# The Prevalence of Erectile Dysfunction in the Primary Care Setting 

## Importance of Risk Factors for Diabetes and Vascular Disease

Steven A. Grover, MD, MPA, FRCPC; Ilka Lowensteyn, PhD; Mohammed Kaouache, MSc; Sylvie Marchand, RN; Louis Coupal, MSc; Emidio DeCarolis, PhD; Joseph Zoccoli, BSc; Isabelle Defoy, PhD

Background: The prevalence of erectile dysfunction (ED) and associated risk factors has been described in many clinical settings, but there is little information regarding men seen by primary care physicians. We sought to identify independent factors associated with ED in a primary care setting.

Methods: We surveyed a cross-sectional sample of 3921 Canadian men, aged 40 to 88 years, seen by primary care physicians. Participants completed a full medical history, physical examination, and measurement of fasting blood glucose and lipid levels. We used the International Index of Erectile Function to define ED as a score of less than 26 on the erectile function domain.

Results: The overall prevalence of ED was $49.4 \%$. The presence of cardiovascular disease (odds ratio [OR], 1.45; $95 \%$ confidence interval [CI], 1.16-1.81; $P<.01$ ) or diabetes (OR, 3.13; 95\% CI, 2.35-4.16; $P<.001$ ) increased
the probability of ED after adjustment for other confounders. Among those individuals without cardiovascular disease or diabetes, the calculated 10-year Framingham coronary risk (OR, 1.03 per 1\% increase; $95 \%$ CI, 1.02-1.05; $P<.001$ ) and fasting blood glucose levels (OR, 1.14 per $18-\mathrm{mg} / \mathrm{dL}$ [ $1-\mathrm{mmol} / \mathrm{L}$ ] increase; $95 \% \mathrm{CI}$, 1.04$1.24 ; P<.01$ ) were independently associated with ED. Erectile dysfunction was also independently associated with undiagnosed hyperglycemia (OR, 1.46; 95\% CI, 1.02$2.10 ; P=.04$ ), impaired fasting glucose (OR, $1.26 ; 95 \%$ CI, $1.08-1.46 ; P=.004$ ), and the metabolic syndrome (OR, $1.45 ; 95 \% \mathrm{CI}, 1.24-1.69 ; P<.001)$.

Conclusions: Cardiovascular disease, diabetes, future coronary risk, and increasing fasting glucose levels are independently associated with ED. It remains to be determined if ED precedes the development of these conditions.

Arch Intern Med. 2006;166:213-219

Author Affiliations: Centre for the Analysis of Cost-Effective Care and the Divisions of General Internal Medicine and Clinical Epidemiology, The Montreal General Hospital, and Departments of Medicine and Epidemiology \& Biostatistics, McGill University, Montreal, Quebec (Drs Grover and Lowensteyn, Messrs Kaouache and Coupal, and
Ms Marchand), and Pfizer Canada, Kirkland, Quebec (Drs DeCarolis and Defoy and Mr Zoccoli).

THE IMPORTANCE OF VASCUlar disease as an underlying cause of erectile dysfunction (ED) is now well established, ${ }^{1-4}$ and diagnosed cardiovascular disease (including ischemic heart disease, cerebrovascular disease, and peripheral vascular disease) is correlated with a higher probability of ED. ${ }^{5-9}$ The presence of diabetes, a condition associated with microvascular and macrovascular complications, is also associated with ED. ${ }^{5-9}$ Cardiovascular risk factors such as high total cholesterol levels, low high-density lipoprotein cholesterol levels, hypertension, obesity, and cigarette smoking have also been shown to increase the risk of ED. ${ }^{5-12}$

The prevalence and severity of ED increases with age in parallel with many conditions such as ischemic heart disease and diabetes. Many risk factors also increase in prevalence with age, including hypertension, lifetime exposure to
cigarette smoking, obesity, and a sedentary lifestyle. Therefore, evaluating the importance of comorbidities or risk factors for ED should include an adjustment for age. If ED, cardiovascular disease, and diabetes also share common risk factors such as cigarette smoking and hypertension, then additional analyses adjusted for these potential confounders are necessary.

## See also pages 201 and 207

Primary care physicians are uniquely positioned to inquire about a patient's sexual function during a routine office visit. ${ }^{13}$ They can also screen for modifiable risk factors and treatable comorbidities. However, there is little information regarding the prevalence of ED among patients seen in this clinical setting. ${ }^{14}$ Most studies to date have used community-
based observational surveys or cohorts of individuals attending specialty clinics. ${ }^{5-12}$ Therefore, primary care physicians are faced with a number of unanswered questions. What is the actual prevalence of ED among the patients whom they commonly see? Which medical conditions, risk factors, or treatments increase the prevalence of ED ? Does the presence of known vascular disease, diabetes, or vascular risk factors increase the probability of diagnosing ED, even after adjustment for potential confounders including increasing age?

The Canadian Study of Erectile Dysfunction (CANSED) was designed to estimate the prevalence of ED among Canadian men seen in primary care physicians' offices and to determine the impact of vascular and nonvascular risk factors and comorbidities on the prevalence of ED.

## METHODS

CANSED was a cross-sectional survey of Canadian men visiting 1 of 75 primary care physicians' offices from July 20, 2001, to November 13, 2002. To approximate the geographical distribution of men across the country, physicians who lived within a $30-\mathrm{km}$ radius of 11 metropolitan centers were selected according to a randomization scheme based on postal code. The actual number of invited physicians in each province was proportional to that province's population. Among 1000 physicians who were invited to attend the investigators' meeting, 94 accepted and 75 enrolled patients in the study. A total of 7305 men were identified as potential participants during an office visit for any problem. Among these individuals, 4146 (57\%) agreed to participate.

Eligible participants included men 40 years or older who were visiting their physician on a scheduled visit for any medical problem. Initially, each investigator attempted to recruit 10 patients in each of the following age strata: 40 to 49,50 to 59, 60 to 69 , and 70 years or older in an effort to provide approximately 1000 patients for analysis in each age group. After approximately 6 months, competitive open enrollment was allowed for all men 40 years and older.

Once informed consent was obtained, the investigators completed a medical history and physical examination. A fasting glucose and plasma lipid profile was obtained for all subjects unless these tests had been completed within the previous 6 months.

The International Index of Erectile Function is a multidimensional, self-administered questionnaire for the clinical assessment of ED. ${ }^{15}$ This validated questionnaire has been shown to discriminate between men with and without ED. The erectile function (EF) domain of the questionnaire has also been shown to provide a reliable measure for classifying the severity of ED. ${ }^{16}$ The International Index of Erectile Function was self-administered to each patient in French or English.

The 6 items on the EF domain included questions concerning erection frequency, firmness, penetration, maintenance frequency, maintenance ability, and erection confidence during the last 4 weeks. Each item was based on a 5-point Likert scale, and the responses to all 6 items were summed to arrive at a total EF score ranging from 1 to 30 . Men who had made no attempt at sexual activity in the past 4 weeks were not included in the present analysis, which was restricted to those individuals with a total score of 6 or more. A higher score indicated relatively better EF. Previous evaluation of the EF domain had determined an optimal cutoff score of less than 26 for those having ED. ${ }^{16}$ The severity of ED was further classified into the following 5 categories: no ED (EF score, 26-30), mild (EF score, 22-
25), mild to moderate (EF score, 17-21), moderate (EF score, 11-16), and severe (EF score, 6-10).

A diagnosis of diabetes was ascribed to anyone using insulin or oral hypoglycemic agents. Undiagnosed hyperglycemia was defined as a fasting glucose level of $127 \mathrm{mg} / \mathrm{dL}$ or more ( $\geq 7 \mathrm{mmol} / \mathrm{L}$ ) in the absence of treatment. Impaired fasting glucose was defined as a glucose level of 100 to $126 \mathrm{mg} / \mathrm{dL}$ (5.5$6.9 \mathrm{mmol} / \mathrm{L})$. The metabolic syndrome was defined as 3 or more of the following: a fasting glucose level of $111 \mathrm{mg} / \mathrm{dL}$ or more ( $\geq 6.1 \mathrm{mmol} / \mathrm{L}$ ); blood pressure of 130/85 or more; triglyceride levels of $150 \mathrm{mg} / \mathrm{dL}$ or more ( $\geq 1.7 \mathrm{mmol} / \mathrm{L}$ ); high-density lipoprotein cholesterol level of less than $39 \mathrm{mg} / \mathrm{dL}(<1.0 \mathrm{mmol} /$ L); and a body mass index (BMI; calculated as weight in kilograms divided by the square of height in meters) of 28.0 or more. (In the absence of abdominal circumference, this cut point was derived from a comparison of BMI and abdominal circumference among men in the Third National Health and Nutrition Examination Survey data set. ${ }^{17}$ )

This study complied with the guidelines of the Declaration of Helsinki and the International Conference on Harmonization and Guidelines for Good Clinical Practice. The appropriate ethics research committees reviewed and approved the protocol and consent forms for each center.

Patients identified with at least mild ED (EF score, $\leq 25$ ) were initially compared with those without ED. Subjects were then stratified into 4 age groups ranging from 40 to 49,50 to 59,60 to 69 , and 70 years and older. Factors associated with ED were identified using univariate statistics including the $\chi^{2}$ test for categorical variables and the 2-tailed $t$ test for continuous variables. Logistic regression analysis was used for all multivariate analyses. To evaluate the robustness of these results, all multivariate analyses were repeated comparing men with at least moderate ED (EF score, $\leq 21$ ) and those without ED.

## RESULTS

Among the 4146 men (57\%) agreeing to participate, 225 subjects were dropped from the study for a variety of reasons, leaving 3921 for analysis. The most common reasons were missing data or response discrepancies on the International Index of Erectile Function questionnaire ( $\mathrm{n}=206$ ).

Among the final study participants, the average age was 56.7 years (range, $40-88$ years), and 3492 ( $89 \%$ ) were white. During the time of the study, 2513 participants ( $64 \%$ ) were employed and 3230 ( $82 \%$ ) were married or cohabiting.

When the baseline characteristics of the participants were stratified by age group, ethnicity and marital status remained fairly constant across all ages (Table 1). Higher education and current employment were less common among older participants. Most physiciandiagnosed medical conditions also increased with advancing age. Cardiovascular disease, including ischemic heart disease, cerebrovascular disease, or peripheral vascular disease, ranged in prevalence from 5\% for subjects aged 40 to 49 years to $40 \%$ for those 70 years and older. Diabetes, hypertension, hyperlipidemia, and previous prostate surgery also increased with advancing age, whereas past or present depression did not appear to be age related. Current cigarette smoking declined with increasing age from $27 \%$ for those aged 40 to 49 years to $11 \%$ for those 70 years and older. Alcohol consumption was consistent across all age groups.

Table 1. Characteristics of 3921 Men Seen by a Primary Care Provider*

| Characteristic | Age Group, y |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
|  | $\begin{gathered} 40-49 \\ (\mathrm{n}=1199) \end{gathered}$ | $\begin{gathered} 50-59 \\ (\mathrm{n}=1250) \\ \hline \end{gathered}$ | $\begin{gathered} 60-69 \\ (\mathrm{n}=854) \\ \hline \end{gathered}$ | $\begin{aligned} & \geq 70 \\ (\mathrm{n} & =618) \end{aligned}$ |
| Ethnicity |  |  |  |  |
| White | 1051 (88) | 1098 (88) | 763 (89) | 580 (94) |
| Asian | 78 (7) | 89 (7) | 54 (6) | 25 (4) |
| Black | 39 (3) | 40 (3) | 29 (3) | 12 (2) |
| Other | 31 (3) | 23 (2) | 8 (1) | 1 (0.2) |
| Marital status |  |  |  |  |
| Married/cohabiting | 984 (82) | 1043 (83) | 712 (83) | 491 (79) |
| Never married | 84 (7) | 53 (4) | 24 (3) | 22 (4) |
| Other | 130 (11) | 154 (12) | 118 (14) | 105 (17) |
| Education $\dagger$ |  |  |  |  |
| Less than high school | 90 (8) | 144 (12) | 178 (21) | 161 (26) |
| High school | 358 (30) | 380 (30) | 274 (32) | 230 (37) |
| Continuing education | 222 (19) | 206 (16) | 124 (15) | 65 (11) |
| University/college degree | 528 (44) | 520 (42) | 278 (33) | 162 (26) |
| Employment status $\dagger$ |  |  |  |  |
| Employed | 1108 (92) | 1010 (81) | 331 (39) | 64 (10) |
| Other | 90 (8) | 240 (19) | 523 (61) | 554 (90) |
| Past or present medical conditions |  |  |  |  |
| Cardiovascular disease | 57 (5) | 163 (13) | 236 (28) | 249 (40) |
| Ischemic heart disease | 39 (3) | 106 (8) | 185 (22) | 185 (30) |
| Cerebrovascular disease | 4 (0.3) | 24 (2) | 22 (3) | 56 (9) |
| Peripheral vascular disease | 19 (2) | 44 (4) | 59 (7) | 56 (9) |
| Diabetes | 87 (7) | 179 (14) | 195 (23) | 128 (21) |
| Depression | 132 (11) | 158 (13) | 85 (10) | 41 (7) |
| Hypertension | 235 (20) | 439 (35) | 415 (49) | 324 (52) |
| Hyperlipidemia | 337 (28) | 469 (38) | 413 (48) | 279 (45) |
| Prostate surgery | 0 | 3 (0.2) | 11 (1) | 14 (2) |
| Smoking status |  |  |  |  |
| Current smoker | 324 (27) | 264 (21) | 134 (16) | 65 (11) |
| Past smoker | 374 (31) | 550 (44) | 481 (56) | 400 (65) |
| Never smoked | 501 (42) | 436 (35) | 239 (28) | 153 (25) |
| Alcohol consumption, mean (SD) drinks per week | 5.3 (7.8) | 5.9 (8.4) | 5.5 (7.9) | 5.2 (7.2) |
| Fasting blood levels, mean (SD), mg/dL |  |  |  |  |
| Total cholesterol | 211 (40) | 209 (41) | 203 (41) | 192 (40) |
| LDL cholesterol | 132 (35) | 129 (35) | 124 (35) | 117 (35) |
| HDL cholesterol | 46 (12) | 47 (12) | 47 (13) | 47 (13) |
| Triglycerides | 174 (122) | 173 (136) | 165 (103) | 146 (79) |
| Glucose | 98 (24) | 106 (33) | 111 (36) | 110 (33) |
| Systolic blood pressure, mean (SD), mm Hg | 125 (13) | 130 (15) | 133 (15) | 135 (16) |
| Diastolic blood pressure, mean (SD), mm Hg | 81 (8) | 81 (9) | 80 (8) | 78 (9) |
| BMI, mean (SD) | 28.2 (4.8) | 28.6 (4.8) | 28.2 (4.1) | 27.3 (3.8) |
| Medications used |  |  |  |  |
| Antidepressants | 90 (8) | 108 (9) | 63 (7) | 34 (6) |
| Lipid-lowering | 154 (13) | 286 (23) | 303 (35) | 232 (38) |
| Antihypertensives | 204 (17) | 442 (35) | 442 (52) | 403 (65) |

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); HDL, high-density lipoprotein; LDL, Iow-density lipoprotein.

SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259 ; glucose to millimoles per liter, multiply by 0.0555 ; triglycerides to millimoles per liter, multiply by 0.0113 .
*Unless otherwise indicated, data are expressed as number (percentage) of participants. Percentages have been rounded and might not total 100.
$\dagger$ Information missing for 1 subject.

Mean fasting blood levels of total cholesterol, lowdensity lipoprotein cholesterol, and triglycerides declined slightly with increasing age. This may be explained, in part, by the use of medication to lower lipid levels, which increased with age. Although diastolic blood pressure remained constant across all age groups, systolic blood pressure increased with age, as did the use of antihypertensive medication. Mean BMI was stable across age, with a range of 27.3 to 28.6 , indicating that participants, on average, were slightly overweight.

Overall, 49.4\% (95\% confidence interval [CI], 48.9\%$52.2 \%$ ) of study participants reported some degree of ED during the past 4 weeks or were taking oral medication for ED. If only moderate or more severe ED is considered, then $33.8 \%$ ( $95 \%$ CI, $32.3 \%-35.3 \%$ ) of men were symptomatic. After excluding those taking sildenafil citrate ( $\mathrm{n}=312$ ), ED was rated as mild among 9.2\% (95\% CI, $8.3 \%-10.1 \%$ ), mild to moderate among $7.1 \%$ ( $95 \%$ CI, $6.3 \%-8.0 \%$ ), moderate among $11.2 \%$ ( $95 \%$ CI, $10.1 \%$ $12.2 \%$ ), and severe among $21.9 \%$ ( $95 \%$ CI, 20.6\%-


Figure 1. The association between age and prevalence of erectile dysfunction (ED). Categories of ED are described in the "Methods" section.


Figure 2. The probability of erectile dysfunction (ED) in the absence of cardiovascular disease (CVD) or diabetes or in the presence of CVD alone, diabetes alone, and both conditions.
$23.3 \%$ ). The age-stratified results are summarized in Figure 1. As expected, the prevalence and severity of ED increased with advancing age.

The presence of cardiovascular disease or diabetes increased the probability of ED in each age group
(Figure 2). After excluding subjects who had prostate surgery ( $\mathrm{n}=28$ ), the impact of cardiovascular disease or diabetes was greatest for those aged 40 to 49 years, among whom the probability of ED in the absence of cardiovascular disease or diabetes was $31 \%$, with increases to $52 \%$ in the presence of cardiovascular disease alone, $57 \%$ in the presence of diabetes alone, and $73 \%$ when both conditions were present. The independent effect of cardiovascular disease or diabetes remained apparent in all age groups but appeared to decline with increasing age. Nonetheless, by 60 years and older, the probability of some degree of ED was $94 \%$ for those aged 60 to 69 years and $100 \%$ for those 70 years and older.

Among those individuals without cardiovascular disease or diabetes, the future risk of developing either condition remained an important determinant of ED. The 10-year coronary risk of each participant was calculated using Framingham risk equations. ${ }^{18}$ In each age stra-


Figure 3. The probability of erectile dysfunction (ED) according to tertiles of Framingham 10 -year coronary risk ${ }^{18}$ for each age group.


Figure 4. The probability of erectile dysfunction (ED) according to tertiles of Framingham 10-year coronary risk and fasting glucose levels. To convert glucose to millimoles per liter, multiply by 0.0555 .
tum, participants were then categorized into tertiles of risk. The probability of ED in each age group increased with higher coronary risk (Figure 3). The same trend was observed for tertiles of blood glucose levels among those not taking diabetes medications. Finally, the independent effects of 10-year coronary risk and glucose levels on the probability of ED were explored using a $3 \times 3$ table. As can be seen in Figure 4, the probability of ED independently increased with 10-year coronary risk or blood glucose levels. Moreover, at each level of coronary risk, an increase in glucose level was associated with a higher probability of ED.

The independent association between cardiovascular disease and diabetes was also evaluated using logistic regression analyses. Multivariate models of increasing complexity were constructed to examine the effects of potential confounding. These analyses also identified a number of risk factors or comorbidities associated with ED. For all participants, the crude odds ratios (ORs) associated with the presence of cardiovascular disease or diabetes are presented in Table 2, along with ORs associated with each condition after adjustment for age. Analyses were also provided where both cardiovascular

Table 2. Independent Comorbidities and Risk Factors for Erectile Dysfunction*

| Variable | OR (95\% CI) |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
|  | Crude | Age-Adjusted | Model $1 \dagger$ | Model $2 \ddagger$ |
| All men |  |  |  |  |
| Age per additional year | 1.09 (1.08-1.10)§ |  | 1.08 (1.07-1.09)§ | 1.08 (1.07-1.09)§ |
| Cardiovascular disease | 3.48 (2.88-4.20)§ | 1.88 (1.52-2.29)§ | 1.69 (1.38-2.09)§ | 1.45 (1.16-1.81)\|| |
| Diabetes | 4.50 (3.47-5.84)§ | 3.57 (2.71-4.69)§ | 3.35 (2.54-4.41)§ | 3.13 (2.35-4.16)§ |
| Antidepressant medication | 1.51 (1.18-1.93)\|| | 1.82 (1.40-2.37)§ |  | 1.62 (1.23-2.13)§ |
| Antihypertensive medication | 2.80 (2.45-3.21)§ | 1.67 (1.44-1.94)§ |  | 1.31 (1.11-1.55)\|| |
| Education at university, college, or $\leq$ high school | 0.53 (0.47-0.60)§ | 0.66 (0.57-0.76)§ |  | 0.73 (0.63-0.85)§ |
| Married, cohabiting, or other | 0.46 (0.39-0.55)§ | 0.40 (0.33-0.49)§ |  | 0.43 (0.35-0.52)§ |
| Current cigarette smoking | 1.08 (0.92-1.27) | 1.60 (1.34-1.92)§ |  | 1.35 (1.12-1.63)\|| |
| Men without cardiovascular disease |  |  |  |  |
| Age per additional year | 1.08 (1.07-1.09)§ |  | 1.06 (1.05-1.07)§ | 1.07 (1.05-1.08)§ |
| Glucose level per $18-\mathrm{mg} / \mathrm{dL}$ (1-mmol/L) increase | 1.30 (1.19-1.41)§ | 1.15 (1.05-1.25)\|| | 1.12 (1.03-1.22)¢ | 1.14 (1.04-1.24)\|| |
| Calculated coronary risk per $1 \%$ increase | 1.10 (1.09-1.12)§ | 1.04 (1.03-1.06)§ | 1.04 (1.03-1.06)§ | 1.03 (1.02-1.05)§ |
| Antidepressant medication | 1.76 (1.33-2.32)§ | 2.13 (1.58-2.85)§ |  | 1.90 (1.39-2.58)§ |
| Antihypertensive medication | 1.98 (1.67-2.35)§ | 1.31 (1.09-1.57)\|| |  |  |
| Education at university, college, or less than high school | 0.55 (0.47-0.64)§ | 0.65 (0.55-0.76)§ |  | 0.71 (0.60-0.84)§ |
| Married, cohabiting, or other | 0.44 (0.37-0.54)§ | 0.38 (0.31-0.47)§ |  | 0.40 (0.32-0.49)§ |
| Current cigarette smoking | 1.22 (1.01-1.47)¢ | 1.73 (1.42-2.12)§ |  |  |

[^0]disease and diabetes were entered simultaneously into a multivariate model after adjustment for age, and where all independent potential confounders were added to the model in a stepwise fashion. In this analysis, the use of antidepressants, current cigarette smoking, the use of antihypertensive medication, not being married or cohabiting, and no education past high school were all independently associated with an increased probability of ED. Nonetheless, the presence of cardiovascular disease and diabetes remained independently associated with ED. A similar analysis for those individuals without cardiovascular disease or diabetes demonstrated that higher levels of cardiovascular risk or fasting blood glucose remained independently associated with ED after adjustment for age, past or present depression, marital status, and education. These analyses were initially completed where ED was defined as an EF score of 25 or less. However, these results remained virtually unchanged when only moderate (or more severe) levels of ED were considered using an EF score of 21 or less as the cutoff point.

We also explored whether the diagnosis of ED might be useful in identifying previously undiagnosed and untreated medical conditions. Undiagnosed hyperglycemia as defined by a fasting glucose level of $126 \mathrm{mg} / \mathrm{dL}$ or more ( $\geq 7 \mathrm{mmol} / \mathrm{L}$ ) in the absence of treatment was significantly ( $P<.001$ ) more common among men with ED ( $10.6 \%$ ) vs those without ( $4.9 \%$ ). Even after adjustment for age, the presence of ED was significantly associated with undiagnosed hyperglycemia (OR, 1.46; 95\% CI, 1.02-
2.10; $P=.04$ ). Impaired fasting glucose level (99-124 $\mathrm{mg} / \mathrm{dL}$ [5.5-6.9 mmol/L] $)$ was also significantly ( $P<.001$ ) more common among men with ( $45.0 \%$ ) vs those without ED (34.3\%). After adjustment for age, the association with ED remained significant (OR, 1.26; 95\% CI, $1.08-1.46 ; P=.004)$. Finally, the metabolic syndrome was more common among men with ED ( $37.9 \%$ vs $29.2 \%$; $P<.001$ ) and remained significant after adjustment for age (OR, 1.45; 95\% CI, 1.24-1.69; $P<.001$ ).

## COMMENT

The results of CANSED demonstrate that nearly one half of Canadian men seen by primary care physicians report some degree of ED. Similar results have been reported in other community studies. ${ }^{5,6}$ Cardiovascular disease and diabetes are independently associated with ED after adjustment for age, as noted by others. ${ }^{5-9}$ However, diabetes is also a major risk factor for cardiovascular disease and may confound the association between cardiovascular disease and ED. ${ }^{19,20}$ Although most studies have been able to adjust for increasing age, only a few have had sufficiently robust data to adjust simultaneously for age, diabetes, and cardiovascular disease and confirm that each is independently associated with ED. ${ }^{6,7}$

There are also other important confounders that should be considered. For instance, a higher level of education is known to be associated with a lower risk of cardiovas-


#### Abstract

G. Ahmed, R. Akhras, J. Ashley, J. M. Auer, J. M. Balaton, G. B. Barrs, D. R. Beegan, A. M. Belliveau, S. K. P. Chan, J. Choquet, F. S. Cogan, A. G. Czaharyn, O. A. David, M. Decarie, B. Dick, M. W. Edgerley, P. M. Erhard, S. K. Gaur, C. Gervais, I. S. Gorfinkel, S. Grunberg, W. G. Hall, D. J. Hancu, R. Hart, P. H. Hebert, M. S. Hirsh, M. S. C. Ho, J. A. Hunt, I. R. Johnston, R. B. Kaasa, S. Kanani, E. Karpinski, K. Keshavjee, B. Kessel, B. W. King, C. P. Kumar, F. Lafleche, P. F. S. Lai, A. K. Lam, N. Levine, E. L. Linzon, J. M. Look, K. D. Louie, G. U. Mahmud, B. P. Malcolm, G. G. McGarry, K. K. Misik, R. Pacis, C. A. M. Pandian, K. K. Patel, V. Patel, A. V. Pavilanis, C. Phaneuf, C. Pinto, L. Pliamm, R. B. Porter, H. Reese, A. R. Rolfe, E. C. Ross, H. W. Sacks, T. Saeed, R. Saksena, C. Savard, E. Silver, J. D. Simmons, E. Sochocka, F. Spicer, M. W. Stender, B. S. Strom, J. A. Syrnyk, R. T. Tanaka, S. Teper, P. C. Twiss, M. S. Weinstock, and J. Werier. *All collaborators are doctors of medicine.


cular disease or diabetes. ${ }^{21,22}$ It was also negatively associated with ED in this study, the Massachusetts Male Aging Study, and a 4-country prevalence study. ${ }^{6,8}$ Antihypertensive medications are commonly prescribed for individuals with diabetes or coronary heart disease and may be an important cause of ED seen in both of these conditions. Depression is also more common among individuals with diabetes or cardiovascular disease and is also one of the major causes of ED. ${ }^{23,24}$ After adjustment for these potential confounders and others such as marital status and cigarette smoking, cardiovascular disease and diabetes were still independently associated with ED.

The mechanism by which cardiovascular disease results in ED remains unclear. The presence of generalized atherosclerosis and vascular impairment is a likely cause. Previous studies have demonstrated decreased penile blood pressure among patients with ED. ${ }^{25,26}$ Increased coronary artery plaque burden as defined by angiography has also been shown to correlate with ED severity. ${ }^{27}$ Among patients with diabetes, endothelial dysfunction has also been shown to correlate with ED. ${ }^{28} \mathrm{Fi}$ nally, comparing men with vascular ED but without cardiovascular disease with age-matched control subjects demonstrated a significant impairment in brachial artery endothelium-dependent and -independent vasodilation. ${ }^{29}$ The men in this study had been shown to have penile vascular disease with reduced Doppler flow rates. These results suggest that vascular ED shares the same endothelial dysfunction and smooth muscle abnormalities observed among patients with coronary artery disease or coronary risk factors. ${ }^{30,31}$

Diabetes is associated with a number of complications that may result in ED, including macrovascular disease, microvascular disease, renal failure, and neuropathy. The obesity and sedentary lifestyle that is common among patients with type 2 diabetes may also play a role in the development of ED. ${ }^{7}$ In the CANSED, a higher BMI was also associated with ED in univariate analyses but was not an independent risk factor in multivariate analyses. Unfortunately, fitness data were not collected. Antihypertensive medication that is commonly used to treat hypertension and preserve renal function among patients with diabetes was also independently associated with ED in the CANSED. This finding has also been reported in other studies. ${ }^{3,7}$

In the absence of diabetes or cardiovascular disease, a strong independent association between calculated cardiovascular risk and ED suggests that the vascular impair-
ment affecting EF may precede the development of symptomatic cardiovascular disease. In this cross-sectional study, it was not possible to determine if the presence of ED identifies men in whom cardiovascular disease is more likely to develop. Nonetheless, this association between coronary risk and ED has been observed in another crosssectional study ${ }^{9}$ and remained significant in the CANSED after adjustment for potential confounders. Prospective results from the Massachusetts Male Aging Study also confirmed that increased coronary risk precedes the development of ED. ${ }^{11}$ Among patients with diabetes accompanied by silent ischemia and asymptomatic coronary disease documented by angiography, the presence of ED was increased compared with that in patients with diabetes but without coronary disease. ${ }^{30}$ It remains to be determined if the presence of ED is actually associated with an increased incidence of future cardiovascular events. If so, ED might be added to the list of risk factors known to precede cardiovascular disease.

The men included in the CANSED population did not undergo evaluation for undetected cardiovascular disease. However, the presence of ED significantly increased the probability of undiagnosed hyperglycemia. Impaired fasting glucose and the metabolic syndrome were more common among men with ED. Each of these conditions has been shown to be associated with an increased probability of development of cardiovascular disease. Diabetes and the metabolic syndrome are among the strongest risk factors currently identified. The presence of either condition is independently associated with a 3- to 4-fold increase in coronary events. ${ }^{32-34}$ These associations further suggest that ED should be a risk factor for future cardiovascular events, at least indirectly through its association with undetected glucose abnormalities.

The CANSED results demonstrate that ED is common in a primary care setting. Given an aging population and growing treatment for ED, these estimates may change. Erectile dysfunction is particularly common among men with cardiovascular disease and/or diabetes. In the absence of either comorbidity, ED is associated with increased calculated coronary risk and increased fasting glucose levels. Finally, the prevalence of ED is positively associated with undiagnosed hyperglycemia and other glucose abnormalities that should be identified and treated. These data demonstrate that primary care physicians may find that taking a sexual history provides important clinical information beyond the detection of ED.

Accepted for Publication: July 22, 2005.
Correspondence: Steven A. Grover, MD, MPA, FRCPC, Division of Clinical Epidemiology, The Montreal General Hospital, 1650 Cedar Ave, Montreal, Quebec, Canada H3G 1A4 (steven.grover@mcgill.ca).
Author Contributions: Dr Grover had full access to all the data in the study and final responsibility for the content of the manuscript and the decision to submit for publication.
Financial Disclosure: Dr Grover has received honoraria and grants from the following companies: Pfizer, Inc; Merck \& Co, Inc; Bristol-Myers Squibb; Sanofi-Aventis; and AstraZeneca. Dr Grover or family members own stock in Merck \& Co, Inc; Bristol-Myers Squibb; Pfizer, Inc; Johnson \& Johnson; and Kos Pharmaceutical, Inc. Dr Defoy owns stock options in Pfizer, Inc.
Funding/Support: The Canadian Study of Erectile Dysfunction (CANSED) was funded by Pfizer Canada, Kirkland, Quebec. For a list of CANSED collaborators, see the box on page 218 .

## REFERENCES

1. Morgentaler A. Male impotence. Lancet. 1999;354:1713-1718.
2. Jackson G, Betteridge J, Dean J, et al. A systematic approach to erectile dysfunction in the cardiovascular patient: a consensus statement: update 2002. Int J Clin Pract. 2002;56:663-671.
3. Bortolotti A, Parazzini F, Colli E, Landon M. The epidemiology of erectile dysfunction and its risk factors. Int J Androl. 1997;20:323-334
4. Lue TF. Erectile dysfunction. N Engl J Med. 2000;342:1802-1813.
5. Feldman HA, Goldstein I, Hatzichristou G, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol. 1994;151:54-61.
6. 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.
7. 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.
8. Johannes CB, Araujo AB, Feldman HA, Derby CA, Kleinman KP, McKinlay JB. Incidence of erectile dysfunction in men 40 to 69 years old: Iongitudinal results from the Massachusetts Male Aging Study. J Urol. 2000;163:460-463.
9. Roumeguère T, Wespes E, Carpentier Y, Hoffmann P, Schulman CC. Erectile dysfunction is associated with a high prevalence of hyperlipidemia and coronary heart disease risk. Eur Urol. 2003;44:355-359.
10. Wei M, Macera CA, Davis DR, Hornung CA, Nankin HR, Blair SN. Total cholesterol and high density lipoprotein cholesterol as important predictors of erectile dysfunction. Am J Epidemiol. 1994;140:930-937.
11. 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.
12. Derby CA, Mohr BA, Goldstein I, McKinlay JB. Modifiable risk factors and erectile dysfunction: can lifestyle changes modify risk? Urology. 2000;56: 302-306.
13. Perttula E. Physician attitudes and behaviour regarding erectile dysfunction in at-risk patients from a rural community. Postgrad Med J. 1999;75:83-85.
14. Slag MF, Morley JE, Elson MK, et al. Impotence in medical clinic outpatients. JAMA. 1983;249:1736-1740.
15. 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.
16. Cappelleri JC, Rosen RC, Smith MD, Mishra A, Osterloh IH. Diagnostic evaluation of the erectile function domain of the International Index of Erectile Function. Urology. 1999;54:346-351.
17. National Center for Health Statistics. Third National Health and Nutrition Examination Survey, 1988-1994 [book on CD-ROM]. Hyattsville, Md: Centers for Disease Control and Prevention; 1997. Series 11, 1A ed.
18. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002;106:3143-3421.
19. American Diabetes Association. Consensus development conference on the diagnosis of coronary heart disease in people with diabetes. Diabetes Care. 1998; 21:1551-1559.
20. Leiter LA, Mahon J, Ooi TC, et al. Macrovascular complications, dyslipidemia and hypertension: Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Can J Diabetes. 2003; 27(suppl 2):S58-S65.
21. Liu K, Cedres LB, Stamler J. Relationship of education to major risk factors and death from coronary heart disease, cardiovascular disease and all causes: findings of three Chicago epidemiologic studies. Circulation. 1982;66:1308-1314.
22. Harris SB. Introduction: Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Can J Diabetes. 2003;27(suppl 2):S1-S3.
23. Anderson RJ, Freedland KE, Clouse RE, et al. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. Diabetes Care. 2001;24: 1069-1078.
24. Egede LE, Zheng D, Simpson K. Comorbid depression is associated with increased health care use and expenditures in individuals with diabetes. Diabetes Care. 2002;25:464-470.
25. Virag R, Bouilly P, Frydman D. Is impotence an arterial disorder? a study of arterial risk factors in 440 impotent men. Lancet. 1985;1:181-184.
26. Morley JE, Korenman SG, Kaiser FE, Mooradian AD, Viosca SP. Relationship of penile brachial pressure index to myocardial infarction and cerebrovascular accidents in older men. Am J Med. 1988;84:445-448.
27. Solomon H, Man JW, Wierzbicki AS, Jackson G. Relation of erectile dysfunction to angiographic coronary artery disease. Am J Cardiol. 2003;91:230-231.
28. De Angelis L, Marfella MA, Siniscalchi M, et al. Erectile and endothelial dysfunction in type II diabetes: a possible link. Diabetologia. 2001;44:1155-1160.
29. Kaiser DR, Billups K, Mason C, Wetterling R, Lundberg JL, Bank AJ. Impaired brachial artery endothelium-dependent and -independent vasodilation in men with erectile dysfunction and no other clinical cardiovascular disease. JAm Coll Cardiol. 2004;43:179-184.
30. Raitakari OT, Seale JP, Celermajer DS. Impaired vascular responses to nitroglycerin in subjects with coronary artherosclerosis. Am J Cardiol. 2001;87: 217-219.
31. Cheitlin MD. Erectile dysfunction: the earliest sign of generalized vascular disease? J Am Coll Cardiol. 2004;43:185-186.
32. Sattar N, Gaw A, Scherbakova O, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. Circulation. 2003;108:414-419.
33. Girman CJ, Rhodes T, Mercuri M, et al. The metabolic syndrome and risk of major coronary events in the Scandinavian Simvastatin Survival Study (4S) and the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS). Am J Cardiol. 2004;93:136-141.
34. Grover SA, Paquet S, Levinton C, Coupal L, Zowall H. Estimating the benefits of modifying risk factors of cardiovascular disease: a comparison of primary vs secondary prevention. Arch Intern Med. 1998;158:655-662.

[^0]:    Abbreviations: Cl , confidence interval; OR, odds ratio.
    *Erectile dysfunction is defined as an erectile function score of 25 or less on the International Index of Erectile Function.
    $\dagger$ Includes adjustment for age, the presence of cardiovascular disease, and the presence of diabetes.
    $\ddagger$ Includes adjustment for age and the other variables indicated by the presence of an OR and $95 \% \mathrm{Cl}$.
    $\S P<.001$.
    $\| P<.01$.
    ॥ $P<.05$.

