The Contribution of Common Medical Conditions and Drug Exposures to Erectile Dysfunction in Adult Males

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Purpose: We examined the association of prevalent erectile dysfunction and coexisting medical conditions in United States men taking into account age and drug exposures.

Materials and Methods: Men older than 40 years who participated in the 2001 to 2002 National Health and Nutrition Examination Survey were asked to report on erectile function. Men who were never able to achieve an erection sufficient for intercourse were defined as having complete erectile dysfunction. Adjusted odds ratios for complete erectile dysfunction prevalence in men with a coexisting condition compared to those without the condition were calculated. Age, race/ethnicity, urinary symptoms, cardiovascular disease, diabetes, hypertension with and without selected antihypertensive therapy (mainly beta blockers and thiazide diuretics), selected antidepressant therapy (mainly, tricyclics and selective serotonin reuptake inhibitors), smoking and alcohol were included in all statistical models.

Results: Of United States men 8% (95% CI 6.0–10.2) reported complete erectile dysfunction. In multivariate analyses, obstructive urinary symptoms (OR 2.0, 95% CI 1.2–3.4), diabetes (OR 2.6, 95% CI 1.3–5.2), hypertension with selected antihypertensive therapy (OR 3.0, 95% CI 1.6–5.9), and selected antidepressant therapy (OR 5.2, 95% CI 1.7–15.9), increased the odds of complete erectile dysfunction prevalence, whereas presence of cardiovascular disease, urinary incontinence and hypertension without selected antihypertensive therapy did not.

Conclusions: Obstructive urinary symptoms, diabetes, hypertension treated with selected medications, and selected antidepressant drug use are independently associated with increased erectile dysfunction risk in United States men. Physicians should carefully consider the potential impact of these medications and comorbid conditions when discussing sexual function with their male patients.

Keywords: impotence; comorbidity; perscriptions, drug; health surveys

Erectile dysfunction is a common disorder, especially among older men, that can affect overall quality of life. Multiple factors have contributing roles in its development[1,2] and community based studies have found that ED occurs more frequently in men with lower urinary tract symptoms,[3–8] diabetes,[8–12] hypertension[7,9,10] and cardiovascular disease[6,8–10] than in men without these comorbidities. However, only a few investigations describing the joint relation of these medical conditions and ED risk in community dwelling men have been performed to date and none in United States men.[8,12] Other studies suggest that drug exposures, including prescribed drugs for hypertension, depression and anxiety disorders, as well as alcohol intake and cigarette smoking, may increase ED risk.[1,2] Only 1 United States study has controlled for typical drug exposures in evaluating risk factors for ED in aging men, and that study was not population based, described healthier men than the general population and did not consider LUTS.[11]

A better understanding of the importance of coexisting chronic medical conditions and drug exposures on the risk of ED in the general population might lead to strategies to reduce the burden of the disorder. We examined the relationship between self-reported complete ED prevalence and certain urological and other chronic medical conditions of aging men (lower urinary tract symptoms, hypertension, diabetes and CVD) in the general population, taking into account the effects of selected drug exposures that may adversely affect erectile function.

METHODS

Data Collection

The National Health and Nutrition Examination Survey, conducted by the National Center for Health Statistics, collects a wide range of health related information from samples of the civilian noninstitutionalized population of children and adults. A 4-stage probability sample design described elsewhere provides a representative sample of residents.[13] During home and MEC scheduled visits, 1,370 male participants in the 2001-2002 NHANES provided the data we analyzed and present here. Men in the sample ranged from 40 to 85 years old. Questionnaires were administered by interviewers and computer assisted self-inter-

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view, the latter used at the MEC to collect information on urogenital system disorders.

Sexual and Urological Function

We categorized erectile dysfunction as none, minimal, moderate or complete using responses to the question (with defining labels), "Many men experience problems with sexual intercourse. How would you describe your ability to get and keep an erection adequate for satisfactory intercourse? Would you say that you are always able or almost always able to get and keep an erection (no ED), usually able to get and keep and erection (minimal ED), sometimes able to get and keep an erection (moderate ED), never able to get and keep an erection?" (complete ED). Our focus is men with complete ED, and we chose this restricted definition because it is potentially less subject to interpretation variation across population subgroups. An obstructive urinary symptom was determined to be present in men who responded yes to "Do you usually have trouble starting to urinate (pass water)?" or no to "After urinating (passing water) does your bladder feel empty?" Three urinary incontinence questions began with the phrase, "During the past 12 months have you leaked or lost control of even a small amount of urine?" Positive responses to leakage in the last year "with an activity like coughing, lifting or exercise?" defined stress UI, "with an urge or pressure to urinate and you could not get to the toilet fast enough?" defined urge UI, and "without an activity like coughing, lifting, or exercise, or an urge to urinate?" defined other UI.

Clinical Parameters

Blood pressure was measured 3 times during each visit. The separate systolic and diastolic readings were averaged. A participant was classified as having hypertension if the mean systolic pressure was 140 mm Hg or greater or mean diastolic pressure was 90 mm Hg or greater, or he self-reported taking medication for control of blood pressure. Previous diagnoses of angina, or heart attack, or coronary heart disease defined respondents with CVD history. Men who reported a prior diagnosis of diabetes or sugar diabetes were defined as diagnosed diabetics. Alcohol use patterns were classified as abstains, 1 to less than 7 drinks per week, 7+ drinks per week. Cigarette smoking categories were current (smokes every day or some days), former (previously smoked in the past but not currently) and never smoker. BMI was calculated as kg/m^2.

Prescription Drugs

During the in-home interview participants were asked about prescription medication use in the last month and to show the interviewer all medication containers. The product name of each medication was entered into a computerized comprehensive prescription drug database, and assigned a standard generic ingredient name and drug code. We used these codes to define 2 drug use indicator variables (yes, no) to connote prescription drug exposures that may adversely affect sexual function.[1] AHBPmed indicated use of antihypertensive drugs such as thiazide diuretics, spironolactone, beta blockers, methyldopa or clonidine. ADEPmed indicated use of the antidepressant drugs selective serotonin reuptake inhibitors, tricyclics except desipramine, any monoamine oxidase inhibitor, thioridazine, fluphenazine or clonazepam.

Analysis

Of the 1,538 men who were at least 40 years old with no history of prostate cancer in the 2001-2002 NHANES 168 had incomplete or missing information on erectile function and were excluded from the analysis. Prevalence of ED was estimated for strata determined by demographic characteristics, coexisting medical conditions, prescription drug use and other health related factors. Age standardized rates were computed using the 2000 Census distribution for adult males as the standard and compared using the independent groups t test. These comparisons revealed variables with a p value less than 0.10 for inclusion in multivariate analyses. Adjusted odds ratios and corresponding 95% confidence intervals for ED prevalence were calculated using logistic regression: age in years (continuous), race/ethnicity and health conditions (presence of urinary symptoms, diabetes, CVD history, hypertension status with and without AHBPmed therapy, ADEPmed use, cigarette smoking and alcohol intake) were included in all models. History of prostate disease was not a variable in these models. All analyses, conducted using SUDAAN®, provided weighted estimates that account for survey design, oversampling and nonparticipation rates. Two-sided p values less than 0.05 were considered statistically significant.

RESULTS

The sample of 1,370 men represents a study population of 51 million community dwelling men at least 40 years old with no history of prostate cancer and a profile of other chronic conditions consistent with expectations (table 1). The mean age was 54.4 years (SE 0.32) and prevalence of complete ED was 8.1% (95% CI 6.1–10.1). Rates of incomplete bladder emptying (10.0%) and urge urinary incontinence (10.8%) were similar, with the latter about twice as common as stress (5.1%) or other (4.0%) urinary incontinence. Prevalence of diagnosed diabetes, cardiovascular disease and hypertension was 10.6%, 13.0% and 34.7%, respectively. More than half (57%) of these men were taking at least 1 prescribed medication during a given month.

As shown in the figure the prevalence of complete ED, incomplete bladder emptying, trouble with urination start and UI of any kind increased with advancing age such that of men 80 years old or older more than half (56%) reported complete ED and 47% reported UI (stress, urge or other). In bivariate analyses that controlled for age, some comorbid conditions (obstructive urinary symptoms, diabetes and hypertension with AHBPmed therapy) but not others (urinary incontinence of any kind, cardiovascular disease, BMI) were significantly associated with increased prevalence of complete ED (table 2).

Multivariate analyses results were adjusted for age, race/ethnicity, diabetes, cardiovascular disease history, hypertension with and without AHBPmed therapy, obstructive urinary symptoms, ADEPmed therapy, cigarette smoking and alcohol intake (table 3). The following factors were associated with increased complete ED prevalence in all men: obstructive urinary symptoms (OR 2.02, 95% CI 1.2–3.4), hypertension with AHBPmed therapy (OR 3.04, 95% CI 1.6–5.9), diabetes (OR 2.57, 95% CI 1.3–5.2), ADEPmed

TABLE 1. *Characteristics of United States men at least 40 years old with no history of prostate cancer*

	Sample Count	Mean % Study Population (SE)*
NonHispanic white	792	79.6 (2.44)
Less than high school completion	416	16.7 (1.39)
Married or cohabiting	973	77.0 (1.96)
Erectile dysfunction:		
None	580	53.2 (1.78)
Minimum	310	21.2 (1.27)
Moderate	298	17.5 (1.05)
Complete	182	8.1 (1.02)
Urinary conditions:		
Bladder emptying incomplete	205	10.0 (0.81)
Trouble with urination start	119	6.2 (0.74)
Urge incontinence	220	10.8 (0.91)
Stress incontinence	94	5.1 (0.61)
Other incontinence	84	4.0 (0.38)
Other comorbidities:		
Diagnosed diabetes	185	10.6 (0.85)
Hypertension	599	34.7 (2.09)
CVD history	242	13.0 (1.31)
Prior stroke	59	2.3 (0.28)
Congestive heart failure	64	3.4 (0.53)
Prostate disease diagnosis	218	12.6 (0.90)
BMI 30 kg/m^2 or greater	384	29.7 (1.06)
Current prescription medications:		
1 or More prescription drugs	817	57.0 (2.05)
AHBPmeds†	228	13.4 (1.70)
ADEPmeds‡	77	6.7 (1.07)
Current cigarette smoker	479	39.7 (2.60)
Alcohol intake:		
Abstains	445	28.2 (0.96)
1–7 Drinks/wk	625	48.1 (1.55)
7 or More drinks/wk	298	29.7 (1.06)

* Statistics represent national estimates produced after application of sampling weights to raw sample counts.
† Antihypertensives that are thiazide diuretics, spironolactone, beta blockers, methyldopa or clonidine.
‡ Antidepressants that are selective serotonin reuptake inhibitors, any tricyclic agent except desipramine, any monoamine oxidase inhibitor, thioridazine, fluphenazine or clonazepam.

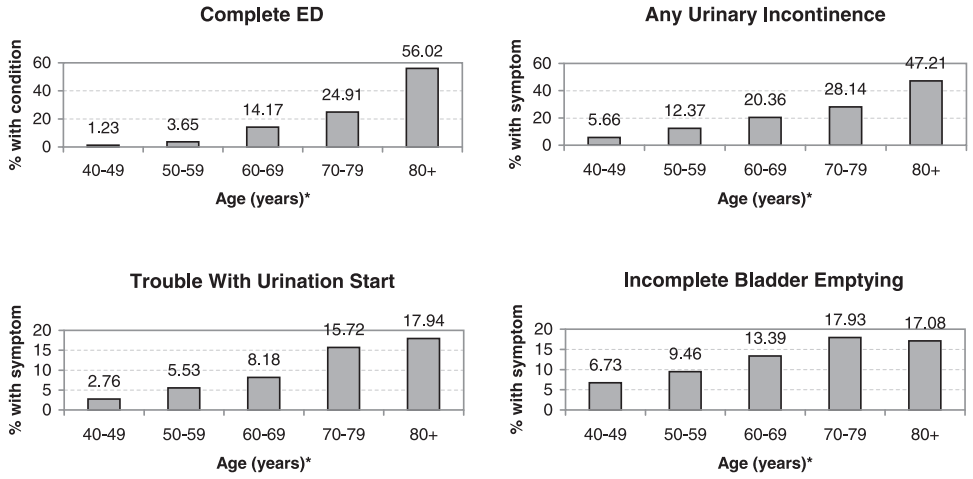
therapy (OR 5.19, 95% CI 1.7–15.9), former cigarette smoking (OR 1.93, 95% CI 1.2–3.2) and age (OR 1.12, 95% CI 1.09–1.14). By contrast, there was no association between complete ED prevalence and race/ethnicity, cardiovascular disease history or hypertension without AHBPmed therapy. When these analyses were repeated by excluding diabetic men, the observed significant associations did not substantively change. Alcohol consumption appeared to be inversely related to complete ED prevalence in the study population: compared with men who did not drink alcohol, men who drank 1 to 6 drinks per week were less likely to report complete ED (OR 0.49, 95% CI 0.3–0.95), but consumers of 7 or more drinks per week were not (OR 0.52, 95% CI 0.3–1.1).

In multivariate analysis models that included any UI as an explanatory variable instead of obstructive urinary symptoms, we found associations of similar magnitude and significance for all study covariates (data not shown). Odds ratios for complete ED prevalence in men with any urinary incontinence compared to those without the problem were not significant (OR 1.13, 95% CI 0.6–2.2 among all men and OR 1.13, 95% CI 0.6–2.3 among men without diagnosed diabetes).

DISCUSSION

We found that 1 of every 12 middle-aged-to-older community dwelling men self-reports complete ED and that potentially modifiable factors are associated with this disorder. Men with obstructive urinary symptoms had a 2-fold increase in the odds of prevalent complete ED compared to those without such symptoms, using fully adjusted models. In addition to confirming previously described independent associations of age, diabetes and antidepressant medication use with ED risk, our results extend published findings by demonstrating that selected prescribed medications for treatment of hypertension, and not the condition itself, contributes significantly to the risk of ED.

Impaired erectile function may result from psychogenic and/or physiological factors. Detection of this disorder in the present study was by computer assisted self-interview questionnaire and men who self-report never being able to get and keep an erection were defined to have complete ED. We believe that complete ED identifies a clinically significant



*Age group sample sizes were 416 (40-49 yrs), 326 (50-59 yrs), 277 (60-69 yrs), 220 (70-79 yrs) and 131 (80+ yrs).

Weighted prevalence of complete erectile dysfunction, any UI, trouble with urination start and incomplete bladder in United States men at least 40 years old with no history of prostate cancer.

TABLE 2. *Prevalence of complete ED by principle analysis variables*

	Sample Count*	% Prevalence Complete ED (SE) Crude†	Age Standardized‡	p Value§
Trouble with urination start:				
Yes	119	29.2 (5.42)	20.3 (3.88)	0.0054
No	1,243	6.7 (0.89)	8.7 (1.00)	
Incomplete bladder emptying:				
Yes	205	16.7 (2.11)	14.1 (1.46)	0.0008
No	1,153	7.1 (1.01)	9.1 (1.03)	
Obstructive urinary symptoms:				
Yes	271	19.3 (2.62)	15.2 (2.29)	0.0069
No	1,098	6.3 (0.92)	8.5 (1.02)	
Urge incontinence:				
Yes	220	19.5 (3.01)	12.3 (2.47)	0.2740
No	1,146	6.6 (1.07)	9.2 (1.30)	
Stress incontinence:				
Yes	94	22.6 (5.74)	16.3 (4.42)	0.1068
No	1,271	7.2 (0.99)	9.3 (1.00)	
Other incontinence:				
Yes	84	26.8 (3.83)	17.6 (3.08)	0.0263
No	1,282	7.3 (1.01)	9.3 (1.06)	
Any incontinence:				
Yes	263	18.0 (2.59)	11.8 (2.00)	0.2883
No	1,107	6.7 (1.09)	9.2 (1.33)	
CVD history:				
Yes	240	20.6 (3.66)	11.7 (1.99)	0.1627
No	1,130	6.2 (0.96)	8.9 (1.09)	
Diagnosed diabetes:				
Yes	185	19.4 (4.67)	17.8 (3.50)	0.0126
No	1,185	6.8 (0.79)	8.5 (0.82)	
Hypertension:				
Yes, uses AHBPmeds	193	23.7 (4.34)	20.6 (5.37)	0.0269
Yes, no AHBPmeds	406	11.9 (1.43)	10.2 (1.22)	0.0694
No	771	4.1 (0.85)	6.6 (1.14)	
Smokes cigarettes:				
Currently	322	4.1 (1.29)	7.0 (1.99)	0.4757
Formerly	567	13.1 (1.86)	11.6 (1.45)	0.1081
Never	479	5.7 (0.96)	8.5 (1.26)	
Alcohol use:				
7+ Drinks/wk	298	5.5 (1.17)	8.3 (1.45)	0.0536
1–7 Drinks/wk	625	5.6 (1.12)	7.5 (1.34)	0.0204
Abstains	445	14.6 (2.85)	14.0 (2.37)	
BMI (kg/m^2):				
Obese (30 or greater)	384	9.7 (2.19)	13.2 (2.07)	0.1392
Overweight (25–30)	594	5.3 (0.79)	6.8 (1.04)	0.2719
Normal (less than 25)	325	7.6 (1.33)	8.8 (1.44)	
ADEPmeds user:				
Yes	77	19.7 (4.83)	22.6 (5.64)	0.0248
No	1,282	7.3 (0.90)	8.9 (0.87)	

* The strata sample counts may not sum to 1,370 because of missing values for some variables.
† National estimate produced after application of sampling weights to raw sample counts.
‡ Standardized to the 2000 Census population using age groups 40 to 49, 50 to 59, 60 to 69, 70+ years.
§ p Value for comparison of age adjusted prevalence estimates.

condition and is less subject to varying respondent interpretation, although other investigations have incorporated less severe degrees of impaired sexual function in definitions of ED. Furthermore, our definition facilitates across-study comparisons. The 8.1% prevalence of complete ED (95% CI 6.1 to 10.1) observed here is within the range reported in the Olmsted County, Minnesota population based study (6.4%)[14] and the Massachusetts Male Aging Study (11.8%),[11] and suggests that our approach identifies men with this condition.

The 2-fold increased odds of ED prevalence associated with obstructive urinary symptoms that we observed in men after controlling for age, race/ethnicity, coexisting disease, adverse drug use and smoking is similar in magnitude to that found in Austrian men,[15] where LUTS were assessed with the International Prostate Symptom Score and ED was assessed with the abridged 5-item version of the International Index of Erectile Function. Other studies have shown that ED prevalence increases with increased LUTS severity independent of age.[6–8,12] Several hypotheses on the link between these 2 conditions have been proposed including decreased nitric oxide levels, autonomic hyperactivity and pelvic atherosclerosis among others.[16]

A number of studies have observed increased ED prevalence associated with hypertension.[7,9–12] However, findings from most community based studies are not fully adjusted for known confounding factors. Among studies that adjusted for antihypertensive medications and other comorbidities, the association between hypertension and ED was found to be weak in one[11] and nonsignificant in another.[8] Importantly, we found hypertensive men who used selected antihypertensive therapy (specifically thiazide diuretics, spironolactone, beta blockers, methyldopa and clonidine) had increased odds of complete ED prevalence that were 3-fold greater than normotensive men and 2.4-fold greater than hypertensive men who did not use these therapies. Since complete ED prevalence was not significantly different between normotensive and hypertensive men who did not use these therapies, our results suggest the specific therapy significantly contributes to prevalent ED. Confounding by disease severity remains a possible explanation for this finding, particularly if the selected antihypertensive medications are more likely to be prescribed in men with more severe disease than other medications for hypertension treatment and control.

Our finding of a strong association between diabetes and complete ED prevalence is similar to results from most[8–12] but not all studies of ED risk factors in community dwelling men.[6] A recent study has revealed that ED is a predictor of the metabolic syndrome,[17] which offers support for an intrinsic link between diabetes and ED. The association between cardiovascular disease and ED prevalence has received considerable research attention,[6–12] with inconsistent results. We found no independent association between cardiovascular disease and complete ED prevalence, which agrees with 4 previous reports[7,9,11,12] but conflicts with 3 other reports.[6,8,10] However, all previous studies but one[8] did not control for LUTS,[9–11] or for use of prescription medications considered here.[6,7,9,10,12]

Previous community based studies of ED risk associated with other drug exposures including antidepressant use,[8,11] alcohol intake[11,12] and cigarette smoking[6–8,11,12] have reported findings that are generally confirmed in our analyses. The 5-fold increase in odds of self-reported complete ED among men who used selected antidepressant therapy (principally selective serotonin reuptake inhibitors and tricyclics) is striking and exceeds the risk of ED attributed to depression symptoms or diagnosis[3,10,12] and general antidepressant use.[8,11] Whether this reflects an effect of the underlying depression/anxiety disorder or the psychotherapeutic agents used to treat the disorder cannot be disentangled since the NHANES did not collect information on symptoms or clinical diagnoses of depression.

Our study has several strengths including use of a nationally representative sample of men, consideration of mul-

TABLE 3. *Odds ratios and 95% confidence intervals for complete ED*

		All Men (1,370)		Nondiabetic Men (1,285)	
Dependent Variables	Categories	Adjusted OR*	95% CI	Adjusted OR*	95% CI
Age	Continuous	1.12	1.09–1.14	1.13	1.10–1.16
Race/ethnicity	NonHispanic white	1.00		1.00	
	NonHispanic black	0.46	0.2–1.0	0.55	0.2–1.4
	Mexican-American	0.93	0.3–2.7	1.44	0.5–4.0
	Other	0.58	0.2–1.7	0.51	0.1–3.3
Obstructive symptoms	No	1.00		1.00	
	Yes	2.02	1.2–3.4	2.17	1.1–4.2
Hypertensive†	No	1.00		1.00	
	Yes, AHBPmed nonuser‡	1.35	0.7–2.6	1.65	0.8–3.5
	Yes, AHBPmed user‡	3.04	1.6–5.9	4.01	1.8–9.0
Diagnosed diabetes	No	1.00			
	Yes	2.57	1.3–5.2	—	—
History of CVD	No	1.00		1.00	
	Yes	0.85	0.4–1.8	0.86	0.4–2.0
User of ADEPmeds§	No	1.00		1.00	
	Yes	5.19	1.7–15.9	9.12	3.0–27.6
Cigarette use	Never	1.00		1.00	
	Former	1.93	1.2–3.2	1.87	1.0–3.7
	Current	1.41	0.6–3.2	1.20	0.6–2.6
Alcohol intake	Abstains	1.00		1.00	
	1–7 Drinks/wk	0.49	0.3–0.95	0.48	0.2–1.1
	7+ Drinks/wk	0.52	0.3–1.1	0.55	0.3–1.2

* Adjusted for all variables in the table.

† Multivariate adjusted odds ratio of complete ED in all men using as the reference group hypertensive men with nonuse of AHBPmed therapy. OR 0.61 (95% CI 0.28–1.29) for normotensive men. OR 2.43 (95% CI 1.34–4.40) for hypertensive men with use of AHBPmed.

‡ AHBPmeds identifies antihypertensives that are thiazide diuretics, spironolactone, beta blockers, methyldopa or clonidine. Among hypertensive men 98 used a beta blocker and no other AHBPmed, 57 used a thiazide diuretic and no other AHBPmed, 2 used spironolactone and no other AHBPmed, 29 used a beta blocker and a thiazide diuretic, 5 used spironolactone and a beta blocker, 1 used spironolactone and a beta blocker and a thiazide diuretic, 1 used methlydopa or clonidine but no other AHBPmed.

§ ADEPmeds identifes antidepressants that are selective serotonin reuptake inhibitors, any tricyclic agent except desipramine, any monoamine oxidase inhibitor, thioridazine, fluphenazine or clonazepam.

tiple risk factors in all men, as well as nondiabetic men, and a low nonresponse rate (7.7%) to the ED question that reduces the likelihood of bias. Some limitations should also be noted. We used a single question to assess erectile function. However, this question closely reflected a National Institutes of Health consensus panel definition of the condition,[18] mirrored approaches used in recently published studies,[11,17] and had similar wording to a question that had been previously shown to accurately predict the clinically diagnosed condition.[19] We assessed obstructive urinary symptoms using 2 of the 4 questions available on the International Prostate Symptom Score, but information on severity and bother of symptoms was not available in the 2001-2002 NHANES. Finally, this was a cross-sectional study and these associations do not imply causal relationships.

CONCLUSIONS

Our findings indicate that obstructive urinary symptoms, diabetes and hypertension with certain therapeutic regimens are independently associated with increased ED prevalence, while cardiovascular disease history and hypertension with other therapeutic regimens have a small nonsignificant effect on ED risk. The strong association between prevalent ED and certain antidepressant use, highlights the need for further research on the temporal relation of ED and depression. Clinicians also need to be sensitive to the dosing implications of antihypertensive and antidepressant medications on their male patient's sexual functioning.

Abbreviations and Acronyms

ADEPmed	=	antidepressant
AHBPmed	=	antihypertensive
BMI	=	body mass index
CVD	=	cardiovascular disease
ED	=	erectile dysfunction
LUTS	=	lower urinary tract symptoms
MEC	=	mobile examination center
NHANES	=	National Health and Nutrition Examination Survey
UI	=	urinary incontinence

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EDITORIAL COMMENT

Erectile dysfunction is commonly associated with aging and cardiovascular risk factors. This article by Francis et al, the third in the trilogy of NHANES articles on sexual dysfunction, reinforces that notion (reference 9 in article).[1] The surprising finding that the presence of CVD, urinary incontinence and hypertension without selected antihypertensive therapy did not increase the odds of ED, is at odds with the currently accepted ED associations. ED is associated with hypertension. Worsening of ED is associated with worsening LUTS symptoms. Urinary incontinence should suggest more advanced ED. ED is considered an early signal for CVD.

While these data are helpful, it is time to delve into the mechanisms underlying these diseases that impact on erectile function. Factor VII, vascular cell adhesion molecule, intracellular adhesion molecule, seem to potential markers.[2] NHANES data reporting these markers might be an interesting sequel to the sexual dysfunction trilogy.

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