High prevalence of erectile dysfunction in diabetes:

A systematic review and meta-analysis of 145 studies

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ABSTRACT

Erectile dysfunction may be common among men with diabetes, but its prevalence is still debated. We aimed to assess the relative prevalence of erectile dysfunction in diabetes searching major databases from inception to November 2016 for studies reporting erectile dysfunction in men with Type 1 and Type 2 diabetes mellitus. We conducted a meta-analysis of the prevalence [and 95% confidence intervals (95% CIs)] of erectile dysfunction in diabetes compared with healthy controls, calculating the relative odds ratios (ORs) and 95% CIs. A random effect model was applied. From 3747 initial hits, 145 studies were included representing 88 577 men (age: 55.8 ` 7.9 years). The prevalence of erectile dysfunction in diabetes overall was 52.5% (95% CI, 48.8 to 56.2) after adjusting for publication bias, and 37.5%, 66.3% and 57.7% in Type 1, Type 2 and both types of diabetes, respectively (P for interaction < 0.0001). The prevalence of erectile dysfunction was highest in studies using the Sexual Health Inventory for Men (82.2%, 17 studies, P for interaction < 0.0001). Studies with a higher percentage of people with hypertension moderated our results (beta = 0.03; 95% CI, 0.008 to 0.040; P = 0.003; R2 = 0.00). Compared to healthy controls (n = 5385) men with diabetes (n = 863) were at increased odds of having erectile dysfunction (OR 3.62; 95% CI, 2.53 to 5.16; P < 0.0001; I2 = 67%, k = 8). Erectile dysfunction is common in diabetes, affecting more than half of men with the condition and with a prevalence odds of approximately 3.5 times more than controls. Our findings suggest that screening and appropriate intervention for men with erectile dysfunction is warranted.

INTRODUCTION

The WHO Global Report on Diabetes states that the number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014, and that the global prevalence among adults has risen from 4.7% to 8.5% over the same period. The main and most considered complications of diabetes weigh on the heart, blood vessels, eyes, kidneys and nerves, and diabetes has been associated recently with specific cancers, physical and cognitive disability, and depression [1,2].

Increasing attention is focusing on erectile dysfunction in men with diabetes due to its multifactorial pathophysiology and the concurrence of the same components as vasculopathy, neuropathy and depression [3]. Erectile dysfunction is defined as the inability to achieve and/or maintain an erection sufficient to permit satisfactory sexual intercourse [3]. Although erectile dysfunction is considered an age- related disease, affecting 20% of men aged > 40 years, it can be present across all the life-span from adolescence, especially when risk factors such as diabetes, metabolic syndrome or cardiovascular diseases coexist [4]. Diabetes is considered the main risk factor for the development of erectile dysfunction and since the 1970s the association between diabetes and the development of erectile dysfunction has been documented both in animal models and humans [5].

Previous studies have suggested that erectile dysfunction is more prevalent in men with diabetes compared with healthy men [6], and increasing evidence emphasises this correlation [7,8]. However, the exact prevalence of this condition and the role of other potential moderators remain unclear in men with diabetes. Several narrative reviews have considered the prevalence of erectile dysfunction in diabetes and the majority agree that the incidence of erectile dysfunction in men with diabetes is two- to three-fold higher than in the general population. It is estimated that erectile dysfunction affects up to 75% of all men with diabetes, it is age correlated and occurs at a younger age in men with diabetes. Although these studies have significantly advanced our knowledge, there appears to be no meta-analysis of the synthesized data which would help provide the most reliable estimates of erectile dysfunction prevalence in men with diabetes compared with controls, and help us understand the moderating factors that might influence the relationship. Given that, for example,

erectile dysfunction is associated with higher cardiovascular risk in men with diabetes, such analysis could be highly beneficial.

Given this, the aim of this study was to conduct a meta- analysis of existing data to estimate prevalence of erectile dysfunction in diabetes and explore potential moderators.

METHODS

This systematic review adhered to the PRISMA [9] and MOOSE [10] statements and followed an a priori defined, but unpublished protocol available upon request.

Data sources and literature search strategy

Two investigators independently conducted a literature search using PubMed, EMBASE and SCOPUS from 1980 to 1 November 2016. In PubMed and other databases, the search strategy was (diabet*) AND (erectile dysfunction OR erectile function OR sexual dysfunction OR sexual function) AND (prevalence or odds or risk). Conference abstracts and the reference lists of included articles were hand-searched to identify and potential additional relevant articles. Any inconsistencies were resolved by consensus with a third author.

Study selection

Studies were included in the meta-analysis if they: (1) reported the prevalence of erectile dysfunction; (2) used a validated instrument for the diagnosis of erectile dysfunction, such as the international index of erectile function (IIEF) [11] or the Sexual Health Inventory for Men (SHIM) [12]; (3) included people with a validated diagnosis of diabetes (e.g. with the criteria suggested by the American Diabetes Association [13]; (4) included male participants. Also abstracts, if suitable with sufficient and quality data, were included.

Studies were excluded if: (1) were not conducted in humans; (2) the sample consisted entirely of participants with both diabetes and erectile dysfunction (i.e. prevalence = 100% and a biased sample); (3) included only females.

Data extraction

Two independent investigators extracted key data from the included articles in a standardized Excel sheet and a third validated data extraction. For each article, we extracted data regarding authors, year of publication, country, setting, demographics (i.e. sample size, mean age), type of diabetes, diagnostic criteria used for erectile dysfunction, duration of diabetes, percentage of participants having the most common complications of diabetes (neuropathy, retinopathy, cardio- vascular disease, kidney failure) and some known risk factors for erectile dysfunction (smoking, obesity, hypertension).

When some information was missing, first and/or corresponding authors of the original article were contacted at least twice in a month to obtain the variables of interest. For 23 eligible papers, we were unable to acquire the full texts and the authors did not respond to our requests. However, these abstracts contained sufficient data for meta-analysis and consequently they were included and treated as conference abstracts.

Outcomes

The main outcome of interest was the prevalence of erectile dysfunction in men with diabetes reported in the original paper both as percentage or as number of erectile dysfunction/number of men with diabetes. Where available, data regarding the prevalence of erectile dysfunction in healthy controls with no diabetes was also extracted.

Assessment of study quality

Two authors assessed the quality of the studies included taking in account the following factors which after discussion we considered to represent important study features with respect to the current topic: (1) clear diagnostic criteria for diabetes; (2) clear diagnostic criteria for erectile dysfunction; (3) reporting the prevalence of at least one diabetic complication; and (4) reporting data on the duration of diabetes.

Data synthesis and statistical analysis

All analyses were performed using Comprehensive Meta- Analysis (CMA) 3 (http://www.meta-analysis.com).

In the primary analysis, we calculated the prevalence of erectile dysfunction in diabetes with its 95% confidence intervals (% CIs) applying a random-effect model due to anticipated heterogeneity [14]. Prevalence was reported as a percentage. In secondary analysis, the prevalence of erectile dysfunction in men with diabetes vs. controls was compared using odds ratios (ORs) with their 95% CIs.

Heterogeneity across studies was assessed by the I2 metric and Cochran's Q chi-square statistics with a value ≥ 50% for the first and $P < 0.05$ indicating the presence of significant heterogeneity [15]. In case of high heterogeneity, sensitivity and meta-regression analyses were run to identify possible moderators of this heterogeneity. In sensitivity analyses, we stratified our results by continent (Africa, Asia, Europe, North and South America, Oceania, multicontinent), type of diabetes (Type 1, 2, and studies including both forms, or not declared), setting (community, outpatients, not declared), type of article (original article or conference abstract), diagnostic tools for the presence of erectile dysfunction (IIEF-5, SHIM or other tools) and mean age (divided into 18–60 years and ≥ 60 years or not declared). In meta-regression analysis, we analysed some potential moderators as

continuous variables in the sample as whole, namely: duration of diabetes (years), study percentage of people with neuropathy, retinopathy, cardio- vascular disease, kidney failure, hypertension, mean BMI, and percentage of actual smokers.

Potential publication bias was assessed by visually inspecting funnel plots and using the Egger bias test [16]. Then, to account for any publication bias, we used the trim-and-fill method, based on the assumption that the effect sizes of all the studies are normally distributed around the centre of a funnel plot; in the event of asymmetries, it adjusts for the potential effect of unpublished (imputed) studies [17]. Finally, we calculated the fail-safe number of negative studies that would be required to nullify each of our comparative analyses.

For all analyses, $P < 0.05$ was considered statistically significant.

RESULTS

Search results

The search yielded 3,747 non-duplicated articles. After excluding 3,441 articles based on title/abstract review, 306 articles were retrieved for full text review and 145 studies were finally included (**Figure 1**).

Study and participants' characteristics

Full descriptive details of the included studies are reported in Table S1.

Altogether, this meta-analysis included 145 studies (for the references see Table S2) and 88 577 male participants with diabetes, with a mean age of 55.8 ` 7.9 years (range: 23.4– 71.7 years).

A majority of the studies was conducted in Asia (61 studies, 41.8%), followed by Europe (48, 32.9%), North America (17, 11.6%) and Africa (15, 10.3%). All except 14 studies were performed among outpatients. Finally, most studies included people having a diagnosis of Type 2 diabetes only (70 studies, n = 44 488 participants), followed by studies that did not declare which type of diabetes was included (45 studies, n = 18,424), both Type 1andType2(18studies,n=20061)andType1 only (12 studies, n = 5604). The presence of erectile dysfunction was diagnosed mainly through the IIEF-5 (n = 90 studies).

The most common source of bias was the absence of data regarding diabetic complications, because this information was present in only 32 (22.1%) of the included studies.

Prevalence of erectile dysfunction in diabetes

As shown in Table 1, the overall prevalence of erectile dysfunction in diabetes was 59.1% (95% CI, 55.5 to 62.7). This finding was characterized by a very high hetero- geneity (I2 = 99%) and by a publication bias (Egger's test = 3.71 ` 1.32, P = 0.006). After conducting the trim and fill analysis, 20

studies missing on the left were adjusted, with an estimated prevalence of erectile dysfunction in diabetes of 52.5% (95% CI, 48.8 to 56.2) (Table 1).

Factors affecting erectile dysfunction prevalence

As shown in Table 1, the prevalence of erectile dysfunction was significantly different across countries ($P < 0.0001$) and highest in studies conducted in South America (prevalence 74.6%; one study), Oceania (prevalence 74.4%; one study) and Africa (prevalence 71.3%; 15 studies) and lowest amongst North American studies (prevalence 34.5%; 17 studies).

The prevalence of erectile dysfunction was significantly higher ($P < 0.0001$) in men with Type 2 diabetes (prevalence 66.3%; 70 studies) compared with Type 1 diabetes (prevalence 37.5%; 12 studies). Moreover, the prevalence of ED was significantly higher in the studies using the SHIM for assessing erectile dysfunction (prevalence 82.2%; 17 studies) and amongst those with a mean age > 60 years (prevalence 66.7%; 23 studies) (Table 1). Conversely, the setting in which the study was performed ($P = 0.37$) and the type of article ($P = 0.79$) did not significantly moderate our findings.

Meta-regression analysis

Because our main outcome was characterized by a high heterogeneity ($I2 = 99\%$) and the stratification shown in Table 1 was not able to explain any heterogeneity, we assessed if other factors could explain this heterogeneity. As shown in Table 2 among some potential possible moderators (including the most common chronic complication of diabetes, duration of diabetes and risk factors for erectile dysfunction such as smoking) only higher percentage of men with hypertension moderated our results (beta = 0.03; 95% CI, 0.008 to 0.040; $P = 0.003$) without, however, explaining any heterogeneity ($R^2 = 0.00$).

Comparison with the controls

Eight studies reported the prevalence of erectile dysfunction in men with diabetes (n = 863) vs. healthy controls (n = 5385). As shown in Fig. 2, the prevalence of erectile dysfunction in men with diabetes vs. controls was almost doubled (51.6% vs. 25.5%), leading to an overall OR of 3.62 (95% CI, 2.53 to 5.16; P < 0.0001; I2 = 67%). No evidence of publication bias was present for this outcome (Egger's test 2.21 ` 1.44; P = 0.17) and the fail-safe number was 311.

DISCUSSION

This is the first meta-analysis to assess the prevalence of erectile dysfunction in diabetes, synthesizing a large volume of international literature (including 145 studies and 88 577 male participants with diabetes). We showed an overall prevalence of erectile dysfunction of 59.1% in men with diabetes (52.5% if adjusted for publication bias). This condition was significantly higher in those with Type 2 diabetes compared with Type 1 diabetes, and in older participants. Men with diabetes tend to develop erectile dysfunction 10–15 years earlier than those without diabetes. In fact, erectile dysfunction is the third most frequent complication of diabetes that affects the quality of life and it is often indicative of underlying vasculopathy representing a predictor of more serious cardiovascular disorders [18]. Because the prevalence of diabetes is rising in high, middle, and low income countries, our work aimed to give an overall estimate of erectile dysfunction in diabetes across several continents [19].

One of our main results is that the odds of erectile dysfunction in men with diabetes is more than three times higher relative to controls, with an overall OR = 3.62 (95% CI, 2.53 to 5.16; $P < 0.0001$; $I2 = 67\%$), and higher among men with a mean age > 60 years. These findings are consistent with the Massachusetts Male Aging Study in which men with diabetes showed a threefold probability of having erectile dysfunction compared with men without diabetes, and the age-adjusted risk of erectile dysfunction was doubled in men with diabetes compared with those without [20]. Notably, the global ageing of the world population as well as the dramatically increasing prevalence of diabetes mellitus may partially explain the worldwide prevalence of erectile dysfunction, which has been estimated to 322 million cases by the year 2025 [21].

A comprehensive review including high-quality studies undertaken by Kamenov and colleagues [22] is consistent with our findings that advanced age and Type 2 diabetes are associated with an increased risk of erectile dysfunction. In addition, as shown in our analyses, the prevalence of erectile dysfunction in men with Type 2 diabetes is higher compared with those with Type 1

diabetes. Indeed, many men may already have erectile dysfunction at the diagnosis of Type 2 diabetes. Erectile dysfunction has been proven to be the first sign of diabetes, diagnosed later in 12–30% of men [23]. Recently, Maseroli et al., found in a sample of 499 men (mean age 58.8 ` 8.8 years) with new or recently diagnosed Type 2 diabetes mellitus: mild erectile dysfunction in 19.4%, mild-to-moderate in 15.4%, moderate in 10.4%, and severe in 21.6% of participants.

Several cross-sectional and longitudinal studies showed an association between erectile dysfunction and most of the classical cardiovascular risk factors, including smoking [24], diabetes [25], hypertension [26], hyperlipidaemia, metabolic syndrome [27], as well as depression. Surprisingly, in our meta- regression analysis, hypertension only was associated with the diabetes-related erectile dysfunction (P = 0.003). However, in a large survey of 7689 men with diabetes and/or hypertension, erectile dysfunction according to the IIEF-5 score was present in 67% of those with hypertension alone, in 71% with diabetes alone, and in 77% of men with both diseases [26].

There is increasing evidence of a direct link between erectile dysfunction and cardiovascular disease. Erectile dysfunction is a marker of early atherosclerosis and it is considered not only as a part of the quality of life, but also as an independent predictor of cardiovascular events and all- cause mortality. Moreover, in men with erectile dysfunction, the prevalence of undiagnosed diabetes is higher than in the general population. Thus, erectile dysfunction should be considered a marker symptom for diabetes and men with erectile dysfunction should be screened for diabetes [28].

Several identified factors contribute to the complex pathogenesis of diabetes-related erectile dysfunction including diabetic neuropathy, micro- and macrovascular arterial disease (oxidative stress, endothelial dysfunction, dyslipidaemia, arterial hypertension, etc.), hypogonadism, psy-chogenic components and drug side effects. The diagnostic process is based on the results of standardized questionnaires, vascular urologic and neurological investigations. One of the most used and practical questionnaires that is administered is the IIEF-5, with a score of ≤ 21 indicating the presence of erectile dysfunction [29]. However, depending on the age, duration and type of diabetes

mellitus, and the used diagnostic criteria, epidemiological data about diabetes- related erectile dysfunction vary significantly between different studies [18]. Our analysis shows large differences in the reported prevalence of erectile dysfunction from approximately 35% to 80% among men with diabetes, which might be due to differences in methodology and population characteristics. Advancing age, duration of diabetes, poor glycaemic control, hypertension, hyperlipidaemia, sedentary lifestyle, smoking and the presence of other diabetic complications have been shown to be associated with diabetes- related erectile dysfunction in cross-sectional studies [18].

Regarding sexual activity and the psychological impact of erectile dysfunction in men with diabetes mellitus, significant and positive associations have been found between depressive symptoms and erectile dysfunction. In addition, erectile dysfunction contributes strongly to poorer quality of life in men with diabetes mellitus. Therefore, early detection of erectile dysfunction is essential to improve the psychological health and men's quality of life. In this way, the management of erectile dysfunction in men with diabetes should involve a multidisciplinary approach in which psychosexual counselling and specialist urologist advice is required in addition to the skills and expertise of the specialist in metabolic diseases and to the traditional pharmacological therapy [30].

Although our data offer novel insight into the extent of erectile dysfunction among men with diabetes, some limitations need to be considered. First, is the difficulty in providing erectile dysfunction prevalence by categories because of incomplete data available in published studies. Second, most information refers to the total population with diabetes and few studies have presented data separately for those with Type 1 and Type 2 diabetes. Third, the analysis of the others risk factors contributing to the diabetes-related erectile dysfunction was limited because of the small number of primary studies that provide complete clinical and biological features of the participants. For example, the use of antidepressant medication, an important contributor of erectile dysfunction in men with diabetes, was not analysable as potential moderator of our findings.

In conclusion, our study provides worldwide data on the prevalence of and risks factors for erectile dysfunction in diabetes. The relationship of erectile dysfunction with certain risk factors, such as age or cardiovascular risk factors (arterial hypertension), are well known and our study corroborates these associations. Future prospective and longitudinal studies in both but separately population with Type 1 and Type 2 diabetes, are needed to characterize others risk factors such as duration of disease or smoking which are involving in the development of erectile dysfunction. Furthermore, men with erectile dysfunction are at an increased risk for cardiovascular morbidity and/or mortality as well as for all-cause death. Thus, clinicians should have in mind that screening of erectile dysfunction in men with diabetes is a part of the assessment of their cardiovascular risk.

Funding sources

None.

Competing interests

None declared.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Descriptive characteristics of the included studies. Table S2. References of the studies included in the meta- analysis. Table 1 Meta-analysis results of prevalence of erectile dysfunction in men with diabetes

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Table 1-Meta-analysis results of prevalence of erectile dysfunction in people with diabetes

Outcome	Number of study estimates	Number of participants	Prevalence (%)	95% CI		Between group p value	I^2 (%)
ED (main analysis)	**145**	**88,577**	**59.1**	**55.5**	**62.7**	**-**	**99**
Continent						*<0.0001*	
Africa	*15*	*2,055*	***71.3***	*63.2*	*78.2*		*92*
Asia	*61*	*36,032*	***67.0***	*60.4*	*73.1*		*99*
Europe	*48*	*3,7300*	***53.6***	*48.7*	*58.3*		*99*
North America	*17*	*10,509*	***34.5***	*26.1*	*44.0*		*99*
South America	*1*	*114*	***74.6***	*65.8*	*81.7*		*-*
Oceania	*1*	*788*	***74.4***	*71.2*	*77.3*		*-*
Multi-continent	*2*	*1,779*	***39.7***	*37.5*	*42.0*		*0*
Type of diabetes						*<0.0001*	
Type 1	*12*	*5,604*	***37.5***	*30.8*	*44.6*		*96*
Type 2	*70*	*44,488*	***66.3***	*61.5*	*70.9*		*99*
Both	*18*	*20,061*	***57.7***	*47.6*	*67.2*		*99*
Not declared	*45*	*18,424*	***53.9***	*45.6*	*62.0*		*99*
Setting						*0.37*	
Community	9	*3,163*	***66.9***	*52.5*	*78.7*		*98*
Outpatients	131	*84,225*	***58.8***	*54.9*	*62.7*		*99*
Not declared	5	*1,189*	***52.8***	*39.0*	*66.2*		*94*
Type of article						*0.79*	
Original article	114	*72,371*	***59.4***	*55.2*	*63.5*		*99*
Conference abstract	31	*16,206*	***58.2***	*50.2*	*65.8*		*99*
Diagnosis of ED						*<0.0001*	
IIEF-5	90	*41,025*	***60.7***	*55.9*	*65.3*		*99*

	SHIM	17	*7,093*	***82.2***	*74.8*	*87.7*	*99*
	Other	38	*40,459*	***42.3***	*37.1*	*47.7*	*99*
Mean age						*0.03*	
	18-60 years	55	*21,220*	***62.2***	*56.1*	*67.9*	*99*
	≥60 years	*23*	*10,432*	***66.7***	*57.5*	*74.8*	*99*
	Not declared	67	*56,925*	***53.8***	*48.3*	*59.3*	*99*

CI, confidence interval; IIEF-5, International Index of Erectile Function; SHIM, Sexual Health Inventory for Men. Values in bold, prevalence in all groups and by strata.

Table 2. Meta regression of continuous moderators of erectile dysfunction presence in people with diabetes.

Moderator*	Number of comparisons	β	95% CI		P-value	R^2
Duration of diabetes (years)	46	-0.02	-0.05	0.00	0.08	0.06
Percentage of people with neuropathy	32	0.02	-0.00	0.04	0.08	0.00
Percentage of people with retinopathy	30	0.004	-0.01	0.02	0.66	0.00
Percentage of people with cardiovascular disease	38	-0.005	-0.03	0.01	0.56	0.00
Percentage of people with kidney failure	22	0.02	-0.005	0.05	0.11	0.05
Mean body mass index	31	0.06	-0.06	0.18	0.30	0.00
Percentage of actual smokers	49	-0.007	-0.03	0.007	0.33	0.00
Percentage of people with hypertension	**50**	**0.03**	**0.008**	**0.04**	**0.003**	**0.00**

CI, confidence interval. Values in bold are significant, $P < 0.05$.

Figure 1. PRISMA flow-chart

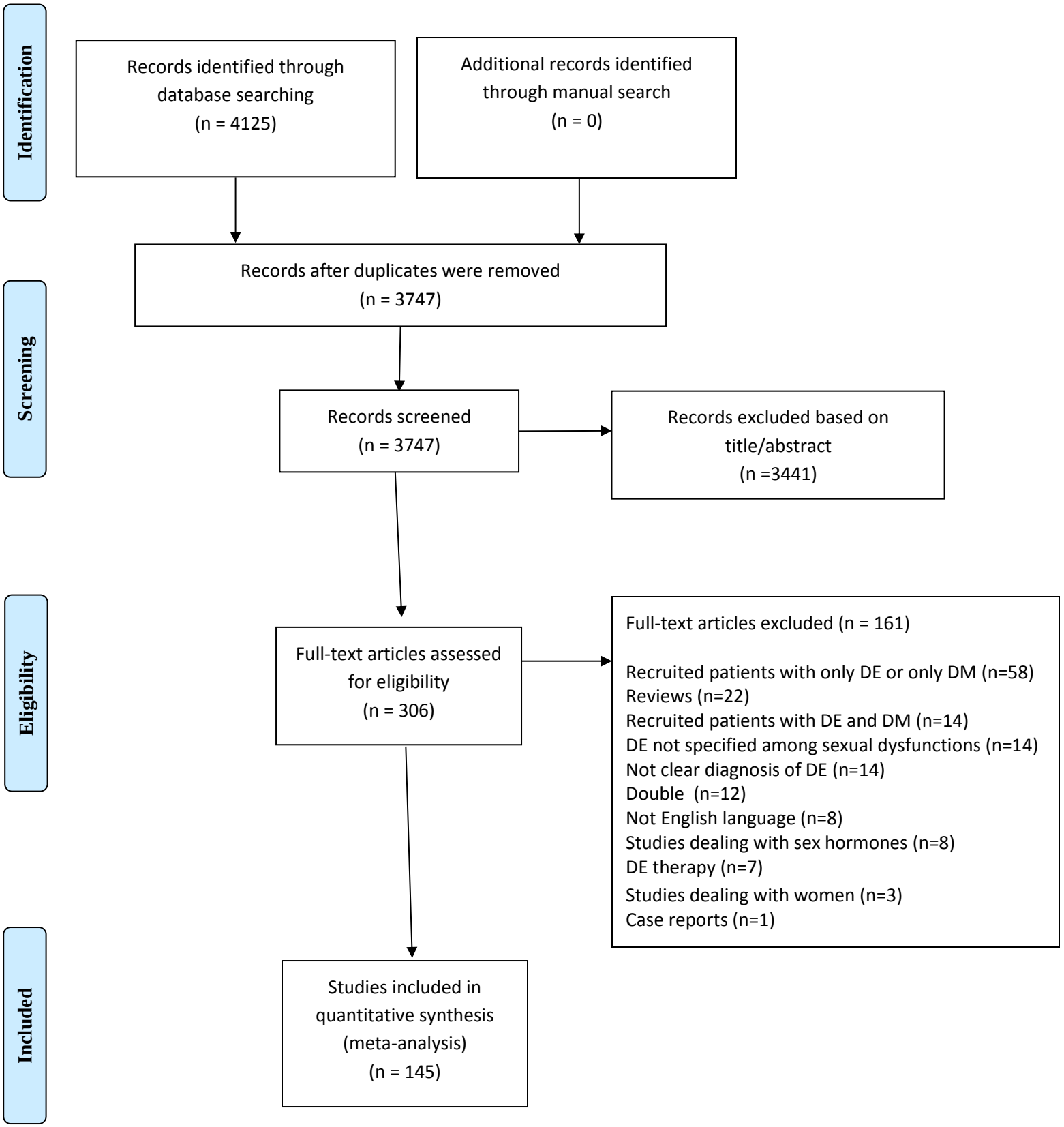
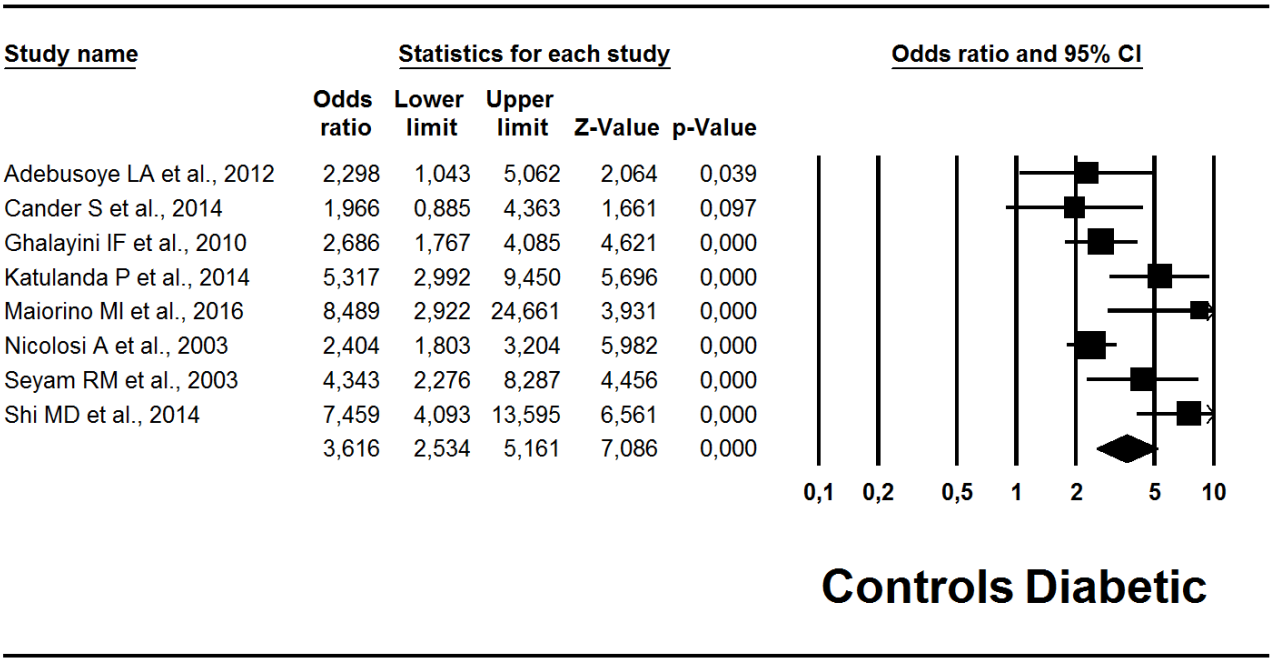


Figure 2. Prevalence of erectile dysfunction in diabetic and control subjects.



Supplementary Table 1. Descriptive characteristics of the studies included.

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Ab Rahman AA et al., 2011	544	Malaysia	Not available	Outpatients	IIEF-5
Adebusoye LA et al., 2012	33	Nigeria	Not available	Outpatients	IIEF-5
Adegite A et al., 2009	66	Nigeria	Type 2	Outpatients	IIEF-5
Ahmad S et al., 2010	281	Malaysia	Not available	Outpatients	IIEF-5
Ahmed A et al., 2011	333	Quatar	Not available	Outpatients	SHIM
Ahmed I et al., 2013	217	Pakistan	Type 2	Outpatients	SHIM
Ahn TY et al., 2007	127	Korea	Not available	Community	IIEF-5
Al Naimi A et al., 2014	209	Quatar	Not available	Outpatients	IIEF-5
Al-Hunayan A et al., 2007	323	Kuwait	Type 2	Outpatients	IIEF-5
AlMogbel TA., 2014	376	Saudi Arabia	Type 2	Outpatients	IIEF-5
Al-Turki YA., 2007	186	Saudi Arabia	Both	Outpatients	Other
Ashok Shenoy K et al., 2012	50	India	Type 2	Outpatients	Other
Awad H et al., 2010	100	Egypt	Type 2	Outpatients	IIEF-5
Bacon CG et al., 2002	2108	USA	Both	Outpatients	Other
Batty GD et al., 2010	6304	United Kingdom	Type 2	Outpatients	Other
Berrada S et al., 2003	34	Marocco	Not available	Community	Other
Bjerggaard M et al., 2015	481	Denmark	Not available	Outpatients	IIEF-5
Blans MCA	90	Netherlands	Both	Outpatients	IIEF-5
Blumentals WA et al., 2003	3160	United Kingdom	Not available	Outpatients	Other
Boyd MJ et al., 2009	180	United Kingdom	Type 2	Outpatients	Other
Brooke JC et al., 2011	356	United Kingdom	Not available	Not available	IIEF-5
Cander S et al., 2014	68	Turkey	Type 2	Outpatients	IIEF-5
Caretta N et al., 2016	92	Italy	Type 2	Outpatients	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Cavan DA et al., 1987	292	Scotland	Not available	Outpatients	Other
Chakraborty K et al., 2013	84	India	Not available	Outpatients	IIEF-5
Chaudhary RK et al., 2016	175	China	Type 2	Outpatients	IIEF-5
Chew SK et al., 2013	324	Singapore	Type 2	Outpatients	Other
Chew SKH et al., 2013	289	Singapore	Type 2	Outpatients	Other
Cho NH et al., 2006	1312	Korea	Type 2	Outpatients	IIEF-5
Chuang YC et al. 2012	455	China	Type 2	Outpatients	SHIM
Cleveringa FGW et al., 2009	1611	Netherlands	Type 2	Outpatients	Other
Corona G et al., 2014	1503	Italy	Type 2	Outpatients	IIEF-5
Dan A et al., 2014	113	India	Both	Outpatients	IIEF-5
De Berardis G et al., 2003	1460	Italy	Type 2	Outpatients	Other
De Berardis G et al., 2007	670	Italy	Type 2	Outpatients	Other
Derosa G et al., 2012	88	Italy	Type 2	Outpatients	IIEF-5
Derosa G et al., 2015	206	Italy	Type 2	Outpatients	IIEF-5
Eardley I et al., 2007	1556	Multicountry	Not available	Community	Other
El Saghier EOA et al., 2015	70	Egypt	Type 2	Outpatients	IIEF-5
Elbendary MA et al., 2009	38	Egypt	Not available	Outpatients	IIEF-5
Fedele D et al., 2000	9756	Italy	Both	Outpatients	Other
Feldman HA et al., 1994	120	USA	Not available	Outpatients	IIEF-5
Fukui M et al., 2011	197	Japan	Type 2	Outpatients	IIEF-5
Furukawa S et al. 2016	332	Japan	Type 2	Outpatients	SHIM
Furukawa S et al., 2016	340	Japan	Type 2	Outpatients	SHIM
Garcia-Malpartida K et al., 2011	154	Spain	Type 2	Outpatients	IIEF-5
Gazzaruso C et al., 2004	260	Italy	Type 2	Outpatients	IIEF-5
Gazzaruso C et al., 2011	293	Italy	Type 2	Outpatients	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Georgescu O et al., 2010	292	Romania	Not available	Outpatients	IIEF-5
Georgescu O et al., 2013	292	Romania	Both	Outpatients	IIEF-5
Ghalayini IF et al., 2010	118	Jordan	Not available	Community	IIEF-5
Ghazi S et al., 2012	391	Egypt	Type 2	Outpatients	IIEF-5
Ghenciu V et al., 2012	45	Moldavia	Type 2	Not available	Other
Giorda CB et al., 2013	1503	Italy	Type 2	Outpatients	Other
Giugliano F et al., 2010	555	Italy	Type 2	Outpatients	IIEF-5
Giuliano FA et al., 2004	2377	France	Both	Outpatients	IIEF-5
Goyal A et al., 2013	348	India	Not available	Outpatients	IIEF-5
Habibi A et al., 2011	171	Iram	Type 2	Outpatients	IIEF-5
Habibi A, 2010	171	Iram	Not available	Outpatients	IIEF-5
Hackett G et al., 2013	190	United Kingdom	Type 2	Outpatients	IIEF-5
Hackett GI et al., 2009	415	United Kingdom	Type 2	Outpatients	SHIM
Hamilton EJ et al., 2016	788	Australia	Type 2	Community	SHIM
Hassan A et al., 2014	429	Saudi Arabia	Type 2	Outpatients	ADAM
Henis O et al., 2011	102	Israel	Type 2	Outpatients	SHIM
Hermans MP et al., 2009	221	Belgium	Type 2	Outpatients	IIEF-5
Hopcan MB et al., 2010	372	Turkey	Not available	Outpatients	IIEF-5
Hotaling J et al., 2010	528	USA	Not available	Outpatients	IIEF-5
Hotaling JM et al., 2012	528	USA	Type 1	Outpatients	IIEF-5
Idung AU et al., 2012	86	Nigeria	Not available	Outpatients	IIEF-5
Jacobson AM et al., 2013	664	USA	Type 1	Outpatients	IIEF-5
Jacobson AM et al., 2015	644	USA	Type 1	Outpatients	IIEF-5
Jamieson F et al., 2008	142	United Kingdom	Type 1	Outpatients	Other
Jayanthy R et al., 2014	60	India	Not available	Not available	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Jayawardena RM et al., 2013	536	Sri Lanka	Not available	Outpatients	IIEF-5
Jiann BP et al., 2009	844	Taiwan	Type 2	Outpatients	SHIM
Justo D et al., 2010	103	Israel	Not available	Outpatients	SHIM
Kalter-Leibovici O et al., 2005	1040	Israel	Both	Outpatients	IIEF-5
Kamenov ZA et al., 2007	150	Bulgaria	Both	Outpatients	Other
Kapoor D et al., 2007	198	United Kingdom	Type 2	Outpatients	ADAM
Katulanda P et al., 2014	125	Sri Lanka	Not available	Outpatients	Other
Kempa T et al., 2015	150	South Africa	Both	Community	SHIM
Khatib FA et al., 2006	988	Jordan	Not available	Outpatients	IIEF-5
Klein R et al., 1996	359	USA	Not available	Outpatients	Other
La Vignera S et al., 2009	110	Italy	Not available	Outpatients	IIEF-5
Liu HY et al. 2016	785	China	Type 2	Outpatients	SHIM
Liu RT et al., 2012	453	China	Type 2	Outpatients	SHIM
Lo WH et al., 2014	603	China	Type 2	Outpatients	IIEF-5
Lu CC et al., 2009	792	Taiwan	Type 2	Outpatients	SHIM
Ma RCW et al., 2008	2306	China	Type 2	Outpatients	Other
Maiorino MI et al., 2015	118	Italy	Type 1	Outpatients	IIEF-5
Maiorino MI et al., 2016	151	Italy	Type 1	Outpatients	IIEF-5
Majzoub A et al., 2015	1052	Quatar	Not available	Outpatients	IIEF-5
Malavige LS et al., 2008	253	Sri Lanka	Type 2	Outpatients	IIEF-5
Malavige LS et al., 2015	232	United Kingdom	Not available	Outpatients	IIEF-5
Malavige LS., 2010	232	United Kingdom	Not available	Outpatients	IIEF-5
Mansour A.A.	2414	Iraq	Type 2	Outpatients	Other
McCulloch DK et al., 1980	541	Germany	Not available	Outpatients	Other
Meena BL et al., 2009	50	India	Type 2	Outpatients	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Mehtiyev TV, 2015	261	Azerbaijan	Type 2	Outpatients	IIEF-5
Meo SA et al., 2011	2250	Saudi Arabia	Not available	Outpatients	IIEF-5
Miccoli R et al., 1985	77	Italy	Not available	Outpatients	Other
Miccoli R et al., 1987	128	USA	Not available	Outpatients	Other
Mofid A et al., 2009	700	Iran	Both	Outpatients	Other
Mota M et al., 2003	310	Romania	Not available	Outpatients	SHIM
Mutagaywa RK et al., 2014	312	Tanzania	Both	Outpatients	IIEF-5
Nakanishi S et al., 2004	112	Japan	Type 2	Outpatients	Other
Nam SM et al., 2010	300	Korea	Type 2	Outpatients	IIEF-5
Nasser J et al., 2015	415	Bahrain	Type 2	Outpatients	IIEF-5
Nicolosi A et al., 2003	223	Multicountry	Not available	Community	Other
Olarinoye JK et al., 2006	77	Nigeria	Type 2	Outpatients	IIEF-5
Owiredu WKBA et al., 2011	274	Ghana	Not available	Outpatients	GRISS
Penson DF et al., 2009	571	USA	Type 1	Outpatients	IIEF-5
Pop-Busui R et al., 2013	644	USA	Type 1	Outpatients	IIEF-5
Pop-Busui R et al., 2014	635	USA	Type 1	Not available	IIEF-5
Pop-Busui R et al., 2015	635	USA	Type 1	Outpatients	IIEF-5
Rombopoulos G et al., 2009	400	Greece	Not available	Outpatients	IIEF-5
Rosen RC et al., 2009	373	USA	Type 2	Outpatients	IIEF-5
Rozhivanov RV et al., 2006	611	Bulgaria	Both	Outpatients	Other
Rutte A et al., 2015	108	Netherlands	Type 2	Outpatients	IIEF-5
Rutte A et al., 2015	154	Netherlands	Type 2	Outpatients	BSSC-M
Sampanis C et al., 2012	93	Greece	Type 2	Not available	IIEF-5
Schaan BD et al., 2013	114	Brazil	Type 2	Outpatients	IIEF-5
Selim S et al., 2015	3790	Bangladesh	Type 2	Outpatients	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Seyam RM et al., 2003	40	Egypt	Not available	Community	Other
Seyoum B., 1998	292	Ethiopia	Both	Outpatients	Other
Shabsigh R et al., 2010	234	USA	Not available	Outpatients	IIEF-5
Shankar A et al., 2013	582	India	Type 2	Outpatients	SHIM
Shi MD et al., 2014	105	Taiwan	Type 2	Outpatients	IIEF-5
Song HJ et al., 2013	124	Korea	Type 2	Outpatients	IIEF-5
Sonomtseren S et al., 2009	146	Mongolia	Type 2	Outpatients	IIEF-5
Taloyan M et al., 2012	190	Sweden	Type 2	Outpatients	Other
Tisdall AR et al., 2009	70	Ireland	Not available	Outpatients	IIEF-5
Turek SJ et al., 2013	301	USA	Type 1	Outpatients	IIEF-5
Vaswani A.S et al., 2011	390	Pakistan	Not available	Outpatients	IIEF-5
Viswanathan V et al., 2009	423	India	Type 2	Outpatients	IIEF-5
Wang CC et al., 2010	226	Taiwan	Type 2	Outpatients	IIEF-5
Wang F et al., 2013	1466	Canada	Both	Outpatients	Other
Webb EM et al., 2015	92	South Africa	Both	Outpatients	SHIM
Wessells H et al., 2011	571	USA	Type 1	Outpatients	IIEF-5
Wu C et al., 2012	127	China	Not available	Community	IIEF-5
Yamasaki H et al., 2004	82	Japan	Type 2	Outpatients	IIEF-5
Yang G et al., 2010	5477	China	Type 2	Outpatients	IIEF-5
Yildiz H et al., 2015	127	Turkey	Both	Outpatients	IIEF-5
Yu LW et al., 2010	313	China	Type 2	Outpatients	IIEF-5
Ziaei-Rad M et al., 2010	199	Iran	Both	Outpatients	IIEF-5

Author, year	Number of participants	Country	Type of diabetes	Setting	Diagnosis ED
Total	**88,577**		**Type 1: 12; type 2: 70; both: 18; not declared: 45**	**Outpatients: 131; community: 9; not declared: 5**	**IIEF-5: 90; SHIM: 17; others: 38**

Supplementary Table 2. References of the studies included in the meta-analysis.

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