Published in final edited form as:

J Sex Med. 2010 February ; 7(2 Pt 1): 712–722. doi:10.1111/j.1743-6109.2009.01600.x.

Risk factors for incident erectile dysfunction among community-dwelling men

Susan A. Hall, Ph.D.¹, Rebecca Shackelton, M.S.¹, Raymond C. Rosen, Ph.D.¹, and Andre B. Araujo, Ph.D.¹

¹New England Research Institute- Community Health Studies, Watertown, Massachusetts, USA

Abstract

Introduction—Compared to the prevalence of erectile dysfunction (ED), fewer studies have focused on the incidence of ED and even fewer have focused on non-medical risk factors.

Aim—We examined psychosocial, demographic/socioeconomic, medical/behavioral, and sexual function risk factors at T1 (1987–1989) and development of incident ED at T2 (1995–1997).

Methods—Longitudinal population-based epidemiologic study of 814 community-dwelling men participating in the Massachusetts Male Aging Study.

Main outcome measure—ED was defined according to a validated, discriminant-analytic formula based on questionnaire responses and categorized as moderate/complete ED vs. none/minimal. Multivariate logistic regression models (odds ratios [ORs] and 95% confidence intervals [CIs]) were used to estimate the association of risk factors with ED.

Results—Among 814 men free of ED at T1, 22% developed moderate/complete ED at T2 (on average approximately 8.8 years later). In a multivariate model, sexual function variables captured at baseline were inversely associated with ED (e.g., more or similar level of sexual arousal compared to adolescence vs. less, OR=0.56, 95% CI: 0.34, 0.92; frequency of sexual thoughts at least 2–3 times weekly vs. less, OR=0.55, 95% CI: 0.33, 0.92) after adjustment for age, education, and other risk factors.

Conclusions—Our results indicate that in the context of other risk factors, sexual desire variables at baseline were associated with incident ED. This in turn suggests that indications of reduced function appear earlier than ED itself, and that there may be a time window for intervention before a loss of erectile function.

Introduction

Few topics in men's health have received as much attention in the past decade as erectile dysfunction (ED). An explosion of clinical research and interest in ED followed the U.S. Food and Drug Administration's approval of the first PDE-5 inhibitor, sildenafil, in March 1998.¹ Since then, much has been learned about the prevalence and epidemiology of ED, in addition to its pathophysiology and clinical management. The public health importance of ED is not insubstantial, as it is now well-recognized as a risk factor or 'upstream' predictor of cardiovascular events.^{2–6} Cross-sectional analyses have repeatedly demonstrated that demographic and medical factors such as advanced age, obesity, diabetes, smoking and hypertension are associated with prevalent ED.^{7–11} The body of ED literature also now includes explorations of longitudinal determinants of incident ED,^{12–14} a recent analysis of how sexual function domains change together over time,¹⁵ and efforts to understand the

Conflict of Interest: All other authors have no conflict of interest.

natural history or 'disease course' of ED over time.^{16, 17} It has been observed that ED is not a stable disease state,¹⁶ and this in turn suggests a need for further in-depth study of factors associated with incident or new-onset ED. This may be of benefit in identifying potential non-pharmacologic targets for intervention, and/or new clinical harbingers of future ED.

Aims

Our objectives in this study were to comprehensively examine a broad range of psychosocial and sexual function parameters (in addition to health status and behavioral factors) to better understand predictors of incident ED in the context of other, more well-established risk factors.

Methods

Study design

The Massachusetts Male Aging Study (MMAS) is a population-based, longitudinal cohort study of aging, health, and endocrine and sexual function among a random sample of men observed at three time points (T1: 1987–89, T2: 1995–97, T3: 2002–04). The sampling design and field protocol have been described previously.¹⁸ Briefly, men aged 40–70 years old were randomly selected from eleven cities and towns near Boston, Massachusetts. Men in older age groups were oversampled to provide approximately equal proportions in each age decade (40–49, 50–59, 60–70). At baseline (T₁, 1987–89), a total of 1709 men (52% of 3,258 eligible) were enrolled in the study. A telephone survey of non-respondents (n=206) revealed that they were similar to respondents in general health and prevalence of chronic diseases.¹⁹ MMAS subjects were observed again in 1995–97 (T₂, n=1,156, 77% response rate) and 2002–04 (T₃, n=853, 65% response rate). These response rates were expected given the requirements for early-morning phlebotomy and extensive in-person interviews. As previously described, MMAS participants were typically white (95%), employed (78%) and married (75%), and most had completed a high school education (71%).¹⁸ The low representation of racial minorities (5%) was similar to the racial composition of the general population of Massachusetts; data from the 1990 United States Census indicate that only 9% of men 40–69 years old in Massachusetts were non-white.²⁰ Participants received no financial incentive at T₁, and \$50 and \$75 remunerations at T₂ and T₃, respectively. MMAS received institutional review board approval, and all participants gave written informed consent.

Data collection and health status variables

A trained field technician/phlebotomist visited each subject in his home and collected non-fasting blood samples within 4 hours of the subject's awakening to control for diurnal variation in hormone levels.²¹ Two samples were drawn 30 minutes apart and pooled for analysis in equal aliquots in order to smooth episodic secretion.²² Blood was kept in an ice-cooled container for transport and centrifuged within 6 hours. Serum was initially stored at –20°C, shipped to the laboratory within one week by same-day courier, and stored at –70°C until time of assay. Sex steroid measurements were performed at The Endocrine Laboratory at the University of Massachusetts Medical School (Worcester, MA). Total testosterone was measured in 1994 on stored T₁ serum by radioimmunoassay (RIA) kit (Diagnostic Products Corporation, Los Angeles, CA). Previous analyses showed negligible assay drift due to storage.²³ The inter-assay coefficient of variation (CV) was 8.0%. Free testosterone was calculated from testosterone and sex hormone binding globulin using the mass action equations described by Södergard,²⁴ with association constants for testosterone taken from Vermeulen.²⁵ High-density lipoprotein (HDL) cholesterol was measured at T₁ by a standard technique at a CDC-certified lipid laboratory (Miriam Hospital, Providence,

RI). Anthropometric data on height, weight, and waist and hip circumference were obtained using standardized procedures developed for large-scale epidemiological field studies.²⁶ Two blood pressure (BP) measures were obtained at time points 25 minutes apart during the interview, and averaged. The following information was collected via interviewer-administered questionnaire: demographics, psychosocial factors, history of chronic disease, self-assessed general health status, tobacco and alcohol use, nutritional intake, a full medication inventory, a set of common complaints (e.g., headaches, backaches, trouble sleeping), and physical activity/energy expenditure during the past seven days.

Sexual function and psychosocial variables

The MMAS self-administered questionnaire on sexual activity included 23 items related to sexual function including quantity and quality of erections and sexual activity, sexual desire, and thoughts about sexual decline.¹⁹ It was adapted from previously validated instruments,^{27, 28} field-tested, and self-administered in private at the end of a hour-long interview presuming that threat associated with answering sensitive questions would be reduced by the rapport developed during the interview. Participants were instructed to place the completed instrument in a sealed envelope and were assured the strictest confidentiality.

The MMAS interviewer-administered instrument included several validated psychosocial or mood scales. Depressive symptoms were measured with the Center for Epidemiological Studies Depression (CES-D) scale.²⁹ This instrument measures current levels of depressive symptoms in community populations and does not indicate a diagnosis of clinical depression. Scores range from 0 to 60, with higher scores indicating more depression symptoms. For the present analysis, the presence of depressive symptoms was indicated by a score greater than or equal to 16 on the CES-D Scale. Dominance was measured using the Jackson dominance scale, a subscale of the Jackson Personality Research Form E.³⁰ This scale consists of 16 items regarding the frequency of attempts to control one's environment, influence others, and express opinions forcefully. The response set for this scale includes "false," "true," and "don't know," coded as 0, 1, and 0.5, respectively. Scores can range from 0 to 16, with higher scores indicating a higher degree of dominance. The anger-in, anger-out, ability to control anger, and frequency anger is aroused and expressed (or suppressed) subscales of the Spielberger Anger Expression Scale were used to measure anger domains. Each subscale consists of eight questions pertaining to feelings of anger and is scored from 1 ("almost never") to 4 ("almost always").³¹ Scores for each subscale can range from 8 to 32, with higher scores indicating a tendency to react or behave in the manner described. Additional psychosocial/mood questions were also included in the study protocol.

Analytic sample and statistical analysis

Our analysis sample was derived from 955 subjects for whom an ED assessment was available at T1 and T2, who were not using available ED drugs (e.g., alprostadil), and who did not have prostate cancer before T1 or T2. 814 men exhibited none or minimal ED symptoms at baseline, and were thus eligible to develop moderate or complete ED (our definition of an incident ED case). The characteristics of these 814 men at T1 by ED status at T2 were described and simple tests of equivalence were performed using t-tests and Wilcoxon tests for continuous variables and chi-squared or Fisher's exact tests for categorical variables. Odds ratios (OR) and 95% confidence intervals (CI) were obtained from a multivariate logistic regression analysis model of ED incidence. All of the variables listed in Figure 1 were included in the preliminary models. Stepwise backwards elimination was then used to define parsimonious models with a significance criterion of $p < 0.15$ for retention in the model. BMI was included in the final model regardless of significance. As a measure of model performance, the area under the receiver operating characteristic (ROC)

curve of the final parsimonious model was calculated. The area under the curve (the c-statistic) is a measure of the model's accuracy. A simple flip of the coin would on average produce a c-statistic of 0.50. All analyses were conducted using SAS version 9.2 (Cary, NC).

Main Outcome Measure

The self-administered questionnaire included 13 items related to ED; e.g., "During the last six months have you ever had trouble getting an erection before intercourse begins?" These items were combined in a discriminant-analytic formula to assign a degree of erectile function to each subject.³² The same discriminant formula was used at both baseline and follow-up. Calibration data for the discriminant formula were taken from an additional single-question, subjective self-assessment of ED, included in the follow-up questionnaire in response to recommendations of the NIH Consensus Panel.³³ Impotence was rated by subjects with reference to the following statement, "being able to get and keep an erection that is rigid enough for satisfactory sexual activity. The subject rated himself as completely impotent ("never able to get and keep an erection ..."), moderately impotent ("sometimes able ..."), minimally impotent ("usually able..."), or not impotent ("always able ..."). In random subsets of the follow-up samples the self-assessment was validated against two established ED measures,³⁴ the International Index of Erectile Function.³⁵ ($r = 0.71$, $n = 254$) and the Brief Male Sexual Function Inventory³⁶ ($r = 0.78$, $n = 251$), as well as an independent urologic assessment.³⁷ We grouped the 4-category ED status variable into absence and presence of ED, the latter defined as moderate or complete ED.

Results

Of the 814 men with no or minimal ED at T1, 178 (22%) developed moderate or complete ED at T2. Bivariate associations between demographic and health status factors at T1 and incident ED (movement from none or minimal at T1 to moderate or complete ED at T2) status are presented in Table 1. Men who developed ED were more likely to be in the lower categories of education and income, and were 5.4 years older on average compared to those who did not. They had more heart disease, diabetes, higher mean systolic blood pressure, greater BMI and waist circumference, used more medications and were not as likely to rate their health excellent compared to men without incident ED. We did not observe significant differences at T1 in mean or median levels of total or free testosterone or HDL cholesterol between men with and without incident ED, however.

Regarding psychosocial parameters, men with incident ED were less likely to report social support than men without incident ED (Table 2), but we observed no association between incident ED status at T2 and depressive symptoms at baseline. There was also no association of incident ED with domains of the Spielberger Anger Scale, but men without incident ED scored higher on the Jackson Dominance Scale (mean 10.7 vs. 9.7 among men with incident ED, $p < 0.002$). Other differences in psychosocial variables were noted in that men with incident ED were generally less likely to report tension, irritability, feeling frazzled or that things are 'out of control'.

Compared to the psychosocial variables we examined, there were more associations with ED among the sexual function variables (Table 3). Men with incident ED consistently reported lower levels of sexual desire and arousal, fewer sexual thoughts, and had poorer erectile function overall compared to men without incident ED. For example, men with incident ED reported an average of 21.5 erections monthly compared to 30.7 monthly among men without incident ED ($p < 0.001$; comparison of medians: 16.0, 30.0, respectively). 30% of

men who developed ED had awakening erections once a month or less compared to 17.3% of men who did not develop ED (overall $p < 0.001$).

Table 4 and Figure 2 present the final parsimonious multivariate model of incident ED at T2. Considering health status variables, age, having diabetes, heart disease, and an increased number of medications were positively associated with incident ED, while reporting very good/excellent health was inversely associated. Having some college or a college degree was associated with ED incidence compared to those with an advanced degree beyond college (OR=2.07, 95% CI: 1.23, 3.48). Psychosocial variables (i.e., nervous or tense or feeling that things were 'out of control') were also inversely associated with developing ED at T2. Having a similar sexual arousal level compared to adolescence, a higher frequency of sexual thoughts and ejaculation by masturbation at T1 also were 'protective' (or inversely associated with) incident ED at T2. Men who reported difficulty getting or maintaining an erection at T1 were more likely to develop incident ED at T2. The area under the ROC curve for this model was 0.787, showing a high level of predictive power.

Discussion

Our population-based study of community-dwelling men was able to consider a broad range of potential risk factors and their association with incident ED approximately nine years later. Previous examination of factors associated with ED incidence in this study population primarily focused on modifiable risk factors related to lifestyle,³⁸ or cardiovascular risk factors and comorbidity,³⁹ or psychosocial factors.⁴⁰ In the current analyses, we included sexual function characteristics at T1 'in the mix', as our objectives were to identify a broader range of 'upstream' determinants that might have predictive value in provoking onset of ED. We conclude that sexual function parameters including arousal levels, frequency of ejaculation by masturbation and sexual thoughts as well as erectile function were predictive of ED, even after adjustment for age, education levels and comorbidity.

Other longitudinal studies have examined sexual function as a predictor of ED. Sexual function (frequency of intercourse) at baseline was found to predict the development of ED after five years of follow-up,⁴¹ while another study found that sexual inactivity (defined as no activity for more than 3 months) predicted worsening of erectile function, perhaps through a proxy of reduced libido.¹⁷ These observations along with the current analyses suggest there are sexual function predictors of erectile dysfunction that in turn reveal opportunities for intervention before a more extensive loss of erectile function.

The exact mechanism by which libido and ejaculatory function may influence subsequent ED in our study is unknown; testosterone was not explanatory in our models. A more in-depth cross-sectional analysis of hormonal factors in this cohort (at T3) has shown that testosterone levels (free and total testosterone) were not associated with ED.⁴² Although we adjusted for self-reported health status, men with desire for sex may be healthier in other ways not measured in this study. Recently, Gades *et al.* have shown that among five domains of sexual function, declines in libido and ejaculatory function were most strongly correlated with declines in erectile function over time, demonstrating the interrelationship among these variables in another cohort.¹⁵ It should be recognized, however, that sexual desire is not necessarily only a function of one's medical health but is related to relationship factors.⁴³ While we included partner availability and other baseline relationship factors in this analysis, they were not related to the development of ED (data not shown). However, since baseline, relationships may have changed in a way that negatively affected desire (with subsequent resulting loss of desire and ED); this would not have been captured by our data.

Of the psychosocial variables we considered, we did not find that personality traits such as dominance or anger expression were predictive of ED in the multivariate model. The presence of nervous tension and feeling things were 'out of control' were associated with better erectile function and may suggest that personality traits related to being 'keyed up' may be related to factors reducing the risk of ED, perhaps through increased physical activity or other unknown mechanisms. However, we had imprecise confidence intervals due to small cell sizes for some of these predictors. Also, our long follow-up interval may be too long to adequately understand transient mood variables or short-term behavioral factors such as 'drinking more than usual' that are likely to fluctuate substantially over time.

We observed that cardiovascular disease (CVD) and diabetes (well-established risk factors for ED), remained resilient predictors of subsequent ED in the presence of other psychosocial and sexual function parameters in the model. This further suggests the importance of underlying comorbidity in increasing risk of erectile dysfunction. Erectile dysfunction (ED) and CVD share pathophysiologic mechanisms (e.g., endothelial dysfunction, oxidative stress, systemic inflammation)^{44–47} while the underlying mechanism for the association of ED with diabetes may also be multifactorial.⁴⁸ Increased risk of ED among those with diabetes has been observed in a prior longitudinal study in Finland,¹³ where diabetes and CVD were the most important non-demographic predictors of risk. In a cohort study in Brazil conducted among a population with more baseline ED risk factors compared to MMAS, the relative magnitude of increased risk conferred by diabetes was similar to our study (2.5-fold vs. our nearly 3-fold) although heart disease was not significantly associated.¹⁴ In our analysis, the total number of medications used was also associated with ED; these may be acting as a proxy for disease severity, or may directly contribute to ED risk, as some studies have shown.^{10, 49}

The strengths of our study include a longitudinal design and the ability to simultaneously evaluate a wider range of risk factors than physiologic characteristics alone, allowing for novel findings to emerge. A population-based design allows for risk factors to be examined in the community, rather than a design based in the clinic and conducted only among those who present to medical care. Our long follow-up time period has revealed that signs of ED may be present years earlier. While our results are generalizable to Massachusetts men aged 40–70 without a history of prostate cancer, they may not be generalizable to all racial/ethnic groups in the U.S. due to their low representation in Massachusetts. There may also be substantial sociocultural differences in self-reported sexual function that should be considered when comparing results across studies.

Conclusions

Our results indicate that in the context of other risk factors, sexual desire variables at baseline were associated with the development of ED. The presence of ED is increasingly recognized as an potential clinical opportunity or 'portal' to improving men's health overall.⁵⁰ Our results identified additional determinants further 'upstream', suggesting there are intervention opportunities before onset of ED. Specifically, men who are experiencing a loss of desire should be considered to be at risk for development of ED. The evaluation of a broader range of sexual function variables beyond erectile function may serve to more broadly improve men's health.

Acknowledgments

Funding for the Massachusetts Male Aging Study was provided by grant AG04763 from the National Institute on Aging, and Grants DK51345 and DK44995 from the National Institute of Diabetes and Digestive and Kidney Diseases. Additional support for these analyses was provided by Eli Lilly and Company. Lead Author Susan A. Hall is a former consultant to and former employee of GlaxoSmithKline but has no equity interest in

GlaxoSmithKline. Raymond Rosen is a paid consultant to and has received research support from Eli Lilly, Bayer Schering, and Ferring Pharmaceuticals.

References

1. U.S. Food and Drug Administration. Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. FDA; 2009.
2. Gazzaruso C, Solerte SB, Pujia A, Coppola A, Vezzoli M, Salvucci F, Valenti C, Giustina A, Garzaniti A. Erectile dysfunction as a predictor of cardiovascular events and death in diabetic patients with angiographically proven asymptomatic coronary artery disease: a potential protective role for statins and 5-phosphodiesterase inhibitors. *J Am Coll Cardiol*. 2008; 51:2040–2044. [PubMed: 18498958]
3. Inman BA, Sauver JL, Jacobson DJ, McGree ME, Nehra A, Lieber MM, Roger VL, Jacobsen SJ. A population-based, longitudinal study of erectile dysfunction and future coronary artery disease. *Mayo Clin Proc*. 2009; 84:108–113. [PubMed: 19181643]
4. Thompson IM, Tangen CM, Goodman PJ, Probstfield JL, Moinpour CM, Coltman CA. Erectile dysfunction and subsequent cardiovascular disease. *Jama*. 2005; 294:2996–3002. [PubMed: 16414947]
5. Schouten BW, Bohnen AM, Bosch JL, Bernsen RM, Deckers JW, Dohle GR, Thomas S. Erectile dysfunction prospectively associated with cardiovascular disease in the Dutch general population: results from the Krimpen Study. *Int J Impot Res*. 2008; 20:92–99. [PubMed: 17728804]
6. Araujo AB, Travison TG, Ganz P, Chiu GR, Kupelian V, Rosen RC, Hall SA, McKinlay JB. Erectile dysfunction and mortality. *J Sex Med*. 2009; 6:2445–2454. [PubMed: 19538544]
7. Selvin E, Burnett AL, Platz EA. Prevalence and risk factors for erectile dysfunction in the US. *Am J Med*. 2007; 120:151–157. [PubMed: 17275456]
8. Nicolosi A, Moreira ED Jr, Shirai M, Bin Mohd Tambi MI, Glasser DB. Epidemiology of erectile dysfunction in four countries: cross-national study of the prevalence and correlates of erectile dysfunction. *Urology*. 2003; 61:201–206. [PubMed: 12559296]
9. Saigal CS, Wessells H, Pace J, Schonlau M, Wilt TJ. Predictors and prevalence of erectile dysfunction in a racially diverse population. *Arch Intern Med*. 2006; 166:207–212. [PubMed: 16432090]
10. Bacon CG, Mittleman MA, Kawachi I, Giovannucci E, Glasser DB, Rimm EB. Sexual function in men older than 50 years of age: results from the health professionals follow-up study. *Ann Intern Med*. 2003; 139:161–168. [PubMed: 12899583]
11. Kupelian V, Link CL, McKinlay JB. Association between smoking, passive smoking, and erectile dysfunction: results from the Boston Area Community Health (BACH) Survey. *Eur Urol*. 2007; 52:416–422. [PubMed: 17383811]
12. Bacon CG, Mittleman MA, Kawachi I, Giovannucci E, Glasser DB, Rimm EB. A prospective study of risk factors for erectile dysfunction. *J Urol*. 2006; 176:217–221. [PubMed: 16753404]
13. Shiri R, Koskimaki J, Hakkinen J, Tammela TL, Huhtala H, Hakama M, Auvinen A. Effects of age, comorbidity and lifestyle factors on erectile function: Tampere Ageing Male Urological Study (TAMUS). *Eur Urol*. 2004; 45:628–633. [PubMed: 15082206]
14. Moreira ED Jr, Lbo CF, Diamant A, Nicolosi A, Glasser DB. Incidence of erectile dysfunction in men 40 to 69 years old: results from a population-based cohort study in Brazil. *Urology*. 2003; 61:431–436. [PubMed: 12597962]
15. Gades NM, Jacobson DJ, McGree ME, St Sauver JL, Lieber MM, Nehra A, Girman CJ, Jacobsen SJ. Longitudinal Evaluation of Sexual Function in a Male Cohort: The Olmsted County Study of Urinary Symptoms and Health Status among Men. *J Sex Med*. 2009
16. Travison TG, Shabsigh R, Araujo AB, Kupelian V, O'Donnell AB, McKinlay JB. The natural progression and remission of erectile dysfunction: results from the Massachusetts Male Aging Study. *J Urol*. 2007; 177:241–246. discussion 46. [PubMed: 17162054]
17. Schouten BW, Bohnen AM, Dohle GR, Groeneveld FP, Willemsen S, Thomas S, Bosch JL. Risk factors for deterioration of erectile function: the Krimpen study. *Int J Androl*. 2009; 32:166–175. [PubMed: 18067566]

18. O'Donnell AB, Araujo AB, McKinlay JB. The health of normally aging men: The Massachusetts Male Aging Study (1987–2004). *Exp Gerontol.* 2004; 39:975–984. [PubMed: 15236757]
19. McKinlay, JB.; Feldman, HA. Age-related variation in sexual activity and interest in normal men: Results from the Massachusetts Male Aging Study. In: Rossi, AS., editor. *Sexuality Across the Lifecourse: Proceedings of the MacArthur Foundation Research Network on Successful Mid-Life Development*, 1992. New York, NY: University of Chicago Press; 1994. p. 261-285.
20. U.S. Census Bureau. [Accessed August 10, 2009] Census of Population and Housing, Summary Tape File 3C - part 1. 1990. http://factfinder.census.gov/servlet/DatasetMainPageServlet?_program=DEC&_tabId=DEC2&_submenuId=datasets_1&_lang=en&_ts=267986374663
21. Bremner WJ, Vitiello MV, Prinz PN. Loss of circadian rhythmicity in blood testosterone levels with aging in normal men. *J Clin Endocrinol Metab.* 1983; 56:1278–1281. [PubMed: 6841562]
22. Brambilla DJ, McKinlay SM, McKinlay JB, Weiss SR, Johannes CB, Crawford SL, Longcope C. Does collecting repeated blood samples from each subject improve the precision of estimated steroid hormone levels? *J Clin Epidemiol.* 1996; 49:345–350. [PubMed: 8676183]
23. Araujo AB, O'Donnell AB, Brambilla DJ, Simpson WB, Longcope C, Matsumoto AM, McKinlay JB. Prevalence and incidence of androgen deficiency in middle-aged and older men: estimates from the Massachusetts Male Aging Study. *J Clin Endocrinol Metab.* 2004; 89:5920–5926. [PubMed: 15579737]
24. Södergard R, Backstrom T, Shanbhag V, Carstensen H. Calculation of free and bound fractions of testosterone and estradiol-17 beta to human plasma proteins at body temperature. *J Steroid Biochem.* 1982; 16:801–810. [PubMed: 7202083]
25. Vermeulen A, Verdonck L, Kaufman JM. A Critical Evaluation of Simple Methods for the Estimation of Free Testosterone in Serum. *J Clin Endocrinol Metab.* 1999; 84:3666–3672. [PubMed: 10523012]
26. McKinlay, S.; Kipp, D.; Johnson, P. A Field Approach for Obtaining Physiological Measures in Surveys of General Populations: Response Rates, Reliability and Costs. In: Services USDoHaH. , editor. *Proceedings of the Fourth Conference on Health Survey Research Methods*; Washington, DC. 1984.
27. Frenken, J.; Vennix, P. *Sexual Experience Scales Manual*. Netherlands: Swets and Zeitlinger B.V.; 1976.
28. LoPiccolo J, Steger JC. The sexual interaction inventory: A new instrument for assessment of sexual dysfunction. *Arch Sex Behav.* 1974; 3:585–595. [PubMed: 4429442]
29. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas.* 1977; 1:385–401.
30. Jackson, DN. *Personality Research Form Manual*. Post Huron, MI: Sigma Assessment Systems, Inc.; 1989.
31. Spielberger, CD.; Johnson, EH.; Russell, SF.; Crane, RJ.; Jacobs, GA.; Worden, TJ. The experience and expression of anger: construction and validation of an anger expression scale. In: Chesney, MA.; Rosenman, RH., editors. *Anger and hostility in cardiovascular and behavioral disorders*. New York: McGraw-Hill; 1985. p. 5-30.
32. Kleinman KP, Feldman HA, Johannes CB, Derby CA, McKinlay JB. A new surrogate variable for erectile dysfunction status in the Massachusetts male aging study. *J Clin Epidemiol.* 2000; 53:71–78. [PubMed: 10693906]
33. NIH Consensus Conference. Impotence. NIH Consensus Development Panel on Impotence. *Jama.* 1993; 270:83–90. [PubMed: 8510302]
34. Derby CA, Araujo AB, Johannes CB, Feldman HA, McKinlay JB. Measurement of erectile dysfunction in population-based studies: the use of a single question self-assessment in the Massachusetts Male Aging Study. *Int J Impot Res.* 2000; 12:197–204. [PubMed: 11079360]
35. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology.* 1997; 49:822–830. [PubMed: 9187685]
36. O'Leary MP, Fowler FJ, Lenderking WR, Barber B, Sagnier PP, Guess HA, Barry MJ. A brief male sexual function inventory for urology. *Urology.* 1995; 46:697–706. [PubMed: 7495124]

37. O'Donnell AB, Araujo AB, Goldstein I, McKinlay JB. The validity of a single-question self-report of erectile dysfunction. *J Gen Intern Med.* 2005; 20:515–519. [PubMed: 15987326]
38. Derby CA, Mohr BA, Goldstein I, Feldman HA, Johannes CB, McKinlay JB. Modifiable risk factors and erectile dysfunction: can lifestyle changes modify risk? *Urology.* 2000; 56:302–306. [PubMed: 10925098]
39. Johannes CB, Araujo AB, Feldman HA, Derby CA, Kleinman KP, McKinlay JB. Incidence of erectile dysfunction in men 40 to 69 years old: longitudinal results from the Massachusetts male aging study. *J Urol.* 2000; 163:460–463. [PubMed: 10647654]
40. Araujo AB, Johannes CB, Feldman HA, Derby CA, McKinlay JB. Relation between psychosocial risk factors and incident erectile dysfunction: prospective results from the Massachusetts Male Aging Study. *Am J Epidemiol.* 2000; 152:533–541. [PubMed: 10997543]
41. Koskimaki J, Shiri R, Tammela T, Hakkinen J, Hakama M, Auvinen A. Regular intercourse protects against erectile dysfunction: Tampere Aging Male Urologic Study. *Am J Med.* 2008; 121:592–596. [PubMed: 18538297]
42. Kupelian V, Shabsigh R, Travison TG, Page ST, Araujo AB, McKinlay JB. Is there a relationship between sex hormones and erectile dysfunction? Results from the Massachusetts Male Aging Study. *J Urol.* 2006; 176:2584–2588. [PubMed: 17085164]
43. Corona G, Petrone L, Mannucci E, Ricca V, Balercia G, Giommi R, Forti G, Maggi M. The impotent couple: low desire. *Int J Androl.* 2005; 28(Suppl 2):46–52. [PubMed: 16236064]
44. Billups KL, Kaiser DR, Kelly AS, Wetterling RA, Tsai MY, Hanson N, Bank AJ. Relation of C-reactive protein and other cardiovascular risk factors to penile vascular disease in men with erectile dysfunction. *Int J Impot Res.* 2003; 15:231–236. [PubMed: 12934049]
45. Guay AT. Relation of endothelial cell function to erectile dysfunction: implications for treatment. *Am J Cardiol.* 2005; 96:52M–56M. [PubMed: 15979432]
46. Jones RW, Rees RW, Minhas S, Ralph D, Persad RA, Jeremy JY. Oxygen free radicals and the penis. *Expert Opin Pharmacother.* 2002; 3:889–897. [PubMed: 12083989]
47. Solomon H, Man JW, Jackson G. Erectile dysfunction and the cardiovascular patient: endothelial dysfunction is the common denominator. *Heart.* 2003; 89:251–253. [PubMed: 12591819]
48. Hidalgo-Tamola J, Chitaley K. Review type 2 diabetes mellitus and erectile dysfunction. *J Sex Med.* 2009; 6:916–926. [PubMed: 19067787]
49. Francis ME, Kusek JW, Nyberg LM, Eggers PW. The contribution of common medical conditions and drug exposures to erectile dysfunction in adult males. *J Urol.* 2007; 178:591–596. discussion 96. [PubMed: 17570434]
50. Shabsigh R, Arver S, Channer KS, Eardley I, Fabbri A, Gooren L, Heufelder A, Jones H, Meryn S, Zitzmann M. Sexual health as a portal to men's health: a problem turned around into an opportunity. *Int J Clin Pract.* 2008; 62:179–181. [PubMed: 18199276]

FIGURE 1.
T1 variables (thematically grouped) considered for models of ED incidence at T2 in the Massachusetts Male Aging Study.

Final model

- Education
- Fidgety, nervous, tense
- Feeling that things are coming apart or out of control
- During the last 6 months, trouble getting an erection before intercourse begins
- Arousal levels compared to adolescence
- Weekly frequency of sexual thoughts, fantasies, or erotic dreams
- Weekly frequency of ejaculation by masturbation
- Age
- Body mass index
- Number of medications
- Heart disease
- Diabetes
- Very Good/Excellent Health (vs. Good/Fair/Poor Health)

FIGURE 2.

T1 variables in final model of ED incidence at T2 in the Massachusetts Male Aging Study.

TABLE 1

Health status at T1 by incident ED from T1 to T2 (N=814, only those eligible to develop moderate/complete ED).

Health Status at T1	Incident ED n=178	No Incident ED n=636	P-value
Education			
High school or less	48 (27.0%)	120 (18.9%)	< 0.001
Some college or BA	84 (47.2%)	247 (38.8%)	
Advanced study beyond BA	46 (25.8%)	269 (42.3%)	
Income			
< \$40,000	58 (33.9%)	156 (24.7%)	0.04
\$40,000–\$79,999	78 (45.6%)	307 (48.7%)	
\$80,000	35 (20.5%)	168 (26.6%)	
Age, Mean $\pm$ SD	56.7 $\pm$ 7.80	51.3 $\pm$ 7.67	< 0.001
Median (IQR)	57.5 (51.4 – 63.1)	50.1 (44.7 – 56.7)	
BMI, Mean $\pm$ SD	27.7 $\pm$ 4.45	26.8 $\pm$ 3.88	0.01
Median (IQR)	27.0 (24.6 – 30.1)	26.3 (24.3 – 28.4)	
Waist circumference, in, Mean $\pm$ SD	38.9 $\pm$ 4.55	37.7 $\pm$ 4.08	< 0.001
Median (IQR)	38.8 (35.5 – 41.5)	37.5 (35.0 – 40.0)	
High-density lipoprotein, mg/dL, Mean $\pm$ SD	43.0 $\pm$ 14.27	43.5 $\pm$ 12.71	0.68
Median (IQR)	41.0 (33.0 – 52.0)	41.0 (34.0 – 51.0)	
Testosterone, ng/dL, Mean $\pm$ SD	518.3 $\pm$ 173.35	528.4 $\pm$ 177.02	0.50
Median (IQR)	525.0 (380.0 – 622.0)	507.0 (410.0 – 629.0)	
Free testosterone, ng/dL, Mean $\pm$ SD	13.3 $\pm$ 5.23	13.7 $\pm$ 5.27	0.43
Median (IQR)	12.9 (9.5 – 16.4)	13.3 (10.1 – 16.8)	
Systolic blood pressure, mmHg, Mean $\pm$ SD	127.3 $\pm$ 15.75	122.7 $\pm$ 13.04	< 0.001
Median (IQR)	126.0 (118.0 – 138.0)	121.0 (114.0 – 130.0)	
Physical activity, kcal, Mean $\pm$ SD	3281.5 $\pm$ 898.77	3274.9 $\pm$ 1024.1	0.93
Median (IQR)	3073.2 (2714.4 – 3697.1)	2987.0 (2671.3 – 3537.8)	
Number of medications, Mean $\pm$ SD	1.5 $\pm$ 1.97	1.0 $\pm$ 1.26	< 0.001
Median (IQR)	1.0 (0.0 – 2.0)	1.0 (0.0 – 2.0)	
Current smoking	39 (21.9%)	131 (20.6%)	0.70
Heart disease	30 (16.9%)	44 (6.9%)	< 0.001
Diabetes	17 (9.6%)	21 (3.3%)	< 0.001
Would you say your health in general is:			
Excellent	48 (27.0%)	254 (40.1%)	< 0.001
Very Good	65 (36.5%)	253 (39.9%)	
Good	44 (24.7%)	110 (17.4%)	
Fair/Poor	21 (11.8%)	17 (2.7%)	

TABLE 2

Psychosocial parameters at T1 by incident ED from T1 to T2 (N=814, only those eligible to develop moderate/complete ED).

Psychosocial factors at T1	Incident ED n=178	No Incident ED n=636	P-value
How pleased are you with the way your life has gone so far?			
Pleased/Very Pleased	93 (52.2%)	340 (53.6%)	0.93
Wish some things were different but generally happy	79 (44.4%)	275 (43.4%)	
Unhappy/Very Unhappy	6 (3.4%)	19 (3.0%)	
Social Support (% Yes)	160 (89.9%)	599 (94.2%)	0.04
Depression (% Yes)	14 (8.1%)	61 (9.7%)	0.53
Depression score (continuous)	6.0 ± 6.83	6.0 ± 6.55	0.95
Median (IQR)	4.0 (1.0 – 9.0)	4.0 (1.0 – 9.0)	
Spielberger Anger Scales (continuous)			
Hold Anger In, Mean ± SD	14.7 ± 3.99	14.9 ± 3.74	0.62
Median (IQR)	14.0 (12.0 – 17.0)	15.0 (12.0 – 17.0)	
Acts Out due to Anger, Mean ± SD	13.7 ± 2.95	13.8 ± 3.10	0.76
Median (IQR)	14.0 (12.0 – 16.0)	14.0 (12.0 – 16.0)	
Ability to control anger, Mean ± SD	25.4 ± 5.02	25.9 ± 4.67	0.24
Median (IQR)	26.0 (22.0 – 30.0)	27.0 (23.0 – 30.0)	
Frequency Anger is aroused and expressed (or suppressed), Mean ± SD	19.0 ± 8.39	18.8 ± 7.56	0.72
Median (IQR)	18.5 (13.0 – 24.0)	18.0 (13.0 – 24.0)	
Jackson Dominance Scale (continuous), Mean ± SD	9.7 ± 4.03	10.7 ± 3.79	0.002
Median (IQR)	10.0 (7.0 – 13.0)	11.0 (8.0 – 14.0)	
Being fidgety, nervous or tense?	34 (19.1%)	161 (25.3%)	0.09
Being irritable	34 (19.1%)	163 (25.6%)	0.07
Smoking more than usual?	6 (3.4%)	30 (4.7%)	0.44
Drinking more than usual?	6 (3.4%)	37 (5.8%)	0.20
Feeling that things are coming apart or out of control?	7 (3.9%)	60 (9.4%)	0.02
Feeling frazzled or at wit's end?	13 (7.3%)	75 (11.8%)	0.09

TABLE 3

Sexual function parameters at T1 by incident ED from T1 to T2 (N=814, only those eligible to develop moderate/complete ED).

Sexual Function at T1	Incident ED n=178	No Incident ED n=636	P-value
Men's interest in sexual activity tends to decline as they get older			
Agree	72 (40.4%)	192 (30.2%)	0.008
Neutral	31 (17.4%)	93 (14.6%)	
Disagree	75 (42.1%)	351 (55.2%)	
During any average month, how often do you have full hard erections? Mean $\pm$ SD	21.5 $\pm$ 19.35	30.7 $\pm$ 24.12	< 0.001
Median (IQR)	16.0 (5.0 – 30.0)	30.0 (15.0 – 30.0)	
During any average month, how often would you like to have sex? Mean $\pm$ SD	9.1 $\pm$ 6.12	12.6 $\pm$ 9.77	< 0.001
Median (IQR)	8.0 (4.0 – 12.0)	12.0 (8.0 – 16.0)	
How frequently do you awaken from sleep with a full erection?			
2–3 times per week or more	72 (40.4%)	353 (55.5%)	< 0.001
Once a week or 2–3 times per month	51 (28.7%)	173 (27.2%)	
Once a month or less	55 (30.9%)	110 (17.3%)	
During the last 6 months, have you ever had trouble getting an erection before intercourse begins?			
No	100 (63.7%)	480 (81.2%)	< 0.001
Yes	57 (36.3%)	111 (18.8%)	
No intercourse in past 6 months	21	45	N/A
During the last 6 months, have you ever had trouble keeping an erection once intercourse has begun?			
No	101 (64.7%)	475 (80.8%)	< 0.001
Yes	55 (35.3%)	113 (19.2%)	
No intercourse in past 6 months	22	48	N/A
Frequency of sexual desire?			
2–3 times per week or more	93 (52.5%)	506 (79.7%)	< 0.001
Once a week or 2–3 times per month	75 (42.4%)	120 (18.9%)	
Once a month or less	9 (5.1%)	9 (1.4%)	
Compared to when you were an adolescent, do you feel sexually aroused?			
More or about the than when an adolescent	47 (26.4%)	281 (44.2%)	< 0.001
Less than when an adolescent	131 (73.6%)	355 (55.8%)	
Compared to when you were in your 40s, do you feel sexually aroused?			
More or about the same now than then	17 (27.0%)	48 (48.0%)	0.008
Less now than then	46 (73.0%)	52 (52.0%)	
How frequently do you have sexual thoughts, fantasies, or erotic dreams?			
2–3 times per week or more	96 (53.9%)	508 (79.9%)	< 0.001
Once a week or 2–3 times per month	51 (28.7%)	87 (13.7%)	
Once a month or less	31 (17.4%)	41 (6.4%)	
How often do you ejaculate by masturbation?			
2–3 times per week or more	18 (12.8%)	143 (26.3%)	< 0.001
Once a week or 2–3 times per month	37 (26.2%)	151 (27.8%)	

Sexual Function at T1	Incident ED n=178	No Incident ED n=636	P-value
Once a month or less	86 (61.0%)	249 (45.9%)	

TABLE 4

Final multivariate logistic regression models for ED incidence (N=814, only those eligible to develop moderate/complete ED) from T1 to T2, by T1 characteristics.

ED Incidence Model		
	Odds ratio & 95% confidence interval	Wald F-test p-value *
Education[†]		
High school or less vs. advanced study beyond college	1.31 0.68 – 2.55	0.42
Some college or BA vs. advanced study beyond college	2.07 1.23 – 3.48	0.006
Psychosocial Parameters		
Being fidgety, nervous or tense?	0.57 0.31 – 1.06	0.08
Feeling that things are coming apart or out of control	0.23 0.06 – 0.94	0.04
Sexual Function Parameters		
During the last 6 months, have you ever had trouble getting an erection (Yes vs. no)	2.33 1.41 – 3.85	< 0.001
Compared to when you were an adolescent, do you feel sexually aroused (more or about the same than when an adolescent vs. less)	0.56 0.34 – 0.92	0.02
How frequently do you have sexual thoughts, fantasies, or erotic dreams? (2–3 times weekly or more vs. once weekly or less)	0.55 0.33 – 0.92	0.02
How often do you ejaculate by masturbation? (2–3+ times weekly vs. once weekly or less)	0.54 0.26 – 1.09	0.08
Health Status		
Age (per 10 years)	1.40 1.03 – 1.91	0.03
BMI (per 10 kg/m ²)	1.08 0.63 – 1.85	0.79
Number of medications (continuous)	1.14 0.99 – 1.31	0.06
Heart disease	2.16 1.08 – 4.33	0.03
Diabetes	2.93 1.12 – 7.62	0.03
Excellent/Very Good Health (vs. Good/Fair/Poor Health)	0.52 0.31 – 0.89	0.02

Note: C-statistic for ED incidence model: 0.787.

* P value shown is from a test of whether the level of the variable is significantly associated with ED.

[†] P value for the test of the significance of the overall variable with ED was 0.02