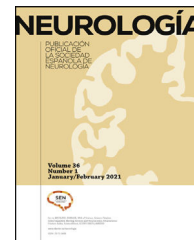




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ORIGINAL ARTICLE

The prevalence of sexual dysfunction and erectile dysfunction in men with multiple sclerosis: A systematic review and meta-analysis

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KEYWORDS

Sexual dysfunction;
Erectile dysfunction;
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Abstract

Background: The prevalence of sexual dysfunction (SD) in men with multiple sclerosis (MS) is reported variously in different studies. The most common form of SD in these patients is erectile dysfunction (ED). The goal of this systematic review and meta-analysis is to determine the pooled prevalence of SD and ED in men suffering from MS.

Methods: We searched PubMed, Scopus, EMBASE, CINAHL, Web of Science, and gray literature (references of references, and congress abstracts) up to 14th November 2020.

Results: We found 3163 studies by primary search, 2246 were included after deletion of duplicates. Finally, 29 studies were included for meta-analysis. A total of 3349 patients were evaluated. The pooled prevalence of SD was 66% (95% CI: 64%–69%). The pooled prevalence of erectile dysfunction was 49% (95% CI: 47%–50%).

Conclusion: Sexual dysfunction is a prevalent complication of MS in male patients which should be considered by clinicians.

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PALABRAS CLAVE

Disfunción sexual;
Disfunción eréctil;
Esclerosis múltiple

La prevalencia de la disfunción sexual y la disfunción eréctil en hombres con esclerosis múltiple: una revisión sistemática y metanálisis

Resumen

Antecedentes: La prevalencia de la disfunción sexual (SD) en hombres con esclerosis múltiple (EM) se informa de forma diversa en diferentes estudios. La forma más común de SD en estos pacientes es la disfunción eréctil (DE). El objetivo de esta revisión sistemática y metanálisis es determinar la prevalencia combinada de SD y DE en hombres que padecen EM.

Métodos: Se realizaron búsquedas en PubMed, Scopus, EMBASE, CINAHL, Web of Science y literatura gris (referencias de referencias y resúmenes de congresos) hasta el 14 de noviembre de 2020.

Resultados: Encontramos 3163 estudios por búsqueda primaria, 2246 permanecieron después de la eliminación de duplicados. Finalmente, 29 estudios fueron incluidos para metanálisis. Se evaluaron en total 3349 pacientes. La prevalencia combinada de SD fue del 66% (IC del 95%: 64%–69%). La prevalencia combinada de disfunción eréctil fue del 49% (IC del 95%: 47%–50%).

Conclusión: La disfunción sexual es una complicación frecuente de la EM en pacientes masculinos que debe ser considerada por los médicos.

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Introduction

Multiple sclerosis (MS) is an autoimmune disease which affects individuals in reproductive age (mostly between 20–50 years of age) and causes a wide range of complications including sexual dysfunction (SD).^{1,2}

Sexual dysfunction in MS may be divided into three categories: primary (due to disease course), secondary (due to fatigue, bowel dysfunction, spasticity), or tertiary (due to psychological complications such as depression),^{3–6} and interferes with quality of life.⁷ Signs and symptoms are widely different in patients and the location of the plaques plays an important role in SD development.⁸

Between 64–91% of men with MS suffer from SD and erectile dysfunction (ED) is the most frequent dysfunction (16%–92%).⁹

For clinicians, it is very important to consider SD in men and manage it to improve marital life and also the quality of life.⁸

Several studies have reported the prevalence of SD in men with MS. As there is no comprehensive study, we designed this systematic review and meta-analysis to determine the pooled prevalence of SD and ED in men suffering from MS.

Methods

Literature search

Two independent researchers searched PubMed, Scopus, EMBASE, Web of Science, and Google Scholar as well as gray literature (references of references and conference abstracts) until 14th November 2020.

Inclusion criteria

We included cross-sectional studies which reported SD and/or ED in men with MS.

Exclusion criteria

Letters to the editor, case-control, case reports, narrative reviews, and systematic reviews were excluded.

Data search and extraction

The search strategy included the MeSH and text keywords as ((Sclerosis[all] AND Multiple[all]) OR MS[all] OR "Multiple Sclerosis"[all]) AND ((Dysfunction[all] AND "Psychological Sexual"[all]) OR "Psychological Sexual Dysfunction"[all] OR "Psychosexual Dysfunctions"[all] OR "Psychosexual Disorders"[all] OR "Hypoactive Sexual Desire Disorder"[all] OR "Sexual Aversion Disorder"[all] OR "Orgasmic Disorder"[all] OR "Orgasmic Disorders"[all] OR "Sexual Arousal Disorder"[all] OR Frigidity[all] OR "Premature Ejaculation"[all] OR "Erectile Dysfunction"[all] OR Dyspareunia[all]).

Risk of bias assessment

We evaluated the risk of potential bias with the NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (NOS) (adapted for cross-sectional studies).¹⁰

Statistical analysis

All statistical analyses were performed using STATA (Version 14.0; Stata Corp LP, College Station, TX, USA). We used the fixed-effects model.

To determine heterogeneity, inconsistency (I^2) was calculated.

Results

We found 3163 studies by primary search. Of those, 2246 articles were screened after deletion of duplicates. Finally, twenty-nine studies were included in the meta-analysis. Twenty-three full texts and 6 conference abstracts were included (Fig. 1).

A total of 3349 patients were evaluated. Fourteen studies provided the frequency of cases with SD and 22 provided the frequency of men with ED.

Basic characteristics of the studies are summarized in Table 1. The NOS ranged between 3 and 9 (Table 2). The pooled prevalence of SD estimated as 66% (95% CI: 64–69%) ($I^2=0$) (Fig. 2). The pooled prevalence of erectile dysfunction estimated was 49% (95% CI: 47–50%) ($I^2=0$) (Fig. 3).

Table 1 Basic characteristics of the included studies.

Title	Type of publication	Author	Year	Country	Sample size	MS Type	Mean age (SD)	Mean Disease duration (Mean \pm sd) or (Medianquartiles range)	Mean EDSS (SD)
Sexual dysfunction in patients with multiple sclerosis from Argentina: what are the differences between women and men? ¹¹	Original article	Contentti et al.	2019	Argentina	65	RRMS = 55 PPMS = 9 SPMS = 1	42.6 (9.7)	7.5 (\pm 0.6)	
Sexual function in multiple sclerosis and associations with demographic, disease and lifestyle characteristics: an international cross-sectional study ¹²	Original article	Marck et al.	2016	Australia	388				
Insular multiple sclerosis lesions are associated with erectile dysfunction ¹³	Original article	Winder et al.	2018	Germany	31		38.2 (11.2)	3.75 \pm 4.2	3.3 (2–4.4)
Correlates of sexual dysfunction in men and women with multiple sclerosis ⁵	Original article	Fraser et al.	2008	US	32		47 (8.9)	6.9 (3.5)	
Sexual dysfunction in multiple sclerosis: Gender differences ¹⁴	Original article	Çelik et al.	2012	Turkey	45				
Sexual dysfunctions and sexual quality of life in men with multiple sclerosis ⁷	Original article	Lew-Starowicz et al.	2014	Poland	67	RRMS = 25 PPMS = 30 SPMS = 8	49.9 (15.5)		5.32 (2.11)
Lower urinary tract symptoms and sexual dysfunction in men with multiple sclerosis ¹⁵	Original article	Tomé et al.	2019	Brazil	39				
Is multiple sclerosis only a neurological problem? Evaluation of sexual dysfunctions in a group of multiple sclerosis patients ¹⁶	Original article	Popek et al.	2018	Poland	40				
Sexual dysfunction and incidence of depression in multiple sclerosis patients ¹⁷	Original article	Zavoreo et al.	2016	Croatia	42				
Sexual function in young individuals with multiple sclerosis: does disability matter? ¹⁸	Original article	Calabrò et al.	2018	Italy	33				
Exploring sexual problems among patients with multiple sclerosis ¹⁹	Original article	Tulek et al.	2011	Turkey	49				
Relationship functioning and sexuality among people with multiple sclerosis ²⁰	Original article	McCabe et al.	2002	Australia	144		46.88		
Identifying barriers to help-seeking for sexual dysfunction in multiple sclerosis ²¹	Original article	Tudor et al.	2018	Croatia	20				
Sexual difficulties for persons with multiple sclerosis in New South Wales, Australia ²²	Original article	Redelman et al.	2009	Australia	68				
Sexual dysfunction in multiple sclerosis: a 6-year follow-up study ²³	Original article	Darija et al.	2015	Serbia	27				

Table 1 (Continued)

The impact of sexual dysfunction on the quality of life measured by MSQoL-54 in patients with multiple sclerosis ²⁴	Original article	Tepavcevic et al.	2008	Serbia	31	RRMS = 19 PPMS = 5 SPMS = 7	41.6 (6.9)	9.0 (5.1)	4.2 (1.9)
Relationship between urodynamic findings and sexual function in multiple sclerosis patients with lower urinary tract dysfunction ²⁵	Original article	Fragala et al.	2014	Italy	60				
Multiple sclerosis patients with and without sexual dysfunction: are there any differences? ²⁶	Original article	Demirkiran et al.	2006	Turkey	18				
Changes over time in sexual and relationship functioning of people with multiple sclerosis ²⁷	Original article	McCabe et al.	2003	Australia	120		48.1		
Exacerbation of symptoms among people with multiple sclerosis: impact on sexuality and relationships over time ²⁸	Original article	McCabe et al.	2004	Australia	57				
Determinants of sexual impairment in multiple sclerosis in male and female patients with lower urinary tract dysfunction: results from an Italian cross-sectional study ²⁹	Original article	Fragalà et al.	2014	Italy	60				
Sexual dysfunction in patients with multiple sclerosis ³⁰	Original article	Orasanu et al.	2013	US	1568				
Sexual dysfunction in male patients with multiple sclerosis ³¹	Conference abstract	Garcia et al.	2016	Spain	32		35.4(6.4)	6.9(5.4)	1.2 (0–5)
Increased risk of erectile dysfunction in men with multiple sclerosis: an Italian cross-sectional study ⁸	Original article	Balsamo et al.	2017	Italy	101	RRMS = 64 PPMS = 28 SPMS = 9	41.26 (11.6)	11.5 (7.5)	3.77 (2.01)
Depression influences erectile dysfunction in multiple sclerosis patients with primary and tertiary sexual dysfunction ³²	Conference abstract	Roy et al.	2018	Germany	41		29.3 (29.3–42.5)		
A study of sexual dysfunction and awareness on its rehabilitation measures in multiple sclerosis ³³	Conference abstract	Mulanur Murugesan et al.	2018	India	7				
Sexual dysfunctions in patients affected by multiple sclerosis: evaluation in a contemporary cohort from a referral center ³⁴	Conference abstract	Sacco et al.	2011	Italy	56				
Sexual dysfunction in young men with relapsing-remitting multiple sclerosis ³⁵	Conference abstract	Zinchenko et al.	2010	United Kingdom	18	RRMS = 18	30.8 (4.3)		
Determinants of sexual dysfunctions and sexual quality of life in men with multiple sclerosis ³⁶	Conference abstract	Balsamo et al.	2016	Italy	90		40 (20–64)		

RRMS: relapsing-remitting multiple sclerosis; PPMS: primary-progressive multiple sclerosis; SPMS: secondary-progressive multiple sclerosis.

Table 2 Number of patients with SD and ED.

NOS score	Number of patients with erectile dysfunction	Number of patients with Sexual dysfunction	Sexual test	Author	Title
8	58		Multiple Sclerosis Intimacy and Sexuality Questionnaire (MSISQ-19) International Index of Erectile Function (IIEF5-ED)	Contentti et al.	Sexual dysfunction in patients with multiple sclerosis from Argentina: what are the differences between women and men?
9	158	193	Sexual function scale satisfaction item	Marck et al.	Sexual function in multiple sclerosis and associations with demographic, disease and lifestyle characteristics: an international cross-sectional study
7	14		IIEF5 MSISQ-19	Winder et al.	Insular multiple sclerosis lesions are associated with erectile dysfunction
3		19	The Guy's Neurological Disability Scale (GNDS)	Fraser et al.	Correlates of sexual dysfunction in men and women with multiple sclerosis
7	9	22	MSISQ scores	Çelik et al.	Sexual dysfunction in multiple sclerosis: gender differences
8	35		IIEF Sexual Quality of Life Questionnaire—Male Version (SQoL-M)	Lew-Starowicz et al.	Sexual dysfunctions and sexual quality of life in men with multiple sclerosis
7	26	29	IIEF-15	Tomé et al.	Lower urinary tract symptoms and sexual dysfunction in men with multiple sclerosis
7	26		IIEF	Popek et al.	Is multiple sclerosis only a neurological problem? Evaluation of sexual dysfunctions in a group of multiple sclerosis patients
6	13		Sexual Satisfaction Scale, SSS	Zavoreo et al.	Sexual dysfunction and incidence of depression in multiple sclerosis patients
3	22		Interview and 40-item questionnaire	Calabrò et al.	Sexual function in young individuals with multiple sclerosis: does disability matter?
2	26		5-item questionnaire	Tulek et al.	Exploring sexual problems among patients with multiple sclerosis
5	53		Nature of the Sexual Problem Subscale of the Sexual Dysfunction Scale (SDS) Sexual Activity Subscale of the Sexual Function Scale (SFS)	McCabe et al.	Relationship functioning and sexuality among people with multiple sclerosis
5	14		Arizona Sexual Experiences Scale (ASEX) MSISQ	Tudor et al.	Identifying barriers to help-seeking for sexual dysfunction in multiple sclerosis
5		50	28-item questionnaire	Redelman et al.	Sexual difficulties for persons with multiple sclerosis in New South Wales, Australia
7	8(loss) 18 (incomplete)	24	16-item questionnaire Szasz sexual functioning scale	Darija et al.	Sexual dysfunction in multiple sclerosis: a 6-year follow-up study

Table 2 (Continued)

NOS score	Number of patients with erectile dysfunction	Number of patients with Sexual dysfunction	Sexual test	Author	Title
7	7(loss) 16(incomplete)	26	16-item questionnaire Szasz sexual functioning scale	Tepavcevic et al.	The impact of sexual dysfunction on the quality of life measured by MSQoL-54 in patients with multiple sclerosis
7		50	IIEF15 MSISQ	Fragala et al.	Relationship between urodynamic findings and sexual function in multiple sclerosis patients with lower urinary tract dysfunction
6	13	14	(MSISQ-19)	Demirkiran et al.	Multiple sclerosis patients with and without sexual dysfunction: are there any differences?
8	53	97	Index of Sexual Satisfaction (ISS) Sexual Dysfunction Scale (SDS) Sexual Function Scale (SFS)	McCabe et al.	Changes over time in sexual and relationship functioning of people with multiple sclerosis
6		29	Index of Sexual Satisfaction (ISS) Sexual Function Scale (SFS) e Sexual Dysfunction Scale (SDS)	McCabe et al.	Exacerbation of symptoms among people with multiple sclerosis: impact on sexuality and relationships over time
8		50	IIEF-15 FSFI MSISQ19	Fragalà et al.	Determinants of sexual impairment in multiple sclerosis in male and female patients with lower urinary tract dysfunction: results from an Italian cross-sectional study
7	639		MSISQ-19	Orasanu et al.	Sexual dysfunction in patients with multiple sclerosis
	10		MSISQ-19 IIEF	Garcia et al.	Sexual dysfunction in male patients with multiple sclerosis
7	75	75	IIEF-15	Balsamo et al.	Increased risk of erectile dysfunction in men with multiple sclerosis: an Italian cross-sectional study
	25		IIEF-5	Roy et al.	Depression influences erectile dysfunction in multiple sclerosis patients with primary and tertiary sexual dysfunction
	7		MSISQ-19 IIEF-5	Mulanur Murugesan et al.	A Study of sexual dysfunction and awareness on its rehabilitation measures in multiple sclerosis
	26	29	IIEF	Sacco et al.	Sexual dysfunctions in patients affected by multiple sclerosis: evaluation in a contemporary cohort from a referral center
	14		IIEF MSISQ-19	Zinchenko et al.	Sexual dysfunction in young men with relapsing remitting-multiple sclerosis
	48	54	IIEF-15	Balsamo et al.	Determinants of sexual dysfunctions and sexual quality of life in men with multiple sclerosis

MSISQ-19: multiple sclerosis intimacy and sexuality questionnaire ;IIFE5: international index of erectile function ; GNDS: the guy's neurological disability scale; SQoL-M: sexual quality of life questionnaire; SSS: sexual satisfaction scale; SDS: sexual dysfunction scale; SFS: sexual function scale; ASEX: Arizona sexual experiences scale; ISS: index of sexual satisfaction.

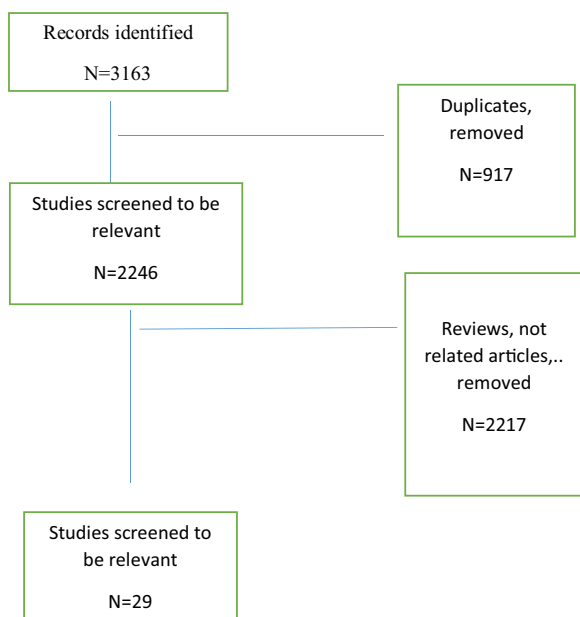


Figure 1 Flow diagram of included studies.

Discussion

To our knowledge, this is the first systematic review and meta-analysis evaluating SD and ED in men with MS. Our results

demonstrated that the pooled prevalence of SD in men with MS was 66% and the pooled prevalence of ED was 49%.

The prevalence of SD in the included studies ranged between 49% and 89% which could be due to different inclusion and exclusion criteria, different applied tests, and different sample sizes.

Men with MS suffer from deterioration in their sexual life affecting their marital life, which is ignored in most cases. Neither physicians nor patients talk about this issue in most clinical settings. There are controversies regarding the role of some factors (including age, disease duration, and disability) in developing SD in men with MS.^{7,37}

Zorzon et al. found that SD is more common in men with MS than patients with other chronic diseases (including rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, and ankylosing spondylitis) as well as healthy controls.³⁸

In another study, Marck et al. evaluated 388 men with MS and reported SD in 49.7%. They found that difficulty in erection was the most frequent problem.¹² Their results also showed that fatigue, depression and antidepressant use were independent predictors of SD.

Low-Starowicz and Rola reported ED as the most common form of SD in men with MS (52.9%). They also investigated that age, disease duration and disability were not related with the incidence or severity of SD.⁷

It should be noted that ED affects sexual satisfaction and sexual self-esteem⁷ and ED diagnosis and treatment would improve marital life and overall quality of life.

In healthy men, the sexual response cycle includes libido, erection, ejaculation and orgasm.³⁹ Men with MS may suffer from ejaculatory dysfunction and/ or orgasmic dysfunction, ejaculatory dysfunction and/or orgasmic dysfunction, and anorgasmia.⁴⁰ Despite its importance, Low-Starowicz reported that only 6% of their

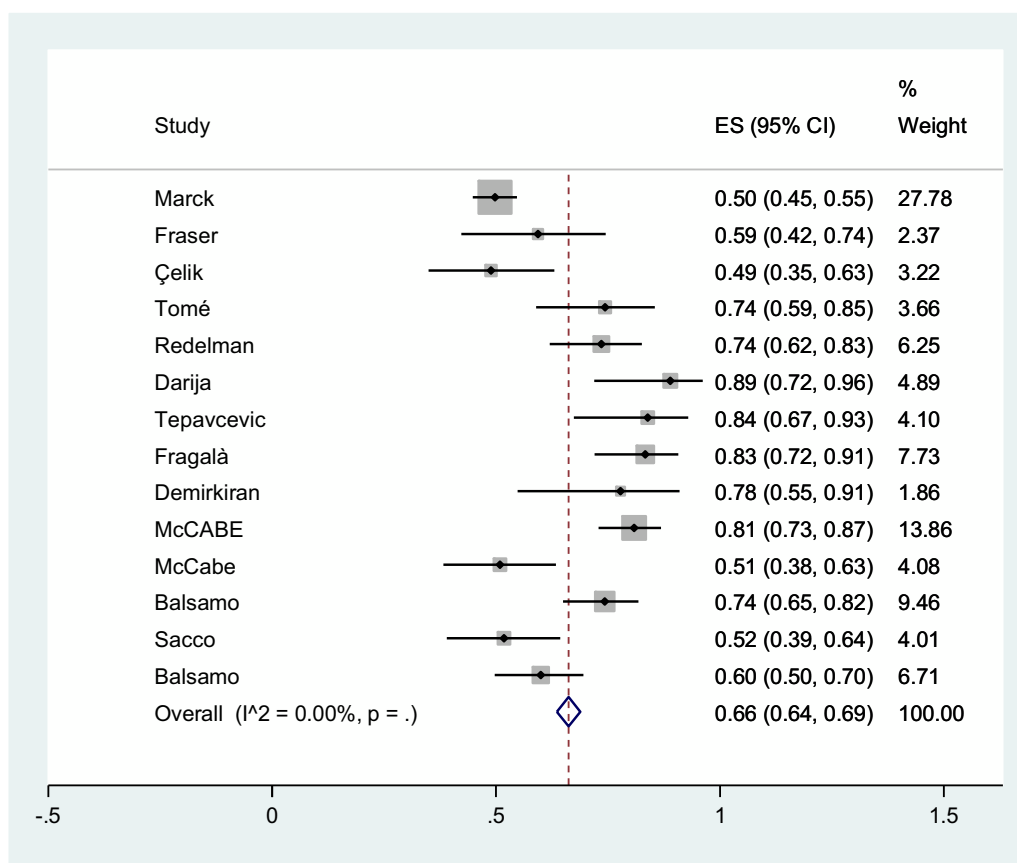


Figure 2 The pooled prevalence of SD.

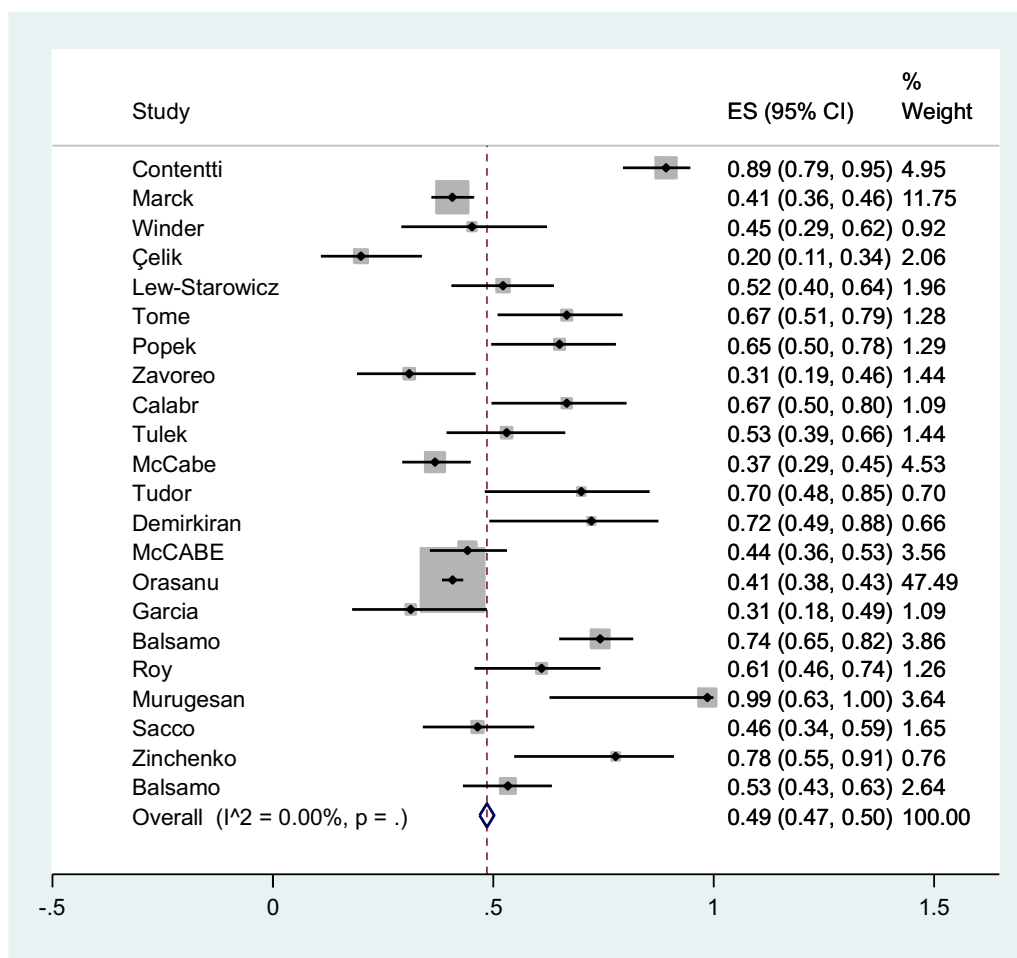


Figure 3 The pooled prevalence of erectile dysfunction.

patients discussed their sexual concerns with their physicians or received treatment for this problem.⁷

Sexual dysfunction is an important issue for patients with MS. Most patients are young and in reproductive age. SD influences mental health, quality of life and intimate relationships, but is not routinely evaluated.¹² Asking a few questions as well as applying suitable questionnaires could help physicians to detect and treat SD. The International Index of Erectile Function is widely used for ED detection.

Sexual dysfunction in MS can be a direct result of neurological changes due to MS which is known as primary SD, or the consequence of medication use (medications which are applied for fatigue, bladder and bowel dysfunctions, spasms, and pain) which is known as secondary SD, or tertiary SD which is the result of psychological complications such as depression, anxiety, decreased self-esteem, fear of being sexually rejected, and body image perception distortion.^{40,41}

Modification of some factors such as smoking cessation, depression and fatigue treatment, and increased physical activity could help improve SD.¹²

This systematic review has several strengths. First, it included 29 studies which used different tests. Second, studies are from different nations.

Conclusion

Sexual dysfunction is a prevalent complication of MS in male patients which should be considered by clinicians.

Ethics approval and consent to participate

All participants filled informed consent forms. All methods were carried out in accordance with relevant guidelines and regulations. All experimental protocols were approved by local ethics committee.

Consent for publication

All authors consent for publication.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors had no conflicts of interest.

Funding

We had no funding.

Authors' contribution

VS: Study conception, data gathering article writing
OM: Data gathering, article writing
SV: Data gathering, article writing
NN: Data gathering, article writing
MG: Study design, data analysis, article writing

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