The global prevalence of Erectile Dysfunction: a review.

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Keywords: Erectile Dysfunction (ED), cardiovascular disease (CVD), benign prostatic hyperplasia (BPH), International Index of Erectile Function (IIEF), Massachusetts Male Ageing Study (MMAS)

Conflict of interests: None declared.

Word count: 230 (abstract) and 3775 (main text)

Abstract

Aims: the aim of this review was to evaluate the global prevalence of erectile dysfunction (ED); as well as its association with physiological and pathological ageing by examining the relationship between ED and cardiovascular disease (CVD), benign prostatic hyperplasia (BPH) and dementia. We also aimed to characterise discrepancies caused by use of different ED screening tools.

Methods: Embase and Medline were searched to find population-based studies investigating the prevalence of ED and the association between ED and CVD, BPH and dementia in the general population.

Results: the global prevalence of ED was 3-76.5%. ED was associated with increasing age. Use of the IIEF and MMAS derived questionnaire identified a high prevalence of ED in young men. ED was positively associated with CVD. Men with ED have an increased risk of all-cause mortality OR 95% CI of 1.26 (1.01-1.57) as well as CVD mortality 1.43 (1.00-2.05). Men with ED are 1.33-6.24 times more likely to suffer from BPH compared to men without ED and 1.68 times more likely to develop dementia compared to men without ED.

Conclusion: ED screening tools in population-based studies are a major source of discrepancy. Non-validated questionnaires may be less sensitive than the IIEF and MMAS derived questionnaire. ED constitutes a large burden on society given its high prevalence and impact on quality of life and is also a risk factor for CVD, dementia and all-cause mortality.

Introduction

Erectile dysfunction (ED) represents an increasing health concern causing significant impact on the quality of life of men globally. It is estimated that 322 million men worldwide will be affected by ED by 2025, an increase from 152 million men in 1995[1]. This is also reflected by a growing economic burden. Annual expenditure in the USA on ED was $330 million in 2000, compared to $185 million in 1994 (excluding pharmaceutical costs)[2]. ED also significantly affects the quality of life of men's partners. Partners of men with ED experience lower sexual satisfaction, correlated to the degree of ED in their partner[3].

The physiology of achieving and maintaining an erection involves integration of psychological, hormonal, neurological and vascular pathways. ED is therefore a symptom of a wide range of pathologies. It is often classified into organic (endocrine, neurological, vascular and structural) and psychogenic aetiologies, however both are often heavily interlinked and difficult to discern[4].

The principal risk factor associated with ED is age, and the increasing prevalence of ED is linked to the global ageing population[4]. Other risk factors independently associated with ED include diabetes, cardiovascular disease (CVD), depression and benign prostatic hyperplasia (BPH)[5,6]. The presence of ED has also been found to be a predictor of cardiovascular disease, dementia and all cause mortality[7,8].

The prevalence of ED is difficult to estimate due to the range of definitions of ED used. The National Institutes of Health (NIH) consensus development conference in 1993, defined ED as 'the inability to achieve or maintain an erection sufficient for satisfactory sexual

performance'[53]. The challenge remains however, to measure ED accurately in population-based studies, particularly given the subjective nature of this definition.

The International Index of Erectile Function (IIEF) is a self-administrable questionnaire developed to detect treatment effects in clinical trials[55]. It consists of 15 items categorised by 5 domains of sexual functioning and therefore represents significant respondent burden. An abridged version of the IIEF was therefore, subsequently developed, the IIEF-5 or Sexual Health Inventory for Men (SHIM), with high sensitivity and specificity to detecting ED in clinical trial subjects for sildenafil citrate (Viagra)[56]. Derby et al. sought to develop a simple tool for assessing ED in population-based studies. A single item questionnaire was created and tested against the IIEF in the Massachusetts Male Aging Study (MMAS), a prospective cohort study from Boston, USA. A high negative agreement between the MMAS-derived questionnaire and IIEF was found[34]. The IIEF and MMAS-derived questionnaires are the most common tools used for identifying ED in population based-studies, however other tools still exist and are used frequently. This remains a major limitation to the translatability of study results.

Methods

A search of Embase and Medline was conducted using the search terms: '[impotence or erectile dysfunction] and [general population or community-based or population-based]' to find studies relating to the global prevalence of ED. To review the association between cardiovascular disease and ED the same databases were used to search '[erectile dysfunction or impotence and cardiovascular disease or atherosclerosis and general population or population-based]'. For the association between ED & BPH, search terms used were: '[Erectile dysfunction or Impotence] and [benign prostatic hyperplasia or lower urinary tract symptoms] and [general population or population-based]'. Finally, the association between ED and dementia was reviewed by using search terms '[Impotence or erectile dysfunction] and dementia and [general population or population-based]. Filters used included English language, title and abstract, human and male.

Initial selection of studies was performed independently, based on title, followed by screening of the full text. Articles were excluded if there was no information on ED prevalence or the association between ED and CVD, BPH or dementia, the study population was not representative of the general population, there was no original data or the full text was not available.

Results

Study Selection

The initial search for studies on the global prevalence of ED yielded 1,501 results, after duplicates were removed and filters applied (n=799) 702 records were screened. 635 articles were excluded based on title and 67 full articles were then assessed for eligibility. 26 studies were excluded due to lack of original data (n=8), specific study population (n=3), abstract only (n=3), text not available (n=1), no information on ED prevalence (n=4), unclear methods (n=7).

Initial search results for the association of ED and CVD yielded 220 articles, after removal of duplicates and filters applied (n=117), 103 titles were screened and 43 articles selected for full text review. 26 studies were subsequently excluded due to lack of original data (n=4), abstract only (n=9), text not available (n=2), specific study population (n=4), irrelevant (n=7).

The association between ED and BPH gave 95 results initially. After deduplication and addition of limits, 44 titles remained. 20 relevant articles were chosen by screening titles of which 8 were excluded due to study population (n=2), abstract only (n=2), full text not available (n=1) and no information on the association between ED and BPH (n=4). The search for the association between ED and dementia resulted in 6 articles, after duplicates were removed (n=2), 4 article titles were screened of which only one study was relevant.

Use of Questionnaires

Out of 41 studies extracted, 15 (36.6%) used the IIEF, 10 (24.4%) used the MMAS derived questionnaire and 16 (39.0%) used other tools.

ED Prevalence

Table 1 displays the prevalence of ED assessed by the IIEF, IIEF-5 or IIEF variants. The overall global prevalence was 13.1-71.2% [12-26]. The prevalence by continent was as follows, North America: 20.7%[16], Europe: 16.8-65.4%[21, 22, 25, 26], Oceania: 40.3-42%[12,15], Asia: 13.1-71.2%[13, 17, 18, 20, 23, 24], Africa: 24-58.9%[14,19]. All studies demonstrated a trend of increasing ED prevalence with increasing age [12-15, 17-25]. Young men (<40 years old) had an exceptionally high prevalence of ED[15, 18, 22, 23]. There was no apparent trend in ED severity. Wu et al. compared self-reported ED prevalence to ED as determined by the IIEF-5 and found a lower prevalence of self-reported ED compared to IIEF-5 defined ED (13.1%, and 26.0% respectively) in all age groups [20].

The global prevalence of ED as assessed by the MMAS-derived self-assessment was 15.5-69.2%[27-36] (Table 2). The prevalence of ED by continent was 22.0-57.8%[31,34,36], 15.5-55.2%[28-30, 33, 35], 17.2%[29], 60.69[27], 22.4-69.2%[29, 32], for North America, South America, Europe, Oceania and Asia, respectively. The prevalence of ED increased with increasing age where the study population was over 40 years old[28, 30-33]. 9.1-49.9% of men under 50 years old[30-33] were affected compared to 54.9-94.7% men over 70 years old [31,32]. Martins et al. studied a young (18-40 years) population of men in Brazil and found a higher prevalence of ED amongst 18-25 year olds (35.6%) compared to 26-40 year olds (30.7%)[28]. The prevalence of ED was inversely associated with ED severity, 25.1-36.7%, 8.5-25.0%, 1.3-16.77% had mild, moderate and severe ED, respectively[27, 30, 32-36]. Derby et al. measured ED prevalence using both IIEF and the MMAS self-assessment methods. The overall and moderate-severe prevalence of ED was the same using both methods[34].

The global prevalence of ED as measured by all other questionnaires was 3-76.5%[37-52] (Table 3). The prevalence by continent was 22-46.3%[42, 46, 49], 14%[49], 10-76.5%[37,38,40, 45, 49, 50, 52], 49.4%[47], 8-65%[39, 40, 41, 43, 44, 48], 53.6%[51] for North America, South America, Europe, Oceania, Asia and Africa, respectively. The prevalence of ED increased with increasing age[38, 40-44, 48, 49, 52]. There was no apparent trend in ED severity throughout all age groups [40, 41, 45, 46, 51, 52].

ED and Cardiovascular Disease

Table 4 describes the association between CVD and ED. When compared to men without ED, men with ED were at increased risk of ischaemic heart disease (1.08-1.87)[59, 60, 64], heart failure (5.19-8.00)[64],hypertension (0.89-3.60) [25, 35, 47, 60, 63], dyslipidaemia (1.14-5.48) [47, 59, 60], peripheral vascular disease (0.93-2.37) [60, 64], cerebrovascular accident (1.43-3.30) [47, 60], angina (1.26)[21], metabolic syndrome (1.35-1.52)[68], and diabetes (0.58-8.94) [21, 25, 35, 47, 59, 63]. The risk of CVD was positively associated with severity of ED[35, 64, 68] and increasing age[25]. The prevalence of CVD was higher in persons with ED[49, 61, 62] and this was correlated with ED severity[61, 66, 67, 70]. The incidence of CVD events per 100 person years in men with normal erectile rigidity was 5.1 (95% CI 4.2-6.1) compared to reduced rigidity 10.1 (95% CI 7.4-13.8) and severely reduced rigidity 19.0 (95% CI 11.5-31.5)[70].

Men with ED also had an increased risk of all-cause mortality OR 95% CI 1.26 (1.01-1.57) as well as CVD mortality 1.43 (1.00-2.05)[66]. Only one study found no significant increase in prevalence of DM, HTN, CVD and DLM in persons with ED[28].

ED and Benign Prostatic Hyperplasia

Table 5 summarises our findings on the association between ED and BPH in the general population. Men with ED are 1.33-6.24 times more likely to suffer from BPH compared to

men without ED [17, 22, 30-32, 35, 62, 72, 74, 76]. Prevalence of ED and BPH ranged from 5.2-40% [73, 75] and prevalence was positively associated with increasing age[73]. Risk of BPH and ED was also correlated to BPH severity; men with severe BPH (IPSS ≥20) were 5.86-6.24 times more likely to suffer from ED compared to men with moderate BPH (IPSS 8-19) 1.7-4.41[30-32]. Similarly, prevalence of BPH and ED was associated with ED severity, prevalence of BPH in men without ED was 10% compared to 16%, 16%, 23% and 26% for mild, mild-moderate, moderate and severe ED, respectively[35, 62].

ED and dementia

Only one study was found which investigated the association between ED and dementia in the general population. Yang et al. conducted a longitudinal cohort study of 4,153 ED cases at baseline and 20,765 matched controls randomly selected from the National Health Insurance Research Database of Taiwan. Over the 7 year follow-up period, 2.5% of cases developed dementia compared to 1.5% of controls. Participants with ED were 1.68 times more likely to develop dementia compared to controls (HR 1.68 [95% CI = 1.34–2.10) P < 0.0001][82].

Discussion

The current review identified that the global prevalence of ED was 13.1-71.2%, 15.5-69.2% and 3-76.5% as determined by studies using the IIEF/ IIEF-5, the MMAS-derived questionnaire or other questionnaires, respectively.

Global Prevalence

The range of ED prevalence has been found to vary widely, which may be reflective of differences in study population ages. Martins et al., studied 18-40 year olds in Brazil and found an overall prevalence of 35.0% ED, whereas Moreira et al. studied 40-70 year olds in Brazil as well and found an overall prevalence of 45.9% ED [28, 33]. The variety of definitions and assessment methods of ED undoubtedly also impact the range of ED prevalence. The global prevalence of ED determined by the IIEF/ IIEF-5 and MMAS derived questionnaire are relatively similar (13.1-71.2% and 15.5-69.2%, respectively), in comparison to that determined by studies using other questionnaires (3-76.5%). Pooled results revealed the highest prevalence was found in Europe (10-76.5%), Asia (8-71.2%), Oceania (40.3-60.69%), Africa (24-58.9%), North America (20.7-57.8%) and the lowest prevalence was found in South America (14-55.2%). The cause of the geographical disparities in ED prevalence is likely to be multifactorial. Genetic, environmental and lifestyle factors are likely to be involved. The main risk factors associated with ED include age, comorbidities (diabetes, cardiovascular disease, obesity, prostate cancer and depression and anxiety treatment), lifestyle factors such as heavy alcohol consumption and smoking were also positively associated with ED[16, 18, 19, 21, 27]. Single, separated or divorced men were also at increased risk, as well as men who are unemployed or of low socio-economic status[15, 16]. Furthermore, due to the sensitive nature of the topic, cultural factors affecting perceptions may influence reporting of ED.

ED and Age

Age as a risk factor for ED was universal across all studies. A linear relationship between increasing ED prevalence and increasing age was also seen in all studies, regardless of the

ED assessment method used[12-15, 17-25, 28, 30-33, 38, 41-45, 49, 50, 53]. Physiological ageing processes mediating vascular changes in the penis have been implicated, however cardiovascular comorbidities such as diabetes and hypertension appear to expedite and exacerbate the process[58]. In studies where young men were included in the study population, young men were found to have an exceptionally high prevalence of ED [15, 18, 22, 23, 28]. This was the case for studies using the IIEF, IIEF-5 or MMAS-derived questionnaire as an ED measurement tool, but not those using other questionnaire types [42, 45, 49, 50, 51]. The relatively high prevalence of ED in young men may be due to psychological factors such as anxiety related to sexual inexperience, performance anxiety as well as life stressors related to independence and joining the workforce. Organic causes for erectile dysfunction, however, should be excluded in young men presenting with ED[59].It is likely that the questionnaires used by Lau, Tan, Rosen and Hendrickx (table 3) are not as sensitive as the IIEF, IIEF-5 or MMAS-derived questionnaires at detecting ED in young persons. The questionnaire used by Hendrickx et al., specifically applies to men who are having sexual intercourse, however a proportion of this age group may not yet be engaging in sexual intercourse which could lead to under-reporting ED. The questionnaire used by Rosen et al. also seems tailored to well-educated men who have had previous sexual experience and therefore may not be sensitive to detecting ED in sexually inexperienced and less educated men. Lau et al. simply asked participants to answer 'yes/no' to the question 'do you have erectile difficulties?', young men may be less willing to identify with this question positively compared to their older counterparts, which may lead to under-reporting ED in this age-group.

ED Severity

In studies using the MMAS-derived questionnaire there was an inverse trend between ED prevalence and severity. 25.1-36.7%, 8.5-25.0%, 1.3-16.77% had mild, moderate and severe ED, respectively[27, 30, 32-36]. This trend was not seen in studies using the IIEF/ IIEF-5 or other questionnaires. Firstly, it is difficult to compare severity measured because the IIEF/ IIEF-5 traditionally classifies severity into four categories: mild, mild-moderate, moderate and severe; whereas the MMAS-derived questionnaire uses three categories: mild, moderate and severe. Furthermore, the IIEF/ IIEF-5 severity is calculated on a points-based system for answers chosen by subjects. Conversely, the MMAS-derived questionnaire requires men to classify themselves subjectively as being mild, moderate or severely impotent. Our results show men are more likely to self-report themselves as having mild ED using the MMAS assessment compared to the IIEF/ IIEF-5 or other questionnaires. This may be due to perceptions or embarrassment surrounding admitting to having ED and its severity as part of certain questionnaires; whereas the points-based IIEF/ IIEF-5 system provides a degree 'blinding', as subjects are not aware of how their answers correlate to ED severity. Wu et al., compared the prevalence of ED defined by the IIEF-5 and self-reported by answering yes or no to the question 'do you think you have ED?'. 26.0% were found to have ED using the IIEF-5, compared to 13.1% who self-reported having ED. 18.8% of those who self-reported not having ED were subsequently found to have ED as defined by the IIEF-5 and 26.2% of those who self-reported ED did not class as ED according to the IIEF-5[20]. This is further evidence that self-reported data may a less sensitive measure of ED in population-based studies.

Association between ED and Cardiovascular Disease

There is a wealth of evidence for the association between ED and CVD. This review identified an increased prevalence and incidence of CVD, including HTN, MI, IHD, angina, stroke/ TIA, arteriosclerosis, HLD, HCL, PVD, MS and DM in study participants with ED. One study found no significant association between ED prevalence and diabetes, hypertension, dyslipidaemia or CVD[28]. Martins et al performed a cross-sectional observational study on men aged 18-40 years old. The relatively young population studied, likely explains the lack of significant association found. Both ED and CVD are associated with increasing age and therefore the effects of the association between ED and CVD may not be evident in this age group[28].

The association between hypertension, dyslipidaemia and ED remains controversial. Lahoz et al. found no significant association between ED and HTN, elevated cholesterol or triglycerides[63]. Equally, de Boer et al found the risk of HTN in ED patients to be 0.83 (95% CI 0.56-1.25)[21]. Use of anti-hypertensives and cholesterol-lowering drugs are ubiquitous in the general population, this is likely to be a strong confounding factor when examining HTN and dyslipidaemia. ED may also be a side-effect of these medications, however this is an area which requires further research and is beyond the scope of this review.

ED as a Risk Marker for CVD

The majority of studies reviewed were cross-sectional population studies and therefore the nature of the association between ED and CVD is difficult to interpret. The Massachusetts Male Ageing Study (MMAS), however, is a longitudinal cohort study of randomly selected men between 40-70 years old. Participants were surveyed at 3 points in time and followed

up for 16.2 years. The CVD incidence for men with moderate-complete ED was 17.9 (95% CI 14.1-22.6) per 1,000 person-years compared to a CVD incidence of 12.5 (95% CI 10.8-14.3) for men with none-minimal ED ($p<0.05$). Frequency of sexual activity was inversely associated with CVD incidence[68]. Using data from the same study, Araujo et al. found an increased risk of all-cause mortality in men with ED as well as an increased risk of CVD death in men with moderate-severe ED 1.87 (95% CI 1.32-2.64) compared to men with none-minimal ED. There was a dose-dependent association between risk of CVD death and ED severity[66]. The authors postulate that sexual activity being physical activity may in itself be cardio protective. Additionally, men engaging in frequent sexual activity may also be likely to have intimate relationships which offer support, decrease stress and therefore improve cardiovascular health[68]. Schouten et al. also conducted a longitudinal community-based study, the Krimpen study, to examine general health and genitourinary problems of men aged 50-75 years[71].Reduced erectile rigidity was associated with an increase in CVD event incidence in a dose-response fashion. HR for CVD events and reduced erectile rigidity was 2.0 (95% CI 1.4-2.7) and 3.8 (95% CI 2.0-7.3) for severely reduced erections. ED is therefore likely to be a 'risk marker' for CVD, rather than a risk factor, reflecting the presence of vascular endothelial dysfunction and atherosclerosis which predispose cardiovascular morbidity and mortality[68].

ED and Benign Prostatic Hyperplasia

The prevalence of ED and concurrent BPH is high, 5.2-40% [72, 74] and men with ED are 1.33-6.24 times more likely to suffer from BPH compared to men without ED [17, 22, 30, 31, 32, 35, 61, 71, 73, 75]. The prevalence of ED and BPH increased with age, as expected as both conditions are associated with age. Furthermore, shared risk factors between ED and BPH, such as

atherosclerosis and diabetes, are also associated with ageing[76]. The bidirectional dose-response relationship between ED and BPH prevalence together with their common risk factors suggest a shared pathophysiology, however this has yet to be elucidated. It is likely that psychological factors are a strong contributor. Kim et al. found that men with lower urinary tract symptoms (LUTS) had a decreased frequency and enjoyment in sexual activity as well as lower sex life satisfaction due to urinary symptoms[72]. Men with LUTS may therefore experience sexual performance anxiety and aversion of sexual activity which may contribute to the development of ED. Evidence is limited on the underlying link between ED and BPH, however, one possible explanation is impaired nitric oxide (NO) or nitric oxide synthase (NOS) production in bladder, prostate and penile smooth muscle. This may impair smooth muscle functioning which is involved in bladder compliance, contractility and vasodilation of erectile tissues[76]. Another proposed hypothesis for the pathophysiology of ED and BPH is pelvic atherosclerosis. Hypoperfusion of the bladder, prostate and penis may cause fibrosis of smooth muscle resulting in LUTS and ED[76].

The relationship between ED & LUTS is important to consider in clinical practice as many therapies for BPH may cause or worsen ED as a side effect, for example finasteride or prostate surgery. Interestingly, Sairam et al. found that men with ED and LUTS treated with sildenafil experienced an improvement in LUTS as well as erections[77]. Men presenting with LUTS and ED may benefit from an initial phosphodiesterase inhibitor trial.

ED and Dementia

Evidence of the association between ED and dementia in the general population is limited. Previous cross-sectional studies have shown an association between ED & dementia,

however due to study design it was not possible to elucidate a directionality to the relationship[79, 80]. Yang et al. have demonstrated a greater prevalence of dementia amongst men with long-standing ED (2.5%) compared to controls (1.5%) and that men with ED are 1.68 times more likely to develop dementia[81]. Moore et al also found that men with ED had poorer cognitive function compared to those without ED[82]. The pathophysiology underlying the relationship between ED and dementia is likely to be complex; vascular, neuronal and psychological factors may all be implicated. Alzheimer's and vascular dementia, however are strongly associated with CVD risk factors. Endothelial dysfunction is thought to be the common denominator[82]. ED may therefore be a culmination of subclinical CVD risk factors which is a risk marker for both cardiovascular disease and dementia.

Limitations

The review is limited by the studies included, no non-English language studies were included. This may lead to certain bias, nevertheless, data from all geographical regions of the world has been presented here. Data is also limited by varying definitions and measurements of ED in population-based studies which make certain studies incomparable. Initial data extraction involved excluding articles based on title, although only unambiguously irrelevant articles were removed in this way, there is a possibility worthy articles were missed.

Conclusion

There is widespread use of unvalidated assessment tools, despite the existence of developed items such as the IIEF and MMAS-derived questionnaire.

The global prevalence of ED is high and represents a significant burden on the quality of life of men and their partners. ED is not simply a consequence of physiological aging, but also a symptom of pathology such as CVD, BPH and dementia. ED has been identified as a risk marker for cardiovascular morbidity and mortality as well as all-cause mortality. Widespread and early detection of ED may, therefore, improve primary prevention of CVD and mortality, as well as improving quality of life by treating ED itself. ED is also strongly associated with BPH, however the aetiology of the relationship remains to be elucidated. ED has also been found to predict development of dementia, early cognitive testing may therefore be warranted in certain ED patients. Young men are also affected by ED, putatively of psychological aetiology. Due to the sensitive nature of the topic, physicians should consider screening for ED in at risk patients, as information may not be volunteered.

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Table 1. Global prevalence of ED measured by the International Index of Erectile Function and variants.

Author	Country	ED Measurement	Study size	Prevalence rates (%) (95% CI)					
				Age (y)	Overall	Mild	Mild-Moderate	Moderate	Severe/complete
Quilter[12]	New Zealand	IIEF-5	562	40-70	42	21.9	10.3	5.9	4.1
				40-49	23.6				
				50-59	37.9				
				60-69	59.4				
Zhang[13]	China	IIEF-5	5,210	≥40	40.56				
				40-49	18.08				
				50-59	23.56				
				60-69	48.37				
				≥70	81.60				
Oyelade[14]	Nigeria	IIEF-5	241	30-80	58.9	47.2		11.3	41.5
				≤49	51.9				
				≥50	72.3				
Chew[15]	Australia	IIEF-5	1,580	20-80	40.3	11.30	5.3	2.60	21.20
				20-29	15.70				
				30-39	8.70				
				40-49	12.90				
				50-59	31.60				
				60-69	52.40				
				70-79	69.4				
				≥80	68.2				
Kupelian[16]	USA	IIEF-5	2,301	30-79	20.7	26	12	6	3
Mariappan[17]	Malaysia	IIEF-5	344	≥40	71.2	25.3		34.9	11.1
				40-49	43.3				
				50-59	83.3				
				60-69	94.1				
				≥70	94.9				
Tan[18]	Singapore	IIEF-5	729	≥30	51.3	23.2 (20.1-26.2)		8.8 (6.7-10.8)	19.3 (16.5-22.2)
				30-39	47.10 (35.3-48.1)				
				40-49	42.8 (37.1-48.1)				
				50-59	64.00 (55.2-72.8)				
				60-69	77.4 (67-87.8)				
				>70	90.0 (80.7-99.3)				
Pallangyo[19]	Tanzania	IIEF-5	441	≥18	24	8.50	22.60	37.80	31.10
				18-39	10.6				
				≥55	37.0				
Wu[20]	Taiwan		990	>40	26.0[1] , 13.1[2]	23.8[1]		1.4 [1]	0.8 [1]

		IIEF-5[1] & self-reported[2]		40-49	16.01[1], 5.32[2]			
				50-59	25.41[1], 15.64[2]			
				60-69	42.75[1], 21.01[2]			
				≥70	54.79[1], 27.7[2]			
De Boer[21]	The Netherlands	IIEF-5 & LIST[3]	2,117	≥18	16.8 (15.2-18.4)	5.9	3.6	6.9
				18-30	4 (1.8-6.3)			
				31-40	5.6 (3.5-7.6)			
				41-50	13.7 (10.8-16.5)			
				51-60	23.7 (19.5-27.8)			
				61-70	40.0 (32.9-47.0)			
				71-80	41.9 (33.6-50.2)			
				>80	33.3 (17.9-48.7)			
Korneyev[22]	Russia	IIEF	1,083	20-77	48.9	34.6	7.2	7.1
				<21	36.4			
				21-30	28.9			
				31-40	37.4			
				41-50	52.2			
				51-60	63.7			
				61-70	76.6			
				71-80	87.0			
Sathyanarayana[23]	India	IIEF	742	>18	15.77	19.7	42.7	28.2	9.4
				18-25	13.00			
				26-30	8.6			
				31-40	9.9			
				41-50	16.9			
				51-60	27.6			
				61-65	15.6			
				66-75	14.3			
Ng[24]	China	IIEF (question item 15 only)	1,506	26-70	36.7 (33.7-39.7)			
				26-30	18.3 (11.1-25.4)			

				31-40	28.6 (23.5-33.6)			
				41-50	37.9 (32.3-43.5)			
				51-60	47.3 (40.1-54.5)			
				61-70	61.1 (51.1-71.0)			
Mak[25]	Belgium	IIEF[4] / IIEF item 15[5]	799	40-70	43.4[4]; 65.4 (62.0-68.7)[4]	11.2[4]; 25.8 (22.8-29.1)[5]	2.9[4]; 27.6 (23.9–30.2)[5]	1.8[4]; 12.7 (10.5–15.2)[5]
				40-49	11.2[4]; 42.8 (36.5-49.3)[5]			
				50-59	18.0[4]; 69.4 (63.2-75.1)[5]			
				60-69	18.1[4]; 80.5 (75.4-84.7)[5]			
Dunn[26]	UK	Adapted IIEF[6]	789	18-75	26 (23-30)[7]; 39 (35-42)[8]			

[1] IIEF-5
[2] Self-reported ED assessed by single question: 'do you think you have ED? Yes/ No.'
[3] Leidse Impostence Scale Test (LIST)
[4] IIEF used in sexually active men
[5] IIEF item 15 was used as a surrogate measure for men not sexually active in past one month: 'how do you rate your confidence that you could get and keep an erection? Very high confidence= no ED, high confidence most times= mild ED, mod-low confidence= moderate ED, very low/ never achieving =complete ED'
[6] 2 items from the IIEF were used to measure ED: 1. 'Have you ever had any difficulties initiating an erection before intercourse 2. Have you ever had any difficulties maintaining an erection throughout intercourse' If both were present then the subject was said to have ED.
[7] in the last 3 months
[8] over lifetime

Table 2. Global prevalence of ED measured by the MMAS-derived self-assessment.

Author	Country	ED Measurement	Study size	Prevalence rates (%) (95% CI)				
				Age (y)	Overall	Mild	Moderate	Severe/complete
Weber[27]	Australia	MMAS self-assessment	101, 674	≥45	60.7 (60.4-61.0)	25.14 (24.9-25.4)	18.79 (18.6-19.0)	16.8 (16.5-17.0)
Martins[28]	Brazil	MMAS self-assessment	1,947	18-40	35.0			
				18-25	35.6			
				26-40	30.7			
Nicolosi[29]	Japan	MMAS self-assessment	2417	40-70	34.5			
	Malaysia				22.4			
	Italy				17.2			
	Brazil				15.5			
Moreira[30]	Brazil	MMAS self-assessment	602	40-70	39.5	25.1	13.1	1.3
				40-50	30.8			
				50-60	43.4			
				60-70	56.7			
Laumann[31]	USA	MMAS self-assessment	2,173	≥40	22.0 (19.4-24.6)			
				40-49	9.1 ((5.9-12.2)			
				50-59	15.2 (11.3-19.1)			
				60-69	29.4 (22.8-35.9)			
				≥70	54.9 (46.9-62.8)			
Akkus[32]	Turkey	MMAS self-assessment	1,982	≥40	69.2	33.2	27.5	8.5
				40-49	49.9			
				50-59	74.8			
				60-69	86.3			
				≥70	94.7			
Moreira[33]	Brazil	MMAS self-assessment	342	40-70	45.9	33.9	8.5	3.5
				40-50	35.40			
				50-60	48.90			
				≥60	85.40			
Derby[34]	USA	MMAS self-assessment[1] & IIEF[2]	505[1]; 254[2]	40-69	50.0 (45-54)[1]; 50.0 (42-57)[2]			25.0 (20-29)[1]; 25.0 (19-32)[2]
Morillo[35]	Colombia	MMAS self-assessment	622	≥40	52.8 (48.9-56.7)	32.3 (25.8-38.7)	16.4 (9.3-23.5)	3.6 (0-11.9)
	Ecuador		670		52.1 (48.3-55.9)	31.8 (25.2-38.1)	16.1 (9.2-23.0)	2.5 (0-9.9)
	Venezuela		654		55.2 (51.4-58.9)	36.7 (30.6-42.8)	15.8	4.1 (0-11.6)

								(8.7-22.8)	
Londono[36]	USA	MMAS self-assessment	37,712	45-69	57.80	28.72	20.53		8.55

Table 3. Global prevalence of ED measured by other questionnaires

Author	Country	ED Measurement	Study size	Prevalence rates (%) (95% CI)				
				Age (y)	**Overall**	**Mild**	**Moderate**	**Severe/complete**
Parish[40]	China	2-item Questionnaire[8] (≥2 months)	1,261	20-64	8.0 (6.0-10.0)			
Shiri[41]	Finland	2-item Questionnaire[8]	1,941	50	67.0			
				75	88.5			
Ansong[42]	USA	2-item Questionnaire[9]	1,408	50-76	46.3			
				50-54	26.0			
				55-59	34.9			
				60-64	46.9			
				65-69	57.8			
				70-76	69.4			
Chen[43]	Taiwan	Checklist: ED yes/ no?	1,002	40-83	17.7			
				40-50	8.2			
				51-60	17.9			
				61-70	27.2			
				≥71	34.4			
Lau[44]	China	Questionnaire: erection difficulties yes/ no?	1,516	18-60	9.6			
				18-19	0.8			
				20-29	4.5			
				30-39	8.9			
				40-49	10.1			
				50-59	23.5			
Buvat[45]	France	Questionnaire: ≥2 months erectile difficulties,- no/ occasionally/ sometimes/ frequently	750	40-80	15.0 (12.2-18.2)	6.0 (4.2-8.3)	7.6 (5.6-10.1)	1.4 (0.6-2.7)
	Southern Europe		1,500		11.7 (10.2-13.4)	4.3 (3.4-5.5)	5.3 (4.2-6.5)	1.9 (1.3-2.7)
	Northern Europe		3,250		13.1 (11.7-14.6)	5.0 (4.1-6.0)	5.3 (4.4-6.4)	2.7 (2.0-3.4)

Lauman[46]	USA	Questionnaire: ≥2 months erectile difficulties,- no/ occasionally/ sometimes/ frequently	742	40-80	22.5 (19.6-25.7)	9.6 (7.6-12.0)	5.9 (4.3-7.9)	6.5 (4.8-8.5)
Hyde[47]	Australia	Questionnaire: 'ever had trouble gaining/ maintaining an erection?'	3,274	75-95	49.4 (47.7-51.1)			
Tan[48]	China,Japan,Korea, Malaysia,Taiwan	Questionnaire[10]	10, 934	Age				
				20-75	3-14			
				20-29	1-7			
				30-39	1-6			
				40-49	1-6			
				50-59	6-21			
				60-75	11-26			
Rosen[49]	USA, UK, Germany, France, Italy, Spain, Mexico, Brazil	Questionnaire[11]	27,839	20-75	16			
				20-29	8			
				30-39	11			
				40-49	15			
				50-59	22			
				60-69	30			
				70-75	37			
Schouten[50]	The Netherlands	International Contience Society Male Sex Questionnaire[12]	1,643	50-75	40			
Berrada[51]	Morocco	Pfizer Cross-National Study of the Prevalence and Correlates of ED Questionnaire[13]	646	≥25	53.6	37.5	15.0	1.1
Hendrickx[52]	Belgium	Sexual Functioning Scale[14]	696	14-80	22.5 (19.4-29.5)	15.6 (12.9-18.3)	3.2 (1.9-4.5)	3.7 (2.3-5.1)
				14-34	0.9 (0-2.1)			
				35-49	3.0 (0.8-5.2)			
				50-64	11.0 (6.2-15.8)			
				65-80	41.3 (30.2-52.4)			
Korfage[37, 38]	The Netherlands	Dutch module on sexual activity[6]	3,299	55-74	19.0			
			3,810	57-78	19.0			

				58-61	12.0
				62-64	14.6
				65-67	18.4
				68-70	21.9
				71-78	26.3
Li[39]	China (Hong Kong)	The Danish Prostatic Symptoms Score[7]	201	50-80	50
	Singapore		204		53
	Malaysia		250		59
	Philippines		250		65
	Thailand		250		65

[6] 'ED was defined as being sexually inactive because of erectile problems or being sexually active but experiencing problems with getting or maintaining an erection, even when erectile aids were used'

[7] 'Can you get an erection? 1. yes with normal stiffness 2. yes with a slight reduction in stiffness 3. Yes with a big reduction in stiffness 4. No, I cannot get erection'

[8] 2 item questionnaire: 1. do you experience difficulty achieving erection to initiate intercourse, 2. do you have difficulty maintaining erection during intercourse ≥2 months

[9] 2 Item questionnaire: 1.'Have you experienced erectile dysfunction (impotence) within the past 6 months? Have you sought treatment for erectile dysfunction (impotence)?'

[10] Questionnaire: "Which of the following best describes your erection difficulty (or the difficulty you used to have)?": (i) I get no erection at all; (ii) I have difficulty getting a sufficiently good erection; (iii) I get satisfactory erections, they just don't last long enough; (iv) The problem is with ejaculation, not with my erection, or (v) other.

[11] Questionnaire: Erection difficulties? ' (A) seen a doctor, pharmacist or therapist about it; (B) tried any kind of remedy, with or without prescription; (C) not done anything about it; or (D) never had it.'

[12] Do you get erections?" were recoded "ED" if the participants reported "yes, with reduced rigidity" or "yes with severely reduced rigidity" or "no, no erections possible" or "no, never had."

[13] Pfizer Cross-National Study of the Prevalence and Correlates of ED Questionnaire[13]

[14] Sexual Functioning Scale: <6 months erectile difficulties initiating erection sufficiently rigid for penetration or maintaining erection throughout intercourse: mild/ moderate/ severe.

Table 4. The association between ED and cardiovascular disease

Author	Country	ED Measurment	CVD measurement	Study Size	Sample Age	Findings (OR/ HR 95% CI)			
Martins[28]	Brazil	MMAS questionnaire	Self-reported	1,947	18-40	No increase in ED prevalence associated with diabetes, hypertension, cardiovascular disease, and dyslipidemia			
Araujo[65]	USA	MMAS questionnaire	NDI	1,709	40-70	All-cause mortality: 1.3 (1.0–1.6); CVD mortality: 1.4 (95% CI, 1.0–2.1)			
Araujo[66]	USA	MMAS questionnaire	Self-reported, NDI	1,057	40-70	CVD incidence: 1.4 (1.1-1.9)			
Bai[59]	China	CIEF-5[1]	Self-reported	2,226	20-86	Heart Disease	3.7 (2.9-4.7)		
						DM	3.5 (2.4-5.2)		
						DLM	2.1 (1.4-3.0)		
Chew[60]	Australia	IIEF-5	Self-reported	1,580	≥20	HTN	1.5 (1.1-2.1)		
						IHD	1.9 (1.2-3.0)		
						Stroke	3.3 (1.1-8.1)		
						DLM	1.1 (0.8-1.6)		
						PAD	2.4 (0.9-6.3)		
Hyde[47]	Australia	'Difficulty gaining or maintaining an erection?'	Self-reported, hospital record	3,274	75-95	CAD	1.5 (1.2-2.0)		
						Stroke/TIA	1.4 (0.9-2.2)		
						HTN	1.4 (1.1-1.7)		
						DM	1.6 (1.1-2.3)		
						DLM	1.1 (0.9-1.4)		
De Boer[21]	The Netherlands	IIEF-5 & LIST	Self-reported	2,117	≥18	DM	1.7 (1.0–3.1)		
						HTN	0.8 (0.6–1.3)		
						Arteriosclerosis	1.2 (0.5–3.1)		
						Angina pectoris	1.3 (0.5–3.0)		
						MI	1.6 (0.7–3.7)		
						Stroke	0.4 (0.1–1.5)		
						CVD[9]	1.7 (1.2–2.4)		
Chao[63]	Taiwan	IIEF	Self-reported, blood tests	238	>40	DM	8.9 (4.7—17.0)**		
						HTN	3.6 (2.0-6.5)**		
						TG abnormal	2.8 (1.3-5.9)*		
						HDL abnormal	5.5 (3.1 -- 9.8)**		
Shabsigh[61]	USA, UK, Germany, France, Italy, Spain	Questionnaire[2]	Self-reported	28,691	20-75		ED		
						CVD %	Mild	Moderate	Severe
						HTN	25	42	39
						HCL			38

							25	35	
						Angina	7	16	34
						DM	8	16	24
						MI/ surgery	7	13	29
						Arterios clerosis	6	10	13
Hall[67]	USA	MMAS questionnaire	Self-reported, NDI	1,165	40-70	CVD incidence/ 1000 person years*	11.4 (8.9-14.5)	16.6 (11.9-23.2)	18.6 (13.8-25.0)
Kupelian[68]	USA	MMAS questionnaire	Self-reported, NDI	928	40-70	MS	1.35 (1.01-1.81)	1.2 (0.8-1.8)	1.5 (1.0-2.2)
Banks[64]	Australia	MMAS questionnaire	Self-reported	95,038	≥45	IHD	1.08 (0.92-1.27)	1.4 (1.2-1.6)	1.6 (1.3-2.0)
						HF	5.19 (1.75-15.4)	5.4 (1.8-16.2)	8.0 (2.6-24.2)
						Stroke	1.01 (0.75-1.37)	1.9 (1.4-2.5)	1.3 (0.9-1.9)
						PVD	0.93 (0.54-1.60)	1.2 (0.7-2.1)	1.9 (1.1-3.3)
						All CVD	0.99 (0.90-1.09)	1.2 (1.1-1.4)	1.4 (1.2-1.5)
Schouten[70]	The Netherlands	ICS[5]	GP records	1,248	50-75	CV event incidence/ 100 person years**	5.1 (4.2-6.1)	10.1 (7.4-13.8)	19.0 (11.5-31.5)
Morillo[35]	Colombia, Ecuador, Venezuela	MMAS questionnaire	Self-reported	1,946	≥40			ED	
							Colombia	Ecuador	Venezuela

							Mild	Mod	Sev	Mild	Mod	Sev	Mild	Mod	Sev
						DM	0.6 (0.2-1.4)	5.1 (2.3-11.0)*	1.9 (0-7.7)	1.1 (0.6-2.2)	1.7 (0.8-3.6)	2.1 (0-8.6)	1.0 (0.6-1.9)	3.3 (1.8-6.2)*	3.1 (1.2-8.3)*
						HTN	1.1 (0.7-1.7)	2.2 (1.4-3.6)	2.4 (1.1-5.4)	1.5 (0.9-2.5)	1.6 (0.9-2.9)	2.5 (0.8-7.6)	1.3 (0.9-1.8)	1.9 (1.2-3.0)	2.3 (1.1-4.8)
						IHD	0.6 (0.3-1.3)	2.4 (1.2-4.9)*	2.1 (0.6-6.9)	1.5 (0.7-3.2)	0.6 (0.2-1.9)	3.1 (0-12.8)	1.1 (0.6-1.8)	5.0 (2.9-8.7)*	0.7 (0-2.8)
Rosen[49]	USA, UK, Germany, France, Italy, Spain, Mexico, and Brazil	Questionnaire[3]	Physician diagnosis or under treatment	27,839	20-75	CVD %						No ED			ED
						HTN**						19			36
						Angina**						7			17
						HCL**						16			29
						DM**						4			14
Lahoz[62]	Spain	IIEF-5	Self-reported, ABPI· Carotid Doppler	614	45-74	CVD%						No ED			ED
						DM						7.5			16.9*
						HTN						34.0			42.1
						HCL						43.6			49.9
						CVD						6.3			13.7*
						MS						38.9			44.3
						Cholesterol (SD)						203 (35)			193 (39)*
						Triglycerides (SD)						126 (14)			129 (16)
						ABPI <0.9						2.5 (0.3-4.6)			4.3 (2.0-6.4)
						Carotid plaques						44.8 (38.3-51.2)			63.8 (58.7-68.8)*

Mak[25]	Belgium	IIEF & Questionnaire[4]	Self-reported	799	40-70		40-49 years	50-59 years	60-69 years
						HTN	0.9 (0.3-2.3)	1.5 (0.9-2.5)	2.4 (1.4-3.9)
						DM	7.0 (1.0-51.3)	1.8 (0.8-3.8)	1.2 (0.6-2.3)
						CVD	0.7 (0.2-2.2)	2.1 (1.1-3.7)	2.3 (1.4-3.8)

CVD (cardiovascular disease), **HTN** (hypertension), **DM** (diabetes mellitus) **IHD** (ischaemic heart disease), **PVD** (peripheral vascular disease), **MS** (metabolic syndrome), **HF** (heart failure), **HCL** (hypercholesterolaemia), **TG** (triglycerides), **ABPI** (ankle-brachial pressure index), **MI** (myocardial infarction), **NDI** (National Death Index). *p<0.05 **p<0.001

[1] Chinese Index of Erectile Function

[2] Questionnaire: participants screened with 'difficulty getting or keeping an erection 1. never had it, 2. had it before but not now, 3. have it now sometimes, 4. have it now always', subsequently confirmed by IIEF.

[3] Questionnaire: Erection difficulties? ' (A) seen a doctor, pharmacist or therapist about it; (B) tried any kind of remedy, with or without prescription; (C) not done anything about it; or (D) never had it.'

[4] IIEF used in sexually active men; IIEF item 15 was used as a surrogate measure for men not sexually active in past one month: 'how do you rate your confidence that you could get and keep an erection? Very high confidence= no ED, high confidence most times= mild ED, mod-low confidence= moderate ED, very low/ never achieving =complete ED'

[5] International Continence Society Male Sex Questionnaire: "Do you get erections?" were recoded "ED" if the participants reported "yes, with reduced rigidity" or "yes with severely reduced rigidity" or "no, no erections possible" or "no, never had."

Table 5. The Association between ED and Benign Prostatic Hyperplasia

Author	Country	ED measurement	BPH measurement	Study size	Age (years)	Findings [OR/ HR 95% Confidence Intervals or Prevalence (%)]	
Zhang[71]	China	IIEF-5	Self-reported	5,210	≥40	1.332 (1.284-1.521)*	
Mariappan[17]	Malaysia	IIEF-5	AUA symptom index[4]	353	≥40	1.4 (1.3-1.6) *p*=0.064	
Shabsigh[61]	USA, UK, France, Germany, Italy, Spain	IIEF & Questionnaire[2]	Self-reported	28,691	20-75	2.0 (1.8-2.5)	
Moreira[73]	Brazil	MMAS questionnaire	Self-reported	654	40-70	3.67 (1.17-11.48)*	
Morillo[35]	Colombia, Ecuador, Venezuela	MMAS questionnaire	Self-reported	1,946	≥40	1.5 (1.0 – 2.1)	
Korneyev[22]	Russia	IIEF	IPSS	1,083	20-77	4.10 (3.16-5.33)	
Kok[73]	The Netherlands	ICS[1]	IPSS[3]	3,924	50-78	1.600 (1.176-2.175)**	
Akkus[32]	Turkey	MMAS questionnaire	IPSS	1,982	≥40	Moderate LUTS	Severe LUTS
						4.41 (3.29-5.90)**	6.24 (3.43-11.35)
Moreira[30]	Brazil	MMAS questionnaire	IPSS	602	40-70	Moderate LUTS	Severe LUTS
						2.14 (1.26–2.63)**	5.86 (2.82 – 12.17)***
Laumann[31]	USA	MMAS questionnaire	IPSS	2,173	≥40	Moderate LUTS	Severe LUTS
						1.7 (1.0-2.6)	6.0 (1.9-19.0)
Glasser[74]	USA	MMAS questionnaire	IPSS	2,173	≥40	Mild LUTS (%)	Moderate LUTS
						22	40
Kim[72]	South Korea	MMAS questionnaire	IPSS variant	1,842	≥40	% ED & LUTS	% ED, no LUTS***
						99	1

*p<0.05 **p<0.01 ***p<0.001

[1] International Continence Society Male Sex Questionnaire: "Do you get erections?" were recoded "ED" if the participants reported "yes, with reduced rigidity" or "yes with severely reduced rigidity" or "no, no erections possible" or "no, never had."

[2] Questionnaire: participants screened with 'difficulty getting or keeping an erection 1. never had it, 2. had it before but not now, 3. have it now sometimes, 4. have it now always', subsequently confirmed by IIEF.

[3] International Prostate Symptom Score: points based 8-item questionnaire on lower urinary tract symptoms and quality of life. Mild= 1-7, moderate= 8-19, severe ≥20

[4] American Urological Association Symptom Index: points based 7-item questionnaire on lower urinary tract symptoms. Identical to IPSS except for quality of life item. Mild= 1-7, moderate= 8-19, severe ≥20