015	0	0	0	0
Tana, 2009	0	0	0	0
ten Berg, 2006	0	0	0	0
Voci, 2009	0	0	0	0
Zhu, 2015	0	0	0	0

Ref: Jadad et al, 1996.

Randomization: 1. Was the study described as randomized? Double blinding: Was the study described as double blind? Withdrawals/dropouts? Was there a description of withdrawals and dropouts? Yes = 1 point, No = 0 points. Additional points for randomization described and appropriate, and double blinding described and appropriate. Deduction of points if randomization described but inappropriate or double blinding described but inappropriate. IBS-QOL = 1 Irritable Bowel Syndrome Quality of Life questionnaire.

not sexual relations specifically. Furthermore, most studies contained a QOL assessment only as a secondary end point. In all 56 studies, sexual dysfunction was measured by only 1 item in a QOL questionnaire.

We engaged the literature with 2 questions in mind: which questionnaires are used to describe sexual functioning in patients with IBS, and what information do these questionnaires provide about sexual dysfunction and if it is more or less prevalent in patients suffering from IBS compared to others.

The use of QOL questionnaires gives a broad idea of the general well-being of patients with IBS, however, this does not address what the problem is, nor whether the patient's psychological state has any influence on the bowel symptoms. It has traditionally been assumed that a low score for sexual relations in a questionnaire equates sexual dysfunction from a clinical perspective. There is no further description of the type and extent of sexual dysfunction and no consideration of which disease or illness the patient may have. In our systematic review, we found that for the IBS-QOL questionnaire only 5 studies had comparable information on healthy controls. The IBS-QOL questionnaire only had information including controls from 1 questionnaire, and these controls were not healthy but were patients with other gastrointestinal disorders. The 1 study making use of the IBS-36 also did not include healthy controls. The review demonstrates that information relating to sexual dysfunction

Table 7. Jadad score for studies using IBSQOL

Jadad score	Randomization	Double blind	Withdrawals/dropout	Total points
Amouretti, 2006	0	0	0	0
Bjorkman, 2015	0	0	0	0
Chassany, 1998	0	0	0	0
Cremonini, 2012	2	2	1	5
Eugenio, 2012	2	0	1	3
Hahn, 1997	0	0	0	0
Johannesson, 2015	2	0	1	3
Lindfors, 2012	2	0	1	3
Lindfors, 2013	2	0	1	3
Ringstrøm, 2007	0	0	0	0
Ringstrøm, 2009	2	0	1	3
Ringstrøm, 2012	2	0	1	3
Simrén, 2009	2	2	1	5
Watson, 2001	0	2	0	2
Williams, 2006	0	0	0	0

 $\mathsf{IBSQOL} = \mathsf{Irritable} \; \mathsf{Bowel} \; \mathsf{Syndrome} - \mathsf{Quality} \; \mathsf{of} \; \mathsf{Life} \; \mathsf{questionnaire}.$

in patients with IBS is very sparse and, in most of the published studies, limited to 1 question. Information on the type of sexual dysfunction and the relation to gastrointestinal symptoms is lacking. Nonetheless, it does seem that there could be a lower score indicating more sexual problems for patients with IBS than for healthy controls, when looking solely at the IBS-QOL studies. More studies, however, are required to confirm this.

It is well known that patients with IBS have low QOL, and it is often referred to as also having sexual dysfunction. The evidence supporting the latter comes primarily from older studies. ^{4,6,70} However, these studies were excluded due to a lack of validated questionnaires or because patients did not fulfil the established Manning or Rome criteria. Whether or not low QOL in patients with IBS results in sexual dysfunction remains to be examined in studies using validated questionnaires.

The present study found the use of only 4 questionnaires, although other questionnaires are also used also to measure QOL and include questions on sexual relations. They are the Patient Health Questionnaire 15, the World Health Organization Quality of Life BREF, and the Modified Manchester Health Questionnaire. Studies using these other questionnaires were excluded due to the lack of specific data on questions regarding sexual relations. For these other QOL questionnaires we expect the same challenges to emerge, as they are constructed for a broad view on health-related QOL and do not specifically focus on sexual relations.

Table 8. Study using IBS-36 questionnaire

Jadad score	Randomization		Withdrawals/ dropout	Total points
Wilson, 2013	2	2	1	5

IBS-36 = Irritable Bowel Syndrome-36 question.

The question, however, is whether or not the use of QOL questionnaires can provide exact knowledge about sexual dysfunction by asking 1 question about sexual relations. Bearing in mind that QOL questionnaires are designed to give an overview of many aspects of life and are not specifically designed to give information on sexual life, one can question if the results answers our question "is sexual dysfunction more common in patients suffering from IBS than healthy controls?" The only study that used both IBSQOL and the specific sexual relations questionnaire, ASEX, 62 detected a difference in scores for patients with IBS with and without sexual dysfunction, as defined by the ASEX questionnaire. In other words, the patients with sexual dysfunction scored lower in their sexual relations subscore than those who do not have sexual dysfunction. This might support the assumption that a low score in the IBSOOL questionnaire indicates sexual dysfunction.

A history of sexual abuse among patients suffering from IBS is more common than in healthy controls or patients suffering from other functional gastrointestinal syndromes. We, therefore, excluded studies on this group as it could be a confounder. Furthermore, none of the included studies contained information regarding the patients' sexual orientations. However, sexuality is a human phenomenon and is independent of gender or sexual orientation. The questionnaires also provide only limited information regarding different sexual domains (desire,

Table 9. study using ASEX questionnaire

Jadad score	Randomization		Withdrawals/ dropout	Total points
Eugenio, 2012	2	0	1	3

ASEX = Arizona Sexual Experience Scale.

arousal, lubrication, orgasmic function, satisfaction, and pain) and only covers 1, 2, or 3 items.

Limitations to the Study

All but 1 of the studies was not intended to solely evaluate sexual dysfunction in patients suffering from IBS. The studies have a great variety in design; some being intervention studies other descriptive, etc. Even though designs for some of the studies may seem similar there are still differences in intervention type, duration of intervention, and control groups. With the use of the Jadad score, we evaluated the quality of the studies (Tables 6, 7, 8, and 9) and found that a majority of the studies using the IBS-QOL questionnaire had a score of 0 or 1 (score 0–5, 0 being the lowest score). For the IBSQOL questionnaire the score overall were higher but still only 2 studies scored 5.

CONCLUSIONS

Information relating to sexual dysfunction in patients with IBS is sparse in the existing literature and emerges primarily from QOL questionnaires where questions regarding sexual dysfunctions are only 1 of many subscores. Such QOL questionnaires, which dedicate just 1 question to the description of sexual function, are not sufficient to describe the complexity of human sexuality. Nonetheless, from the available research it seems that patients with IBS may have more sexual problems compared to healthy controls. The type and extent of the sexual dysfunction remains unknown and further studies focusing specifically on the patients' sexuality are needed in order to provide further insight and sufficient treatment for patients with IBS.

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REFERENCES

- 1. Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: A meta-analysis. Clin Gastroenterol Hepatol 2012;10:712-721.
- 2. Schmulson MJ, Drossman DA. What is new in Rome IV. J Neurogastroenterol Motil 2017;23:151-163.
- Gralnek IM, Hays RD, Kilbourne A, et al. The impact of irritable bowel syndrome on health-related quality of life. Gastroenterology 2000;119:654-660.
- 4. Fass R, Fullerton S, Naliboff B, et al. Sexual dysfunction in patients with irritable bowel syndrome and non-ulcer dyspepsia. Digestion 1998;59:79-85.
- Whorwell PJ, McCallum M, Creed FH, et al. Non-colonic features of irritable bowel syndrome. Gut 1986;27:37-40.
- Guthrie E, Creed FH, Whorwell PJ. Severe sexual dysfunction in women with the irritable bowel syndrome: Comparison with inflammatory bowel disease and duodenal ulceration. Br Med J (Clin Res Ed) 1987;295:577-578.
- Rivière P, Zallot C, Desobry P, et al. Frequency of and factors associated with sexual dysfunction in patients with inflammatory bowel disease. J Crohns Colitis 2017;11:1347-1352.
- 8. O'Toole A, de Silva PS, Marc LG, et al. Sexual dysfunction in men with inflammatory bowel disease: A new IBD-specific scale. Inflamm Bowel Dis 2018;24:310-316.
- 9. Quigley EM. Overlapping irritable bowel syndrome and inflammatory bowel disease: Less to this than meets the eye? Therap Adv Gastroenterol 2016;9:199-212.
- Barbara G, Cremon C, Stanghellini V. Inflammatory bowel disease and irritable bowel syndrome: Similarities and differences. Curr Opin Gastroenterol 2014;30:352-358.
- 11. Graugaard C. Sexuality as a health-promoting factor theoretical and clinical considerations. Nat Rev Urol 2017;14:577-578.
- Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Ann Intern Med 2013;151:264-269.
- 13. Ahn J, Ehrenpreis ED. Emerging treatments for irritable bowel syndrome. Expert Opin Pharmacother 2002;3:9-21.
- Patrick DL, Drossman DA, Frederick IO, et al. Quality of life in persons with irritable bowel syndrome: Development and validation of a new measure. Dig Dis Sci 1998;43:400-411.
- Hahn BA, Kirchdoerfer LJ, Fullerton S, et al. Evaluation of a new quality of life questionnaire for patients with irritable bowel syndrome. Aliment Pharmacol Ther 1997;11:547-552.
- Groll D, Vanner SJ, Depew WT, et al. The IBS-36: A new quality of life measure for irritable bowel syndrome. Am J Gastroenterol 2002;97:962-971.

 McGahuey CA, Gelenberg AJ, Laukes CA, et al. The Arizona Sexual Experience Scale (ASEX): Reliability and validity. J Sex Marital Ther 2000;26:25-40.

- Abbasnezhad A, Amani R, Hajiani E, et al. Effect of vitamin D on gastrointestinal symptoms and health-related quality of life in irritable bowel syndrome patients: A randomized double-blind clinical trial. Neurogastroenterol Motil 2016; 28:1533-1544.
- Choi CH, Jo SY, Park HJ, et al. A randomized, double-blind, placebo-controlled multicenter trial of saccharomyces boulardii in irritable bowel syndrome: Effect on quality of life. J Clin Gastroenterol 2011;45:679-683.
- De Gucht V. Illness perceptions mediate the relationship between bowel symptom severity and health-related quality of life in IBS patients. Qual Life Res 2015;24:1845-1856.
- 21. Drisko J, Bischoff B, Hall M, et al. Treating irritable bowel syndrome with a food elimination diet followed by food challenge and probiotics. J Am Coll Nutr 2006;25:514-522.
- 22. El-sathy M, Elli L, Astrid R, et al. Effects of a health program comprising reassurance, diet management, probiotics administration and regular exercise on symptoms and quality of life in patients with irritable bowel syndrome. Gastroenterol Insights 2010;2:21-26.
- Frändemark A, Törnblom H, Jakobsson S, et al. Work productivity and activity impairment in irritable bowel syndrome (IBS): A multifaceted problem. Am J Gastroenterol 2018; 113:1540-1549.
- 24. Gholamrezaei A, Zolfaghari B, Farajzadegan Z, et al. Linguistic validation of the irritable bowel syndrome-quality of life questionnaire for Iranian patients. Acta Med Iran 2011; 49:390-395.
- 25. Graham DP, Savas L, White D, et al. Irritable bowel syndrome symptoms and health related quality of life in female veterans. Aliment Pharmacol Ther 2010;31:261-273.
- 26. Huang WW, Zhou FS, Bushnell DM, et al. Cultural adaptation and application of the IBS-QOL in China: A disease-specific quality-of-life questionnaire. Qual Life Res 2007;16:991-996.
- 27. Jang AL, Hwang SK, Kim DU. The effects of cognitive behavioral therapy in female nursing students with irritable bowel syndrome: A randomized trial. Eur J Gastroenterol Hepatol 2014;26:918-926.
- 28. Kang SH, Choi SW, Lee SJ, et al. The effects of lifestyle modification on symptoms and quality of life in patients with irritable bowel syndrome: A prospective observational study. Gut Liver 2011;5:472-477.
- Abel JL, Carson RT, Andrae DA. The impact of treatment with eluxadoline on health-related quality of life among adult patients with irritable bowel syndrome with diarrhea. Qual Life Res 2019;28:369-377.
- Kim YS, Choi SC, Park JM, et al. The effect of tegaserod on symptoms and quality of life in Korean women with irritable bowel syndrome with constipation. J Neurogastroenterol Motil 2010;16:61-70.
- 31. Kopczyńska M, Mokros Ł, Pietras T, et al. Quality of life and depression in patients with irritable bowel syndrome. Prz Gastroenterol 2018;13:102-108.

32. Lauche R, Janzen A, Lüdtke R, et al. Efficacy of caraway oil poultices in treating irritable bowel syndrome—A randomized controlled cross-over trial. Digestion 2015;92:22-31.

- Lee V, Guthrie E, Robinson A, et al. Functional bowel disorders in primary care: Factors associated with health-related quality of life and doctor consultation. J Psychosom Res 2008; 64:129-138.
- Park JM, Choi MG, Oh JH, et al. Cross-cultural validation of irritable bowel syndrome quality of life in Korea. Dig Dis Sci 2006;51:1478-1484.
- Park JM, Choi MG, Kim YS, et al. Quality of life of patients with irritable bowel syndrome in Korea. Qual Life Res 2009; 18:435-446.
- Remes-Troche JM, Torres-Aguilera M, Montes-Martinez V, et al. Prevalence of irritable bowel syndrome in caregivers of patients with chronic diseases. Neurogastroenterol Motil 2015:27:824-831.
- Schmulson M, Ortiz O, Mejia-Arangure JM, et al. Further validation of the IBS-QOL: Female Mexican IBS patients have poorer quality of life than females from North Carolina. Dig Dis Sci 2007;52:2950-2955.
- Sherwin LB, Leary E, Henderson WA. Effect of illness representations and catastrophizing on quality of life in adults with irritable bowel syndrome. J Psychosoc Nurs Ment Health Serv 2016;54:44-53.
- 39. Tana C, Umesaki Y, Imaoka A, et al. Altered profiles of intestinal microbiota and organic acids may be the origin of symptoms in irritable bowel syndrome. Neurogastroenterol Motil 2010;22:512-519.
- 40. Abdulmajeed A, Rabab MA, Sliem HA, et al. Pattern of irritable bowel syndrome and its impact on quality of life in primary health care center attendees, Suez governorate, Egypt. Pan Afr Med J 2011;9:5.
- ten Berg MJ, Goettsch WG, van den Boom G, et al. Quality of life of patients with irritable bowel syndrome is low compared to others with chronic diseases. Eur J Gastroenterol Hepatol 2006;18:475-481.
- Voci SC, Cramer KM. Gender-related traits, quality of life, and psychological adjustment among women with irritable bowel syndrome. Qual Life Res 2009;18:1169-1176.
- 43. Zhu L, Huang D, Shi L, et al. Intestinal symptoms and psychological factors jointly affect quality of life of patients with irritable bowel syndrome with diarrhea. Health Qual Life Outcomes 2015;13:49.
- 44. Begtrup LM, de Muckadell OB, Kjeldsen J, et al. Long-term treatment with probiotics in primary care patients with irritable bowel syndrome—a randomised, double-blind, placebo controlled trial. Scand J Gastroenterol 2013:48:1127-1135.
- Boltin D, Sahar N, Gil E, et al. Gut-directed guided affective imagery as an adjunct to dietary modification in irritable bowel syndrome. J Health Psychol 2015;20:712-720.
- 46. Cañón M, Ruiz AJ, Rondón M, et al. Prevalence of irritable bowel syndrome and health-related quality of life in adults aged 18 to 30 years in a Colombian University: An electronic survey. Ann Gastroenterol 2017;30:67-75.

- 47. Cash BD, Pimentel M, Rao SSC, et al. Repeat treatment with rifaximin improves irritable bowel syndrome-related quality of life: A secondary analysis of a randomized, double-blind, placebo-controlled trial. Therap Adv Gastroenterol 2017; 10:689-699.
- 48. Ki Cha B, Mun Jung S, Hwan Choi C, et al. The effect of a multispecies probiotic mixture on the symptoms and fecal microbiota in diarrhea-dominant irritable bowel syndrome: A randomized, double-blind, placebo-controlled trial. J Clin Gastroenterol 2012;46:220-227.
- Cho HS, Park JM, Lim CH, et al. Anxiety, depression and quality of life in patients with irritable bowel syndrome. Gut Liver 2011;5:29-36.
- 50. Ringel Y, Williams RE, Kalilani L, et al. Prevalence, characteristics, and impact of bloating symptoms in patients with irritable bowel syndrome. Clin Gastroenterol Hepatol 2009; 7:68-72; quiz 3.
- Balboa A, Mearin F, Badia X, et al. Impact of upper digestive symptoms in patients with irritable bowel syndrome. Eur J Gastroenterol Hepatol 2006;18:1271-1277.
- 52. Jafari P, Asadollahi Z, Moini M, et al. Health related quality of life in Iranian patients with irritable bowel syndrome: Reliability and validity of the Persian version of the IBS-QOL. Iran Red Crescent Med J 2013;15:723-728.
- Le Nevé B, Brazeilles R, Derrien M, et al. Lactulose challenge determines visceral sensitivity and severity of symptoms in patients with irritable bowel syndrome. Clin Gastroenterol Hepatol 2016;14:223-233.
- 54. Amouretti M, Le Pen C, Gaudin AF, et al. Impact of irritable bowel syndrome (IBS) on health-related quality of life (HRQOL). Gastroenterol Clin Biol 2006;30:241-246.
- 55. Björkman I, Jakobsson Ung E, Ringström G, et al. More similarities than differences between men and women with irritable bowel syndrome. Neurogastroenterol Motil 2015; 27:796-804.
- Ringström G, Störsrud S, Simrén M. A comparison of a short nurse-based and a long multidisciplinary version of structured patient education in irritable bowel syndrome. Eur J Gastroenterol Hepatol 2012;24:950-957.
- 57. Simrén M, Ohman L, Olsson J, et al. Clinical trial: The effects of a fermented milk containing three probiotic bacteria in patients with irritable bowel syndrome a randomized, double-blind, controlled study. Aliment Pharmacol Ther 2010; 31:218-227.
- 58. Watson ME, Lacey L, Kong S, et al. Alosetron improves quality of life in women with diarrhea-predominant irritable bowel syndrome. Am J Gastroenterol 2001;96:455-459.

- 59. Williams RE, Black CL, Kim HY, et al. Stability of irritable bowel syndrome using a Rome II-based classification. Aliment Pharmacol Ther 2006;23:197-205.
- Chassany O, Bergmann JF. Quality of life in irritable bowel syndrome, effect of therapy. Eur J Surg Suppl 1998; 583:81-86.
- Cremonini F, Nicandro JP, Atkinson V, et al. Randomised clinical trial: Alosetron improves quality of life and reduces restriction of daily activities in women with severe diarrhoea-predominant IBS. Aliment Pharmacol Ther 2012; 36:437-448.
- 62. Eugenio MD, Jun SE, Cain KC, et al. Comprehensive self-management reduces the negative impact of irritable bowel syndrome symptoms on sexual functioning. Dig Dis Sci 2012; 57:1636-1646.
- 63. Johannesson E, Ringstrom G, Abrahamsson H, et al. Intervention to increase physical activity in irritable bowel syndrome shows long-term positive effects. World J Gastroenterol 2015;21:600-608.
- 64. Lindfors P, Unge P, Arvidsson P, et al. Effects of gut-directed hypnotherapy on IBS in different clinical settings-results from two randomized, controlled trials. Am J Gastroenterol 2012; 107:276-285.
- 65. Lindfors P, Ljótsson B, Bjornsson E, et al. Patient satisfaction after gut-directed hypnotherapy in irritable bowel syndrome. Neurogastroenterol Motil 2013;25:169-e86.
- 66. Ringström G, Abrahamsson H, Strid H, et al. Why do subjects with irritable bowel syndrome seek health care for their symptoms? Scand J Gastroenterol 2007;42:1194-1203.
- 67. Böhn L, Störsrud S, Törnblom H, et al. Self-reported foodrelated gastrointestinal symptoms in IBS are common and associated with more severe symptoms and reduced quality of life. Am J Gastroenterol 2013;108:634-641.
- **68.** Mearin F, Baró E, Roset M, et al. Clinical patterns over time in irritable bowel syndrome: Symptom instability and severity variability. Am J Gastroenterol 2004;99:113-121.
- 69. Wilson D, Evans M, Weaver E, et al. Evaluation of serumderived bovine immunoglobulin protein isolate in subjects with diarrhea-predominant irritable bowel syndrome. Clin Med Insights Gastroenterol 2013;6:49-60.
- 70. Whorwell PJ, McCallum M, Creed FH, et al. Non-colonic features of irritable bowel syndrome. **Gut 1986;27:37-40.**
- 71. Leroi AM, Bernier C, Watier A, et al. Prevalence of sexual abuse among patients with functional disorders of the lower gastrointestinal tract. Int J Colorect Dis 1995;10:200-206.