

ERECTILE DYSFUNCTION

Erectile Dysfunction in 45-Year-Old Heterosexual German Men and Associated Lifestyle Risk Factors and Comorbidities: Results From the German Male Sex Study



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ABSTRACT

Background: Erectile dysfunction (ED) is a common public health issue with a significant impact on quality of life. The associations between ED and several risk factors have been reported previously. The continuously increasing incidence of these factors is contributing to the increasing prevalence of ED.

Aim: To assess ED prevalence and severity in a representative sample of 45-year-old German men and to analyze the association with risk factors (lifestyle risk factors/comorbidities).

Methods: Data were collected within the German Male Sex-Study. Randomly selected 45-year-old men were invited. A total of 10,135 Caucasian, heterosexual, sexually active men were included in this analysis. The self-reported prevalence of ED was assessed using the Erectile Function domain of the International Index of Erectile Function. Risk factors for ED were ascertained using self-report questionnaires. An anamnesis interview and a short physical examination were performed.

Main Outcome Measure: ED prevalence and severity were evaluated in a cross-sectional design. The associations of ED with comorbidities (eg, depression, diabetes, hypertension, lower urinary tract symptoms) and lifestyle factors (ie, smoking, obesity, central obesity, physical inactivity, and poor self-perceived health-status) were analyzed by logistic regression.

Results: The overall prevalence of ED was 25.2% (severe, 3.1%; moderate, 9.2%; mild to moderate, 4.2%; mild, 8.7%). Among the men with ED, 48.8% had moderate or severe symptoms. ED prevalence increased with the number of risk factors, to as high as 68.7% in men with 5–8 risk factors. In multiple logistic regression with backward elimination, the strongest associations with ED were found for depression (odds ratio [OR] = 1.87), poor self-perceived health status (OR = 1.72), lower urinary tract symptoms (OR = 1.68), and diabetes (OR = 1.38).

Conclusion: One out of 4 men already had symptoms of ED at age 45. Almost one-half of the men with ED had moderate to severe symptoms. ED was strongly associated with each analyzed risk factor, and the prevalence and severity of ED increased with an increasing number of risk factors. **Hallanzy J, Kron M, Goethe VE, et al. Erectile Dysfunction in 45-Year-Old Heterosexual German Men and Associated Lifestyle Risk Factors and Comorbidities: Results From the German Male Sex Study. Sex Med 2019;7:26–34.**

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Key Words: Erectile Dysfunction; Prevalence; Severity; Risk Factors; Middle-Aged Men; German Male Sex-Study

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INTRODUCTION

Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance.¹ Frequently discussed epidemiologic studies on ED, such as the Massachusetts Male Aging Study, evaluated the prevalence of ED using a self-administered sexual activity questionnaire.² That study reported an overall ED prevalence of 52% in men aged 40–70 years. In 40-year-old men, the prevalence of moderate and complete ED was 17% and 5%, respectively. In a multinational analysis, the prevalence of self-reported ED was 15% in men aged 40–49.³ In the 1998 Cologne Male Survey investigating the prevalence of ED in a sample of German men aged 30–80 years, 9.5% of the men aged 40–49 reported symptoms of ED.⁴ Comparing reported ED prevalences is difficult, owing to differences in methodology among studies, such as varying age ranges and divergent assessment of ED.⁵

Currently, the most common measure for standardized self-assessment of ED is the International Index of Erectile Function (IIEF), which has been validated in 32 languages.^{6,7} The 6-item short form, the Erectile Function domain (IIEF-EF), has been implemented in many clinical trials, including the latest German epidemiologic study that evaluated ED prevalence more than a decade ago.⁸ In that study, comprising 441 men aged 40–49 years, the prevalence of ED was 19.5%. The higher prevalence in that study could be related to a higher number of patients with comorbidities.

Comorbidities are known risk factors for ED, and much research has focused on elderly men and cohorts of men with certain disorders, such as diabetes and cardiac disease.^{9–11} A strong association between ED and comorbidities can be found in younger men as well, however. In an online survey of Middle Eastern men aged 40–49, the prevalence of ED analyzed with the IIEF was 45.6% and was strongly associated with various risk factors, including hypertension, diabetes, and depression.¹² The steady increase in risky lifestyle behaviors, such as a fat diets, physical inactivity, or obesity, and comorbidities that negatively affect the cardiovascular system is a current issue, and thus the prevalence of ED is expected to increase as well. There has been a statistically significant increase in the prevalence of obesity in white American men aged 40–59 years, with rates increasing from 28.5% in 1999–2000.^{13,14} In Germany, the prevalence of obesity in men aged 25–69 years increased from 18.9% in 1990–1992 to 23.3% in 2008–2011.¹⁵ Similarly, the prevalence of diabetes in men aged 18–79 years increased from 4.7% in 1997 to 7.0% in 2008–2011.¹⁶

The aims of the present analysis were to evaluate the current prevalence and severity of ED in sexually active German men using the IIEF-EF, as well as to analyze the associations between ED and various risk factors, categorized into lifestyle risk factors and comorbidities.

MATERIALS AND METHODS

Data were collected within the German Male Sex-Study (GMS-Study), an accompanying project of the ongoing PROBASE trial. This German prostate cancer screening trial, initiated in April 2014, has been described in detail previously.¹⁷ The GMS-Study assesses information on male sexuality by surveying a community-based random sample of 45-year-old men.¹⁸ Aspects of sexual activity, sexual function, and self-concept are examined in cross-sectional and longitudinal designs.¹⁹ An anamnesis interview is conducted by a study physician, and anthropometric data are acquired. In addition, all men complete self-report questionnaires eliciting information on sexuality and lifestyle factors. All men participating at the PROBASE trial who completed information on sexual identity (heterosexuality/homosexuality/bisexuality) were included in the GMS-Study. Ethical approval for the study was provided by an internal Ethics Committee, and written informed consent was obtained from each participant.

Inclusion Criteria

Caucasian heterosexual men with no history of previous pelvic surgery who had been sexually active in the past 4 weeks were included. The current analysis was limited to men recruited during the first 2 years of the study.

Erectile Function

Erectile function was evaluated using the IIEF-EF.²⁰ The severity of ED was classified as mild (IIEF-EF score 22–25), mild to moderate (IIEF-EF score 17–21), moderate (IIEF-EF score 11–16), or severe (IIEF-EF score 6–10). The presence of ED was defined as an IIEF-EF score ≤ 25 .

Lifestyle Risk Factors

To classify obesity and central obesity, height, weight and waist circumference were measured by a study physician. According to World Health Organization guidelines, obesity and central obesity were defined as a body mass index (BMI) ≥ 30 kg/m² and a waist circumference ≥ 102 cm.²¹ Smoking habits (regular smoker vs non- or ex-smoker) and physical activity (≤ 1 day a week vs ≥ 2 days a week for a minimum of 30 minutes, including mild exercise like walking or gardening) were ascertained using self-report questionnaires.

Self-perceived health status was assessed with the first question from the 12-item Short Form survey (SF12) with responses on a 5-point Likert scale. The responses were dichotomized into poor (poor/fair) vs good (good/very good/excellent).²²

Comorbidities

The presence of 3 comorbidities—hypertension, diabetes, depression—was ascertained during anamnesis by the study physicians. Lower urinary tract symptoms (LUTS) were assessed

using the International Prostate Symptom Score (IPSS) and were dichotomized as IPSS > 7 (moderate to severe symptoms) vs IPSS ≤ 7 (no or mild symptoms).²³

Statistics

The data were analyzed using descriptive statistics, calculating counts and percentages for categorical variables. The prevalence of ED was estimated overall and in a subgroup of “healthy” men, defined as men who did not smoke regularly; had a waist circumference < 95 cm; were physically active ≥ 4 times per week (see Lifestyle Risk Factors), were without hypertension, diabetes, or depression; and had an IPSS of 0. The impact of comorbidities and lifestyle risk factors on ED was analyzed by simple and multiple logistic regression with backward elimination (selection level 5%). Odds ratios (ORs) with 95% confidence interval (CIs) and *P* values were calculated.

RESULTS

A total of 12,646 men were recruited in the first 2 years of the GMS-Study. The final study group consisted of 10,135 men (80.1%) after the exclusion of non-Caucasian men (*n* = 292), non-heterosexual men (*n* = 605), men with previous pelvic surgery (*n* = 55), men with incomplete data on erectile function (*n* = 1,242), and men with no sexual activity (*n* = 317). An overview of the sociodemographic characteristics of the study population has been published previously.¹⁸ Self-reported lifestyle risk factors and comorbidities were recorded (Table 1).

The overall prevalence of erectile dysfunction was 25.2% (*n* = 2,565), including 8.7% with mild ED, 4.2% with mild to moderate ED, 9.2% with moderate ED, and 3.1% with severe ED (Figure 1A). Among the men with ED, 48.8% had moderate to severe symptoms. Only 2.1% of cohort (*n* = 216) met the criteria for healthy men; the prevalence of ED in these men was 14.4% (Figure 1B).

ED prevalence and degree of severity were higher in men with lifestyle risk factors and/or comorbidities. In the men with ED, the highest rates of moderate and severe ED were seen in men with depression (61.0%), poor self-reported health status (52.7%), and diabetes (50.6%) (Figure 2).

On simple logistic regression, each lifestyle risk factor and each comorbidity was associated with the presence of ED (Table 2). The highest crude ORs were achieved for depression (OR = 2.44), self-perceived health status (OR = 2.29), diabetes (OR = 1.96), and LUTS (OR = 1.84).

In multiple logistic regression with backward elimination, all risk factors except BMI were identified as an important risk factor for ED (Table 2). In this analysis, depression still had the highest impact on ED prevalence (OR = 1.87), followed by self-perceived health status (OR = 1.72), LUTS (OR = 1.68), and diabetes (OR = 1.38).

The prevalence of ED increased with the more lifestyle risk factors present, with the highest prevalence of 40.9%

Table 1. Distribution of lifestyle risk factors and comorbidities

Parameter	%	n
Lifestyle risk factors		
Smoking regularly		
Yes	18.6	1,864
No	81.4	8,143
Physical activity		
≤ 1 time/wk	19.2	1,927
≥ 2 time/wk	80.8	8,121
Obesity		
BMI ≥ 30 kg/m ²	17.8	1,799
BMI < 30 kg/m ²	82.2	8,298
Central obesity		
WC ≥ 102 cm	29.2	2,908
WC < 102 cm	70.8	7,048
Self-perceived health status		
Poor (fair/poor)	5.0	492
Good (good/very good/excellent)	95.0	9,457
Comorbidities		
Hypertension		
Yes	13.0	1,315
No	87.0	8,820
Diabetes		
Yes	2.0	200
No	98.0	9,935
LUTS		
IPSS > 7	10.3	1,012
IPSS ≤ 7	89.7	8,804
Depression		
Yes	2.7	276
No	97.3	9,859

BMI = body mass index; IPSS = International Prostate Symptom Score; LUTS = lower urinary tract symptoms; WC waist circumference.

(Figure 3A). In this subanalysis for multiple lifestyle risk factors, only waist circumference was included (and not BMI), to avoid overestimating the influence of obesity. Important to note is that regardless of number of lifestyle risk factors, among the men with ED, the proportion of moderate and severe ED was approximately 50%.

Likewise, ED prevalence steadily increased with the number of comorbidities, up to 64.3% in men with 3 or 4 comorbidities (Figure 3B). Among these men, the prevalence of moderate and severe ED was as high as 38.1% (resulting in a proportion of 59%). When examining the simultaneous impact of all risk factors, including both lifestyle risk factors and comorbidities, the prevalence of ED was 68.7% in the group with 5–8 risk factors (Figure 3C).

DISCUSSION

In this study, roughly 1 in 4 (25.2%) sexually active 45-year-old German men reported being affected by ED. Almost one-half of the men with ED (48.8%) suffered from moderate to severe symptoms.

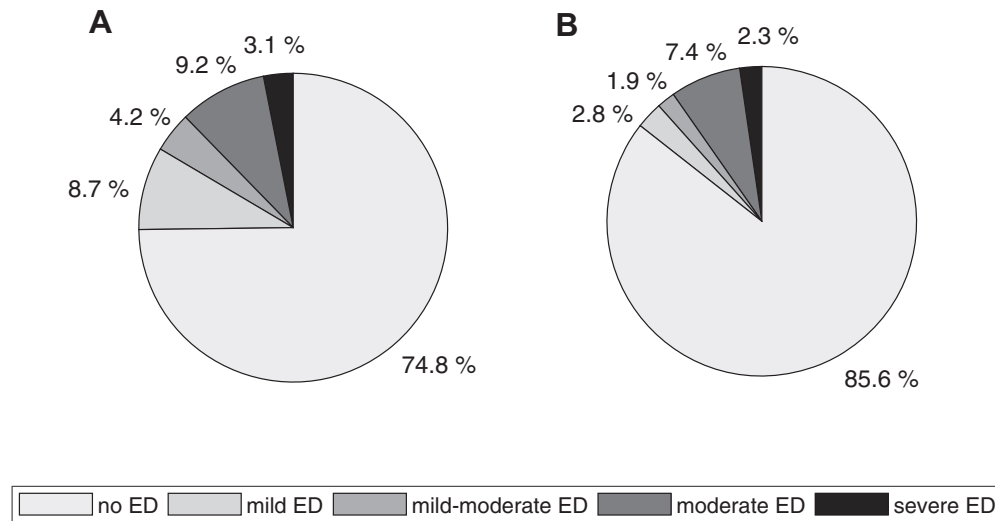


Figure 1. Prevalence of ED with distribution of degrees of severity. A, Overall ED prevalence in the 45-year-old men. B, ED prevalence in a subgroup of “healthy” men (nonsmoker, waist circumference < 94 cm, physical activity >4 time per week, no hypertension/diabetes/depression, IPSS = 0). ED = erectile dysfunction; IPSS = International Prostate Symptom Score.

In 2 large German studies on ED conducted more than a decade ago, ED prevalence (IIEF-EF <25) was 17%–19.5% in the 40- to 49-year age group.^{8,24} Furthermore, previous epidemiologic investigations reported lower prevalences of severe ED than found in our analysis (0.5% and 2.1% vs 3.1%).^{8,25}

The Berlin Male Study found that prevalence rates including only sexually active men might underestimate the actual prevalence of ED, given that sexual inactivity may result from low confidence in achieving and/or maintaining an erection.²⁴ Because we excluded sexually inactive men from our analysis, the true ED prevalence in 45-year-old German men might be even higher than 25.2%. The high prevalence of severe ED in our study may reflect the increasing prevalence of risk factors with an impact on ED.

The prevalence of lifestyle risk factors and comorbidities in 45-year-old men was higher than expected; for example, > 10% of men had LUTS with an IPSS > 7, and almost 30% of the men had central obesity, defined as a waist circumference > 102 cm.

In our analysis, significant associations between ED and all analyzed risk factors, both lifestyle risk factors and comorbidities, were observed. All 5 lifestyle risk factors showed higher odds for an association with ED ($P \leq .001$ for all). The highest odds were found for poor self-perceived health status, central obesity, obesity, and physical inactivity. Besides the self-perceived health status, the association of all assessed lifestyle risk factors with ED has been reported in previous studies, because these are vascular risk factors that lead to endothelial dysfunction and increased inflammation.^{26–28}

The subjective perception of one’s health status is not an objectifiable risk factor per se, but our data suggest that overall sense of well-being is associated with erectile function. In our analysis, only 5% of men reported a poor self-perceived health status. In these men, ED was more prevalent (42.5% vs 24.46%

in men with a good self-perceived health status) and more severe (22.0% vs 11.9% with moderate or severe symptoms).

Obesity has been associated with an increased risk of developing ED. In another study, the relative risk of ED was nearly twice as high (RR 1.9) in obese men compared with men with normal BMI.²⁹ In our sample, symptoms of ED were present in 32.1% of obese men (vs 24.1% of men with a BMI <30 kg/m²), and in 30.3% of men with central obesity (vs 23.2% in men with a waist circumference < 102 cm). Other studies have shown that the prevalence of ED increased from 32.1% to 74.5% with increasing waist circumference.³⁰ In our cohort, almost 20% of the men were physically inactive (defined as mild exercise once per week or less), and the prevalence of ED was 30.3% in these men compared with 24.0% in men who were physically active twice or more weekly. A significant independent association between ED and a self-reported lack of physical activity has been observed in a US study as well; adjusted by age, the prevalence of ED increased from 28.0% to 45.8% with declining physical activity.³¹ An association between smoking and ED is controversial, with some studies showing a significant association.^{32,33} In our analysis, we found a minor association between smoking and ED (OR = 1.2). We assume that smoking will gain importance as the vessel damage manifests in aging men.

All 4 analyzed comorbidities—hypertension, diabetes, LUTS, and depression—were associated with higher odds for ED. The most significantly associated comorbidity was depression. The prevalence of ED in men with depression was 44.6%, compared with 24.8% in those without depression. Previous studies have shown a significant association of depression with ED.³⁴ A significant increase in the incidence of depressive symptoms has been reported in men with ED (OR = 4.34).³⁵ In a study among middle-aged men in northern Finland, depression was associated with a 66% higher risk for ED.³⁶ Nonetheless, conclusions on

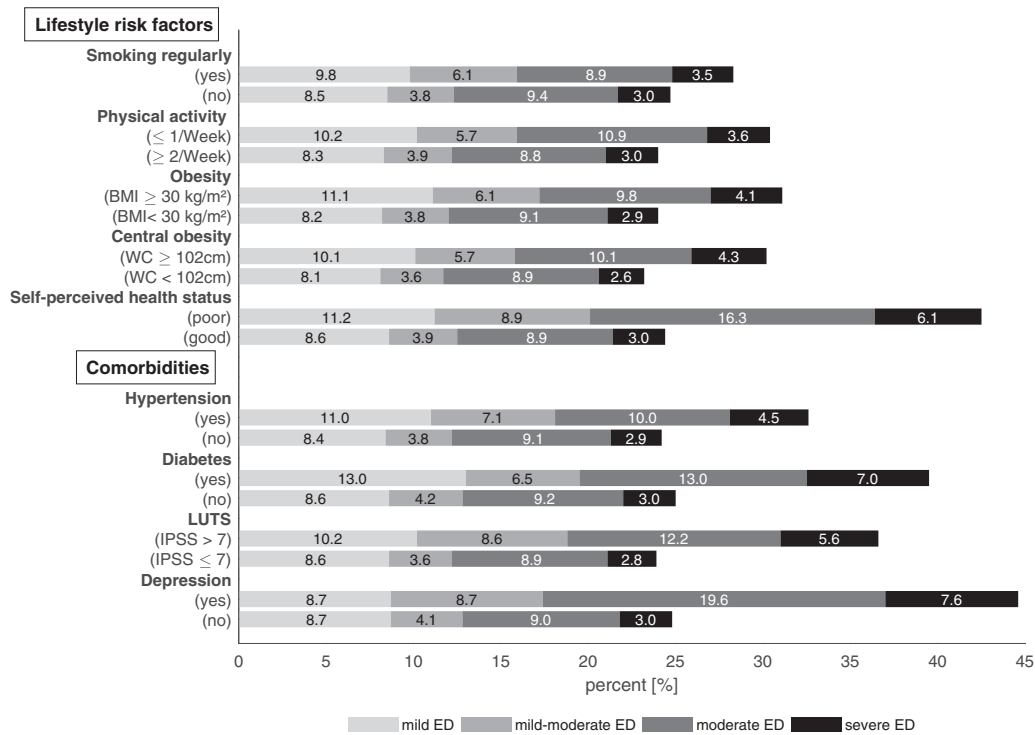


Figure 2. Degree of severity of ED depending on lifestyle risk factors and comorbidities. ED = erectile dysfunction; BMI = body mass index; WC = waist circumference; LUTS = lower urinary tract symptoms; IPSS = International Prostate Symptom Score.

the causal relationship between ED and depression cannot be drawn, given the possibility that ED can be either the symptom or the cause of depression. In addition, sexual dysfunction is a common adverse effect of antidepressant treatment.³⁷

The reported prevalence of ED in men with diabetes ranges from 35% to 90% as analyzed in cohorts with a wide age range, with most studies reporting on patients with a mean age of 54–66.³⁸ In our analysis, the prevalence of ED in 45-year-old

men with diabetes was 39.5%. The etiology of ED in diabetes is considered multifactorial, including vasculopathy, neuropathy, hypogonadism, and local factors such as fibrosis.³⁸ Likewise, LUTS and ED share the same pathophysiological mechanisms: alteration of the nitric oxide–cyclic guanosine monophosphate (cGMP) pathway, enhancement of RhoA–Rho-kinase contractile signaling, autonomic adrenergic hyperactivity, and pelvic atherosclerosis.³⁹ In the Cologne Male Survey, a statistically

Table 2. Logistic regression for the prevalence of ED in men assessing the impact of lifestyle risk factors and comorbidities

Parameter	Separate logistic regression			Multiple logistic regression after backward elimination (selection level 5%)		
	OR	95% CI	P value	OR	95% CI	P value
Lifestyle risk factors						
Smoking regularly (yes vs no)	1.20	1.08–1.35	.001	1.15	1.02–1.29	.024
Physical activity (< 1/wk vs ≥ 2/wk)	1.38	1.23–1.54	<.001	1.23	1.13–1.42	<.001
Obesity (BMI ≥ 30 kg/m² vs BMI < 30 kg/m²)	1.42	1.27–1.59	<.001	-	-	-
Central obesity (WC ≥ 102 cm vs WC < 102 cm)	1.44	1.31–1.59	<.001	1.31	1.18–1.45	<.001
Self-perceived health status (poor vs good)	2.29	1.90–2.75	<.001	1.72	1.41–2.10	<.001
Comorbidities						
Hypertension (yes vs no)	1.51	1.33–1.71	<.001	1.22	1.06–1.40	.005
Diabetes (yes vs no)	1.96	1.47–2.61	<.001	1.38	1.01–1.89	.043
LUTS (IPSS > 7 vs IPSS ≤ 7)	1.84	1.60–2.11	<.001	1.68	1.46–1.94	<.001
Depression (yes vs no)	2.44	1.92–3.11	<.001	1.87	1.44–2.43	<.001

BMI = body mass index; CI = confidence interval; ED = erectile dysfunction; IPSS = International Prostate Symptom Score; LUTS = lower urinary tract symptoms; OR = odds ratio; WC = waist circumference.

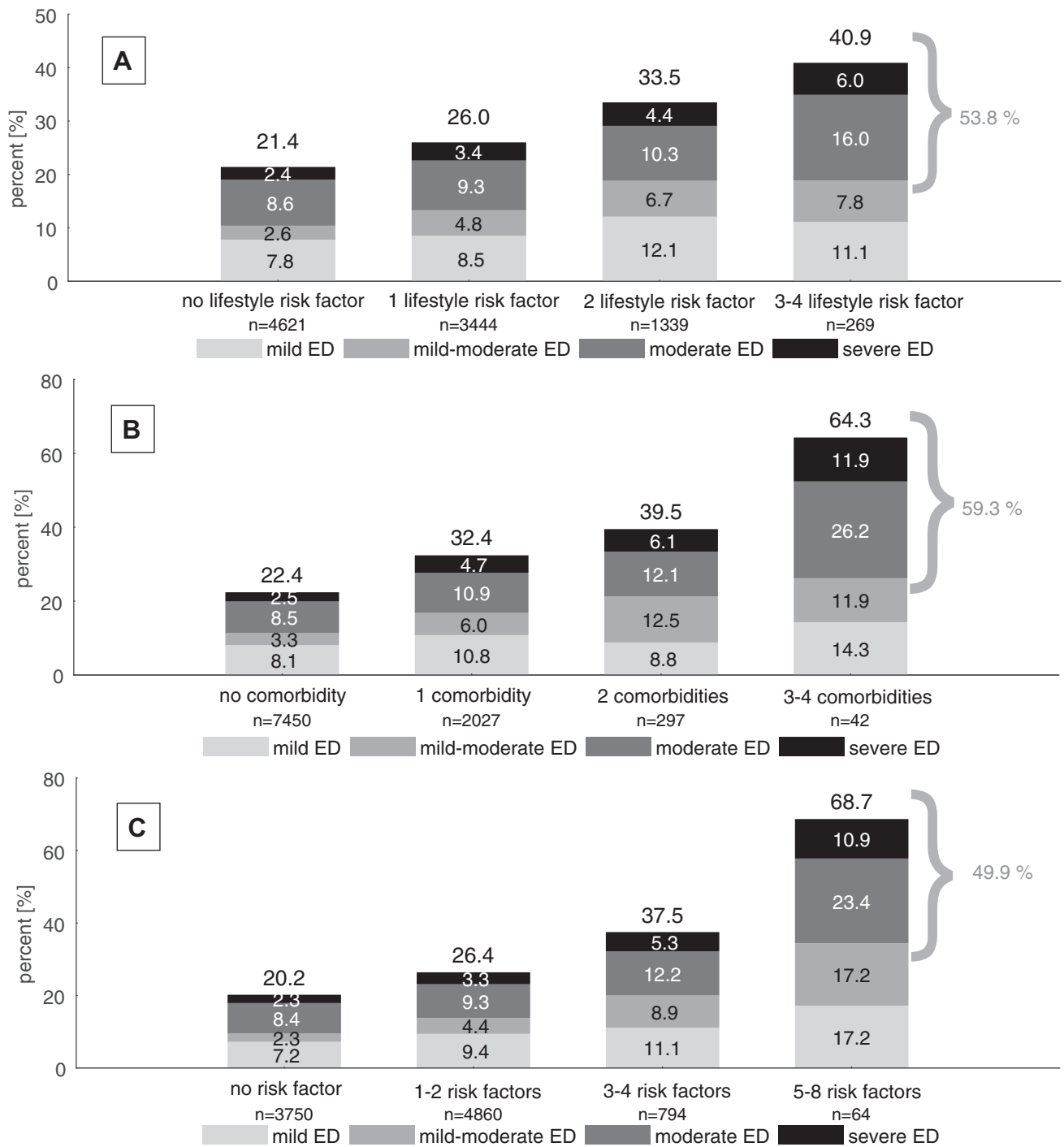


Figure 3. Distribution of degree of severity of ED by A, number of lifestyle risk factors (including smoking regularly, central obesity, physical inactivity, poor self-perceived health status); B, number of comorbidities (ie, hypertension, diabetes, lower urinary tract symptoms, or depression); and C, number of all 8 risk factors. ED = erectile dysfunction. *There were only 2 men with 7 risk factors, both with moderate ED; no subject had the concurrent presence of all 8 risk factors.

significant association between LUTS and ED was identified for the first time. The prevalence of LUTS was 72.2% in men with ED vs 37.7% in those without ED (OR = 2.11).⁴⁰ In our sample, we confirmed the impact of LUTS on ED, with an ED prevalence of 38.6% in men with LUTS vs 23.9% in those without LUTS.

Hypertension and most of the assessed lifestyle risk factors, including smoking, physical inactivity, and obesity, can induce arteriosclerotic changes and vascular obstruction.⁴¹ The pathophysiological link between ED and diseases affecting the cardiovascular system is attributed to endothelial dysfunction and veno-occlusive dysfunction due to limited blood flow.¹¹ In our

sample, the OR for ED in men with hypertension was 1.51. Previous research has identified ED as a marker for subclinical systemic vascular disease and has suggested that ED may serve as a sentinel for future cardiac events, such as apoplexy or myocardial infarction 3–5 years later.^{11,42} The threshold for symptoms due to arteriosclerotic involvement in vessels differs based on the extent of the reduction in lumen artery size; therefore, arteriosclerotic plaques will clinically manifest earlier in penile arteries than in coronary arteries.⁴³ This is why ED should be viewed as a warning signal for future vascular events. As in our investigation, 25.2% of 45-year old sexually active men reported on symptoms of ED, a screening for ED should be recommended in even younger men. Herewith it would be possible to select a group of men with ED that would benefit from prevention of cardiac events due to early medical treatment and lifestyle modifications.

In the present analysis, multiple logistic regression identified 8 of 9 assessed risk factors as significantly associated with ED. Only BMI was eliminated. Likewise, several studies have shown that waist circumference is more significant than BMI in evaluating obesity-related health risks.^{44,45}

We also analyzed the combination of all acquired risk factors except for BMI. We found that the presence of multiple comorbidities was associated with an increased ED prevalence of 64.3%, and that when including all 8 risk factors (lifestyle risk factors and comorbidities), the prevalence increased to 68.7%. The prevalence of multiple comorbidities had the strongest impact on the severity of ED; in affected men, almost 60% of those with ED had moderate or severe symptoms. The coexistence of several risk factors has been described previously^{46,47}; however, to our knowledge, the present study is the first to show the cumulative impact of lifestyle risk factors and comorbidities on ED prevalence and severity in 45-year-old men. Owing to the low numbers of subjects with 5–8 risk factors ($n = 64$) and subjects with 3–4 comorbidities, our data must be interpreted with caution. Nevertheless, the data clearly show an increase in risk with an increasing number of risk factors.

Several studies have indicated that a healthy lifestyle, like physical activity, can prevent ED or induce an improvement of existing ED.^{48,49} To estimate this preventive effect, we assessed ED prevalence in a subgroup of “healthy” men who were physically very active and had a healthy lifestyle without any assessed comorbidities; only 2.1% of the men met these criteria. Still, 14.4% of these healthy men had symptoms of ED. This rather high risk of ED in even healthy men suggests the presence of even more risk factors for ED. Clearly, early adoption of a healthy lifestyle is one approach to reduce the burden of ED.⁵⁰

The strengths of our analysis are that we provide reliable data on current ED prevalence in a large community-based, randomly selected cohort of same-aged men. Furthermore, all men were surveyed by physicians onsite, and ED was assessed using the IIEF-EF as a validated assessment tool, allowing for comparison of results. Limitations of our analysis include that use of the

IIEF-EF restricted our sample to only heterosexual and sexually active men. Moreover, some known risk factors, such as dyslipidemia and hypogonadism (verified via blood analysis), could not be ascertained in our study cohort comprising more than 10,000 participants. Moreover, the cohort of the GMS-Study as part of a screening trial might be oversampling more health-conscious men; previous studies have identified a “healthy user effect,” with healthier men more likely to use preventive health services such as screening.⁵¹ Consequently, our prevalences of obesity (17.8%), central obesity (29.2%), physical inactivity (19.2%), and smoking (18.6%) might be even higher in the general German population.

CONCLUSION

In our sample of 45-year-old German men, 1 in 4 already exhibited symptoms of ED. Almost one-half of the men with ED reported moderate or severe symptoms. Focusing on risk factors for ED, an increasing prevalence was observed, and all factors except BMI were identified as important risk factors for ED, with the strongest associations for depression, poor self-perceived health status, lower urinary tract symptoms, and diabetes. In addition, there was a direct association between increasing ED prevalence and increasing number of lifestyle risk factors and/or comorbidities. Thus, we conclude that it is important to identify modifiable risk factors in men with ED, and that in men with known risk factors, screening for ED is recommended for early vascular system evaluation. General practitioners may proactively ask about erectile complaints even in men as young as 45, with inquiries about ED integrated into routine examinations.

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REFERENCES

1. NIH Consensus Conference. Impotence. NIH Consensus Development Panel on Impotence. *JAMA* 1993;270:83-90.
2. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: Results of the Massachusetts Male Aging Study. *J Urol* 1994;151:54-61.
3. Rosen RC, Fisher WA, Eardley I, et al. The multinational Men's Attitudes to Life Events and Sexuality (MALES) study: I. Prevalence of erectile dysfunction and related health concerns in the general population. *Curr Med Res Opin* 2004;20:607-617.
4. Braun M, Wassmer G, Klotz T, et al. Epidemiology of erectile dysfunction: Results of the Cologne Male Survey. *Int J Impot Res* 2000;12:305-311.
5. McCabe MP, Sharlip ID, Lewis R, et al. Incidence and prevalence of sexual dysfunction in women and men: A consensus statement from the Fourth International Consultation on Sexual Medicine 2015. *J Sex Med* 2016;13:144-152.
6. Rosen RC, Riley A, Wagner G, et al. The international index of erectile function (IIEF): A multidimensional scale for assessment of erectile dysfunction. *Urology* 1997;49:822-830.
7. Rosen RC, Cappelleri JC, Gendrano N 3rd. The International Index of Erectile Function (IIEF): A state-of-the-science review. *Int J Impot Res* 2002;14:226-244.
8. May M, Gralla O, Knoll N, et al. Erectile dysfunction, discrepancy between high prevalence and low utilization of treatment options: Results from the Cottbus Survey with 10 000 men. *BJU Int* 2007;100:1110-1115.
9. Giuliano FA, Leriche A, Jaudinot EO, et al. Prevalence of erectile dysfunction among 7689 patients with diabetes or hypertension, or both. *Urology* 2004;64:1196-1201.
10. Guay AT. Sexual dysfunction in the diabetic patient. *Int J Impot Res* 2001;13(Suppl 5):S47-S50.
11. Hackett G, Krychman M, Baldwin D, et al. Coronary heart disease, diabetes, and sexuality in men. *J Sex Med* 2016;13:887-904.
12. Shaeer O, Shaeer K. The Global Online Sexuality Survey (GOSS): Erectile dysfunction among Arabic-speaking internet users in the Middle East. *J Sex Med* 2011;8:2152-2160 [quiz: 2160-2163].
13. Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* 2006;295:1549-1555.
14. Flegal KM, Kruszon-Moran D, Carroll MD, et al. Trends in obesity among adults in the United States, 2005 to 2014. *JAMA* 2016;315:2284-2291.
15. Mensink GB, Schienkiewitz A, Haftenberger M, et al. [Overweight and obesity in Germany: Results of the German Health Interview and Examination Survey for Adults (DEGS1)]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2013;56:786-794 [in German].
16. Heidemann C, Du Y, Schubert I, et al. [Prevalence and temporal trend of known diabetes mellitus: Results of the German Health Interview and Examination Survey for Adults (DEGS1)]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2013;56:668-677 [in German].
17. Arsov C, Becker N, Hadaschik BA, et al. Prospective randomized evaluation of risk-adapted prostate-specific antigen screening in young men: The PROBASE trial. *Eur Urol* 2013;64:873-875.
18. Goethe VE, Angerer H, Dinkel A, et al. Concordance and discordance of sexual identity, sexual experience, and current sexual behavior in 45-year old men: Results from the German Male Sex-Study. *Sex Med* 2018;6:282-290.
19. Kögel AM, Dinkel A, Marten-Mittag B, et al. [Self-concept and erectile dysfunction in 45-year-old men: Results of a corollary study of the PROBASE trial]. *Urologe A* 2016;55:1321-1328 [in German].
20. Cappelleri JC, Rosen RC, Smith MD, et al. Diagnostic evaluation of the erectile function domain of the International Index of Erectile Function. *Urology* 1999;54:346-351.
21. World Health Organization. Waist circumference and waist-hip ratio: Report of a WHO expert consultation. Geneva: World Health Organization; December 8-11, 2008.
22. Radoschewski M, Bellach BM. [The SF-36 in the Federal Health Survey: Possibilities and requirements for application at the population level]. *Gesundheitswesen* 1999;61; Spec No: S191-S199 [in German].
23. Barry MJ, Fowler FJ Jr, O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. Measurement Committee of the American Urological Association. *J Urol* 1992;148:1549-1557 [discussion: 1564].
24. Englert H, Schaefer G, Roll S, et al. Prevalence of erectile dysfunction among middle-aged men in a metropolitan area in Germany. *Int J Impot Res* 2007;19:183-188.
25. Pohnholzer A, Temml C, Mock K, et al. Prevalence and risk factors for erectile dysfunction in 2869 men using a validated questionnaire. *Eur Urol* 2005;47:80-85 [discussion: 85-86].
26. Giugliano F, Esposito K, Di Palo C, et al. Erectile dysfunction associates with endothelial dysfunction and raised proinflammatory cytokine levels in obese men. *J Endocrinol Invest* 2004;27:665-669.

27. Esposito K, Giugliano F, Ciotola M, et al. Obesity and sexual dysfunction, male and female. *Int J Impot Res* 2008;20:358-365.
28. Akbartabartoori M, Lean ME, Hankey CR. Smoking combined with overweight or obesity markedly elevates cardiovascular risk factors. *Eur J Cardiovasc Prev Rehabil* 2006;13:938-946.
29. Bacon CG, Mittleman MA, Kawachi I, et al. A prospective study of risk factors for erectile dysfunction. *J Urol* 2006;176:217-221.
30. Lee RK, Chung D, Chughtai B, et al. Central obesity as measured by waist circumference is predictive of severity of lower urinary tract symptoms. *BJU Int* 2012;110:540-545.
31. Selvin E, Burnett AL, Platz EA. Prevalence and risk factors for erectile dysfunction in the US. *Am J Med* 2007;120:151-157.
32. McVary KT, Carrier S, Wessells H. Smoking and erectile dysfunction: Evidence-based analysis. *J Urol* 2001;166:1624-1632.
33. Feldman HA, Johannes CB, Derby CA, et al. Erectile dysfunction and coronary risk factors: Prospective results from the Massachusetts Male Aging Study. *Prev Med* 2000;30:328-338.
34. Araujo AB, Durante R, Feldman HA, et al. The relationship between depressive symptoms and male erectile dysfunction: Cross-sectional results from the Massachusetts Male Aging Study. *Psychosom Med* 1998;60:458-465.
35. Shabsigh R, Klein LT, Seidman S, et al. Increased incidence of depressive symptoms in men with erectile dysfunction. *Urology* 1998;52:848-852.
36. Suija K, Kerkelä M, Rajala U, et al. The association between erectile dysfunction, depressive symptoms and testosterone levels among middle-aged men. *Scand J Public Health* 2014;42:677-682.
37. Gregorian RS, Golden KA, Bahce A, et al. Antidepressant-induced sexual dysfunction. *Ann Pharmacother* 2002;36:1577-1589.
38. Malavige LS, Levy JC. Erectile dysfunction in diabetes mellitus. *J Sex Med* 2009;6:1232-1247.
39. Gacci M, Eardley I, Giuliano F, et al. Critical analysis of the relationship between sexual dysfunctions and lower urinary tract symptoms due to benign prostatic hyperplasia. *Eur Urol* 2011;60:809-825.
40. Braun MH, Sommer F, Haupt G, et al. Lower urinary tract symptoms and erectile dysfunction: Co-morbidity or typical "Aging Male" Symptoms? Results of the Cologne Male Survey. *Eur Urol* 2003;44:588-594.
41. Fung MM, Bettencourt R, Barrett-Connor E. Heart disease risk factors predict erectile dysfunction 25 years later: The Rancho Bernardo Study. *J Am Coll Cardiol* 2004;43:1405-1411.
42. Roumeguère T, Wespes E, Carpentier Y, et al. Erectile dysfunction is associated with a high prevalence of hyperlipidemia and coronary heart disease risk. *Eur Urol* 2003;44:355-359.
43. Montorsi P, Montorsi F, Schulman CC. Is erectile dysfunction the "tip of the iceberg" of a systemic vascular disorder? *Eur Urol* 2003;44:352-354.
44. Després JP, Lemieux I, Prud'homme D. Treatment of obesity: Need to focus on high-risk abdominally obese patients. *BMJ* 2001;322:716-720.
45. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* 2004;79:379-384.
46. Litwin MS, Nied RJ, Dhanani N. Health-related quality of life in men with erectile dysfunction. *J Gen intern Med* 1998;13:159-166.
47. Esposito K, Giugliano F, Martedì E, et al. High proportions of erectile dysfunction in men with the metabolic syndrome. *Diabetes Care* 2005;28:1201-1203.
48. Esposito K, Giugliano F, Di Palo C, et al. Effect of lifestyle changes on erectile dysfunction in obese men: A randomized controlled trial. *JAMA* 2004;291:2978-2984.
49. Agostini LC, Netto JM, Miranda MV Jr, et al. Erectile dysfunction association with physical activity level and physical fitness in men aged 40–75 years. *Int J Impot Res* 2011;23:115-121.
50. Derby CA, Mohr BA, Goldstein I, et al. Modifiable risk factors and erectile dysfunction: Can lifestyle changes modify risk? *Urology* 2000;56:302-306.
51. Brookhart MA, Patrick AR, Dormuth C, et al. Adherence to lipid-lowering therapy and the use of preventive health services: An investigation of the healthy user effect. *Am J Epidemiol* 2007;166:348-354.