

# Clinical, Socioeconomic, and Lifestyle Parameters Associated With Erectile Dysfunction Among Diabetic Men

OFRA KALTER-LEIBOVICI, MD<sup>1,2</sup>  
 JULIO WAINSTEIN, MD<sup>3</sup>  
 ARNONA ZIV, MA<sup>4</sup>  
 ILANA HARMAN-BOHEM, MD<sup>5</sup>

HAVI MURAD, MA<sup>6</sup>  
 ITAMAR RAZ, MD<sup>7</sup>  
 FOR THE ISRAEL DIABETES RESEARCH GROUP  
 (IDRG) INVESTIGATORS\*

**OBJECTIVE** — Erectile dysfunction is frequently observed in diabetes. The current study aims to assess the association of a comprehensive set of clinical, socioeconomic, and lifestyle parameters with erectile dysfunction in diabetic men.

**RESEARCH DESIGN AND METHODS** — Participants were randomly selected from male patients (age >18 years) treated in 26 diabetes clinics in Israel. Participants completed a self-reported questionnaire on demographic, socioeconomic, and lifestyle characteristics and on erectile function, using the IIEF-15 (International Index of Erectile Function). Information on diabetes type, duration, treatment, and control; microvascular complications and cardiovascular disease; drug therapy; blood pressure; and lipid levels was also obtained.

**RESULTS** — Information on erectile function was obtained in 1,040 patients. Their mean age was 57 years, and their median diabetes duration was 8 years (range <1–50). Normal erectile function was found in 13.5% of the patients and severe erectile dysfunction in 30.1%. The characteristics found to be significantly associated with erectile dysfunction [associations presented as adjusted odds ratio (95% CI)] were: patient's age (5-year increments): 1.38 (1.29–1.48); diabetes duration (5-year increments): 1.16 (1.07–1.26); current HbA<sub>1c</sub> level (1% increment): 1.10 (1.01–1.19); any microvascular disease: 1.43 (1.09–1.88); cardiovascular disease: 1.78 (1.27–2.48); and diuretic treatment: 1.78 (1.09–2.91). Leisure time and work-related physical activity and consumption of small amounts of alcohol were found to be protective: 0.51 (0.36–0.72) and 0.70 (0.51–0.97), respectively.

**CONCLUSIONS** — In diabetic men, erectile dysfunction severity increases with age and diabetes duration, poor glycemic control, presence of microvascular complications, diuretic treatment, and cardiovascular disease. Physical activity and alcohol intake may be protective. These findings can guide clinicians in taking preventive measures and undertaking early screening and treatment in high-risk patients.

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From the <sup>1</sup>Unit of Cardiovascular Epidemiology, Gertner Institute for Epidemiology and Health Policy Research, Sheba Medical Center, Tel-Hashomer, Israel; the <sup>2</sup>Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel; the <sup>3</sup>Diabetes Unit, Wolfson Medical Center, Holon, Israel; the <sup>4</sup>Information and Computer Unit, Gertner Institute for Epidemiology and Health Policy Research, Sheba Medical Center, Tel-Hashomer, Israel; the <sup>5</sup>Department of Internal Medicine C and the Diabetes Unit, Soroka University Medical Center, Beer-Sheba, Israel; the <sup>6</sup>Unit of Biostatistics, Gertner Institute for Epidemiology and Health Policy Research, Sheba Medical Center, Tel-Hashomer, Israel; and the <sup>7</sup>Diabetes Unit, Hadasa Medical Center, Jerusalem, Israel.

Address correspondence and reprint requests to Ofra Kalter-Leibovici, Unit of Cardiovascular Epidemiology, Gertner Institute for Epidemiology and Health Policy Research, Sheba Medical Center, Tel-Hashomer, Ramat-Gan, 52621, Israel. E-mail: ofrak@post.tau.ac.il.

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\*A complete list of the IDRG Investigators can be found in the APPENDIX.

**Abbreviations:** CVD, cardiovascular disease.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Diabetic men are at high risk of developing erectile dysfunction (1–7). Hyperlipidemia, hypertension, and cardiovascular disease (CVD), which frequently complicate diabetes, and drugs that are commonly given to diabetic patients (i.e., antihypertension agents) are associated with higher frequency of erectile dysfunction (1,5,8–10).

The prevalence of erectile dysfunction is expected to double by the year 2025, and the growing global epidemic of diabetes contributes to this forecast (11). Despite being associated with poor quality of life, erectile dysfunction is seldom addressed by primary-care physicians and specialists (12). The current study aims to define, from a comprehensive set of socioeconomic, lifestyle, and clinical characteristics reported to be associated with erectile dysfunction in population studies, attributes that are significantly and independently associated with greater risk for erectile dysfunction in diabetic men. This will allow physicians to identify patients at increased risk for erectile dysfunction who could benefit from preventive measures and timely treatment.

## RESEARCH DESIGN AND METHODS

The study participants included diabetic men treated in ambulatory secondary and tertiary diabetes care clinics in Israel.

A random sample of calendar days was obtained for each clinic participating in the study. During these days, all scheduled visits of diabetic male patients (age >18 years) were registered. Patients with comorbidities that might have caused erectile dysfunction regardless of diabetes (i.e., congenital or acquired spinal, pelvic, or penile malformations and injuries; prostate cancer; alcohol or drug abuse; depression; and schizophrenia) were excluded. Eligible patients were included in the study after obtaining their informed consent. The study protocol was approved by the local ethics committees.

Participants completed a questionnaire containing information on sociodemographic and lifestyle characteristics.

They were asked how many hours a day they were engaged in nonleisure strenuous physical activity at work and/or at home and how many hours per week they spent in leisure-time physical activity. Participants were asked about current or past cigarette smoking, the number of cigarettes smoked per day, age at the start of smoking, and age at smoking cessation. Based on this information, we calculated for each individual the number of pack-years (1 pack-year is smoking 20 cigarettes per day for 1 year; individuals who never smoked have 0 pack-years) as a single measure that quantifies lifetime cigarette smoking. Participants were asked whether they drink alcoholic beverages and the number of portions consumed per week.

Participants were asked to answer the IIEF-15 (International Index of Erectile Function) questionnaire, a reliable and valid self-administered measure of erectile function used in epidemiological studies and clinical trials on erectile dysfunction. The questionnaire includes five domains, derived by factor analysis, which assess erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. For the current analysis, we used items 1–5 and 15, which are the components of the erectile function domain. Participants were asked how often they were able to get an erection during sexual activity, how often their erections were hard enough for penetration, how often they were able to penetrate their partner when attempting sexual intercourse, how often they were able to maintain their erection after penetration, how difficult it was to maintain their erection to completion of intercourse, and how they rate their confidence in being able to get and keep an erection. Scores for the first five questions ranged from 0 for “Did not attempt intercourse” to 5 for “Almost always/always.” The score for the last question ranged from 1 for “Very low” to 5 for “Very high.” Erectile function score was calculated as the sum of scores of these items (possible range: 1–30) and further recoded as a five-category ordinal variable (previously defined), ranging from normal function (score 26–30) to severe dysfunction (score 1–10), to present a clinically meaningful gradient of erectile dysfunction severity (13–15).

Information on patients' height, weight, age at diagnosis of diabetes, dia-

betes type and mode of treatment, presence of diabetic microvascular and macrovascular complications, presence of hypertension and/or hyperlipidemia, and drug therapy was obtained from the medical records using a standard questionnaire completed by the participating physicians. An abbreviated questionnaire containing pertinent information on patients who refused to participate was also completed. Data collection began in December 2001 and ended by June 2003.

#### Sample size calculation, data management, and analysis

The sample size calculations, using formula with continuous outcome for unequal group sizes and unequal variances (16), were based on our previous findings on the associations between erectile dysfunction with age, diabetes duration, and HbA<sub>1c</sub> (A1C) level (7). According to these calculations, and assuming a 75% response rate, we aimed at a sample of at least 1,000 eligible patients. Data entry and analyses were performed using the 8.2 release of SAS computer software. Associations of contingency tables were tested using the  $\chi^2$  statistic, whereas associations between erectile function and continuous variables were tested using ANOVA and the Kruskal-Wallis test, as appropriate. To test for variables that are significantly and independently associated with erectile dysfunction severity, ordinal logistic regression analysis was used (17). Variables associated with erectile dysfunction on univariate analysis with a *P* value < 0.1 were entered into the multivariate model. All analyses were two-tailed, and the critical value for statistical significance was set at  $\alpha = 0.05$ .

**RESULTS** — Of 1,510 eligible male patients treated in 26 clinics, 1,301 (86%) agreed to participate in the study, and 1,040 (69%) provided complete information on erectile function. Normal erectile function was reported in 140 men (13.5%), whereas mild, mild-to-moderate, moderate, and severe erectile dysfunction was found in 216 (20.8%), 193 (18.5%), 178 (17.1%), and 313 (30.1%) patients, respectively.

The patients' age (mean  $\pm$  SD) was 57.0  $\pm$  11.8 years, and the median diabetes duration was 8 years (range <1–50). Most of the patients (88%) had type 2 diabetes. Of the patients, ~50% had some microvascular disease (diabetic ret-

inopathy, nephropathy, and/or neuropathy) in one or more sites. Ischemic heart disease was reported in 20% of the patients and CVD (defined as having ischemic heart disease, peripheral vascular disease, and/or stroke) in 25%.

#### Associations between patients' characteristics and erectile dysfunction

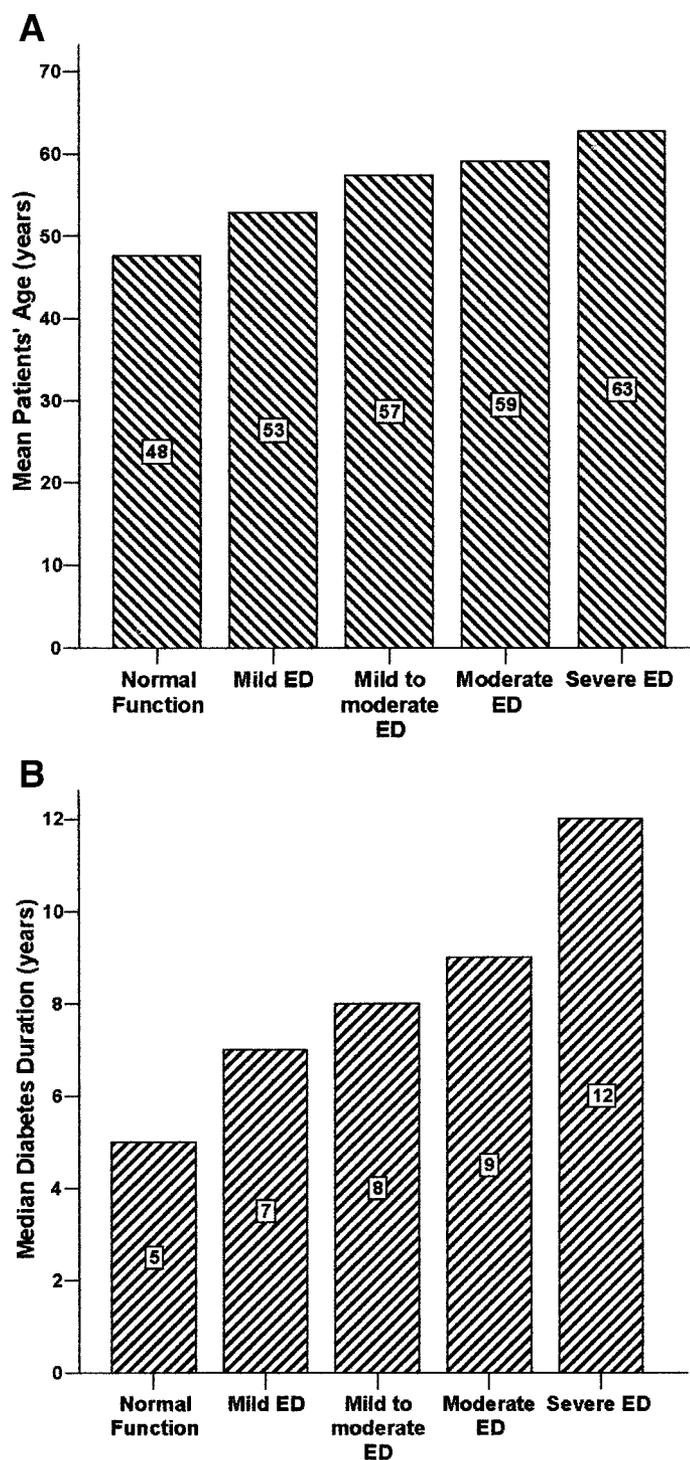
The prevalence and severity of erectile dysfunction increased significantly with age (Fig. 1A). Patients with greater erectile dysfunction severity were more likely to be born outside Israel, be currently unemployed, avoid alcohol, be physically inactive, have a blue-collar profession, and have a history of cigarette smoking (measured in pack-years). BMI was not significantly associated with erectile dysfunction (Table 1).

Because patients born in Israel were significantly younger than patients born elsewhere (mean age: 53.9  $\pm$  12.2 vs. 61.3  $\pm$  11.1 years, *P* < 0.001), we studied the association between country of birth and erectile dysfunction after controlling for the effect of age. The age-adjusted association between the country of birth and erectile dysfunction was no longer statistically significant (adjusted odds ratio [OR] 0.87, 95% CI 0.68–1.11).

#### Associations between characteristics of diabetes and its complications and erectile dysfunction

The prevalence and severity of erectile dysfunction increased significantly with diabetes duration (Fig. 1B). Patients with erectile dysfunction had higher current A1C values, and erectile dysfunction severity increased with increasing prevalence of microvascular disease, ischemic heart disease, and CVD (Table 1).

The severity of erectile dysfunction was inversely related to the proportion of patients with type 1 diabetes. Because type 1 diabetic patients were significantly younger than type 2 patients (mean age: 45.6  $\pm$  15.0 vs. 49.7  $\pm$  10.6 years, *P* < 0.001), we tested for the association between diabetes type and erectile dysfunction after controlling for the effect of age. Diabetes type was no longer significantly associated with erectile dysfunction after controlling for the effect of age (adjusted OR: 0.96, 95% CI: 0.66–1.39).



**Figure 1**—Erectile function by age (A) and diabetes duration (B). ED, erectile dysfunction.

### Associations between hypertension and hyperlipidemia and erectile dysfunction

Patients with erectile dysfunction had a higher prevalence of physician-diagnosed hypertension, and the mean systolic blood pressure increased with increasing

erectile dysfunction severity. All types of antihypertension drugs were significantly associated with erectile dysfunction in univariate analyses (Table 2).

Although erectile dysfunction severity was found to be associated with greater prevalence of physician-diagnosed hyper-

lipidemia, plasma triglycerides were the only plasma lipid parameter found to be significantly associated with erectile dysfunction (Table 2).

### Multivariate analysis

To test for variables significantly and independently associated with the five-category erectile dysfunction parameter, we entered the following characteristics into the multivariate model: patient's age, country of birth, profession (blue-collar versus other), any alcohol consumption, lifetime exposure to cigarette smoking (in pack-years), physical activity, diabetes type and duration, current A1C level, presence of any microvascular and cardiovascular disease, physician-diagnosed hypertension and hyperlipidemia, and the type(s) of antihypertension drug therapy.

The attributes found to be positively associated with erectile dysfunction severity in the multivariate model were patient's age, diabetes duration and current A1C level, having any microvascular disease, CVD, and diuretic drug therapy. Both work-related and leisure-time physical activity and any alcohol consumption were inversely related to erectile dysfunction severity (Table 3). It should be noted that most of the study participants (79.7%) avoided alcohol completely, 17.5% had up to one alcoholic drink per day, and only 2.8% reported more frequent alcohol consumption.

Physician-diagnosed hypertension and antihypertension drugs other than diuretics (i.e.,  $\beta$ -adrenergic receptor blockers, calcium channel antagonists, ACE inhibitors, and angiotensin receptor antagonists) were not found to be significantly associated with erectile dysfunction in the multivariate model.

Cigarette smoking was not found to be significantly associated with erectile dysfunction in the multivariate analysis. To further investigate the association between cigarette smoking and erectile dysfunction, we stratified the patients according to the presence or absence of CVD. The association between cigarette smoking and erectile dysfunction was not found to be statistically significant in patients with and without CVD (data not shown). We thus conclude that the association between cigarette smoking and erectile dysfunction is probably mediated by CVD.

Table 1—Associations between demographic, lifestyle, and diabetes-related characteristics and erectile function

	Total	Normal erectile function	Mild erectile dysfunction	Mild to moderate erectile dysfunction	Moderate erectile dysfunction	Severe erectile dysfunction	P
n (%)	1,040 (100)	140 (13.5)	216 (20.8)	193 (18.5)	178 (17.1)	313 (30.1)	—
Patients' characteristics							
Age (years)	57.0 ± 11.8	47.6 ± 11.8	52.8 ± 11.3	57.3 ± 9.1	59.0 ± 10.2	62.6 ± 10.9	<0.0001
Region/country of birth							
Asia/Africa	19.9	9.0	20.5	25.3	22.3	20.1	—
Europe/America	33.5	32.3	31.0	29.3	32.5	38.7	0.0078
Israel	46.6	58.6	48.4	45.4	45.2	41.2	—
Currently employed*	70.3	85.4	77.4	67.3	65.2	57.0	<0.0001
Blue-collar profession	30.0	20.2	24.1	32.0	38.6	33.2	0.0044
Number of pack-years (median)†	12.55	4.0	11.0	12.65	16.5	17.5	0.0168
Any alcohol consumption	20.4	29.4	21.4	19.0	20.7	16.3	0.0361
Physically active							
None	33.8	27.7	26.2	26.5	34.7	45.7	—
Leisure time	26.5	28.5	28.1	25.9	22.3	27.3	—
At work	16.2	15.3	18.1	20.1	14.7	13.8	—
Both	23.5	28.5	27.6	27.5	28.2	13.2	—
BMI (kg/m <sup>2</sup> )	28.5 ± 4.4	28.0 ± 4.1	28.5 ± 4.5	28.6 ± 4.5	28.5 ± 4.2	28.8 ± 4.5	0.50
Characteristics of diabetes and its complications							
Median diabetes duration (years)	8	5	7	8	9	12	<0.0001
Type 1 diabetes	12.1	25.7	15.4	8.8	11.2	6.1	<0.0001
Current A1C (median)	7.7	7.6	7.3	7.6	7.9	7.8	0.0176
Any microvascular complications	50.1	37.1	38.4	47.7	55.6	62.3	<0.0001
Ischemic heart disease	20.0	5.1	11.4	20.9	22.0	30.6	<0.0001
CVD	24.8	6.6	13.4	26.3	27.1	38.4	<0.0001

Data are the means ± SD or %, unless otherwise indicated. \*Patient's age is <65 years; †1 pack-year = smoking one pack of cigarettes per day for 1 year. One pack contains 20 cigarettes. BMI is calculated as body weight (kg) divided by height squared (m<sup>2</sup>).

### Comparisons of participants and nonparticipants

The study participants had significantly shorter diabetes duration compared with those who refused to participate (median duration: 9 vs. 11 years, respectively;  $P = 0.016$ ). They also had lower prevalence of diabetic retinopathy (corresponding rates: 23.95 vs. 32.85%,  $P = 0.029$ ). Participants and nonparticipants did not differ by age, current A1C, and prevalence of CVD (data not shown).

Among participants, those who provided complete information on erectile function were significantly younger and had shorter diabetes duration compared with patients who provided incomplete information (median age: 57 vs. 64 years,  $P < 0.0001$ ; median diabetes duration: 8 vs. 12 years,  $P = 0.002$ ). They had also significantly less CVD compared with participants who failed to provide complete information (24.8 vs. 39.8%,  $P < 0.0001$ ).

**CONCLUSIONS**— Our main findings are that erectile dysfunction is common among men treated in diabetes clinics, and its severity increases with age, diabetes duration and poor diabetes control, presence of microvascular complications, CVD, and diuretic drug therapy.

Previous studies have also reported the association between erectile dysfunction and increasing age (7,18–21), poor diabetes control (7,20–22), presence of microvascular complications (17–20), and CVD (20,21). The association between diabetes duration and erectile dysfunction has been reported in some but not all studies (7,20,21,23). Our finding that diuretics, rather than hypertension per se, are significantly associated with erectile dysfunction confirms previous reports (7,20,24).

We found no residual effect of lifetime exposure to cigarette smoking, after controlling for the confounding effects of age and presence of CVD. This finding is

similar to that reported by Klein et al. (20) and contradicts that reported by Fedele et al. (21). Similarly, we found no residual effect of diabetes type on erectile dysfunction, after controlling for patients' age, unlike a previous report on greater frequency of erectile dysfunction in type 1 diabetic patients (21).

Finally, we found that both leisure time and work-related physical activity and consumption of small amounts of alcohol may have a protective effect against erectile dysfunction. Recently, physical activity together with weight reduction were reported to improve erectile function in nondiabetic obese men (25). The protective effect of consumption of alcohol in small amounts on the risk to develop erectile dysfunction in diabetic men should be confirmed in prospective studies.

Our study is cross-sectional and therefore inferences on causal relationships should be made with caution. Considering the fact that nonparticipants in our study

Table 2—Associations between hypertension, antihypertension therapy, hyperlipidemia, and erectile function

Variable	Total	Normal erectile function	Mild erectile dysfunction	Mild to moderate erectile dysfunction	Moderate erectile dysfunction	Severe erectile dysfunction	P
n (%)	1,040 (100)	140 (13.5)	216 (20.8)	193 (18.6)	178 (17.1)	313 (30.1)	—
Hypertension and antihypertension drug therapy							
Systolic blood pressure (mmHg)	134.1 ± 18.8	128.3 ± 15.3	132.5 ± 18.9	135.2 ± 19.5	133.2 ± 17.2	137.5 ± 20.0	0.0001
Hypertension*	440 (43.0)	36 (26.5)	81 (38.6)	78 (40.6)	77 (43.7)	168 (54.4)	<0.0001
Subjects on diuretics	103 (9.9)	6 (4.3)	19 (8.8)	9 (4.7)	14 (7.9)	55 (17.6)	<0.0001
Subjects on β-adrenergic receptor blockers	155 (14.9)	5 (3.6)	39 (18.1)	27 (14.0)	26 (14.6)	58 (18.5)	0.0007
Subjects on Calcium channel antagonists	164 (15.8)	11 (7.9)	26 (12.0)	23 (11.9)	28 (15.7)	76 (24.3)	<0.0001
Subjects on ACE inhibitors or angiotensin receptor antagonists	487 (46.8)	50 (35.7)	93 (43.1)	93 (48.2)	85 (47.7)	166 (53.0)	0.0102
Plasma lipid levels and hyperlipidemia							
Total cholesterol (mmol/l)	4.9 ± 1.0	4.8 ± 0.9	4.9 ± 1.0	5.0 ± 1.1	5.0 ± 1.2	4.9 ± 1.0	0.64
LDL cholesterol (mmol/l)	3.0 ± 0.8	2.9 ± 0.8	2.9 ± 0.7	3.0 ± 0.9	2.9 ± 0.9	2.9 ± 0.8	0.81
Triglyceride level (median) (mmol/l)	1.7	1.3	1.5	1.8	1.8	1.9	0.0017
HDL cholesterol (mmol/l)	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	0.32
Hyperlipidemia*	56.1	45.2	51.4	56.0	59.3	62.3	0.0077

Data are the means ± SD, n (%), or %, unless otherwise indicated. \*Physician diagnosed.

and participants who failed to provide complete information on erectile function had higher prevalence of erectile dysfunction risk markers, we assume that the true prevalence and severity of erectile dysfunction in the study population may have been even greater than those described.

The comprehensive assessment of sociodemographic, lifestyle, and disease-related characteristics allowed an in-depth investigation of the characteristics

that are significantly associated with erectile dysfunction severity in diabetic men. Our study points at potentially modifiable factors associated with erectile dysfunction severity in diabetic men (i.e., diabetes control and diuretic treatment) and suggests possible protective effects of physical activity and moderate alcohol consumption. Awareness of factors associated with erectile dysfunction should guide the clinician in taking preventive

measures, making timely detection, and treating erectile dysfunction.

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## APPENDIX

### Israel Diabetes Research Group (IDRG) Investigators

Afula: Dagan B; Beer-Sheba: Harman Bohem I and Khanina DH; Haifa: Abdul-Ghani MA, Minuchin O, and Orlovsky S; Herzelia: Roitman A; Holon: Ashkenazy B and Wainstein J; Jaffa: Cohen J and Stern E; Jerusalem: Raz I, Shilo S, and Tsur A; Kiron: Lifshitz A; Nahariya: Herskovits TA; Nazareth: Zoabi M; Netanya: Norymberg C; Petach-Tiqva: Dux S and Loewinger Z; Rehovot: Knobler H; Rishon-le-Zion: Arad J and Bar-Or IS; Tel-Aviv: Rubinstein A and Yerushalmy Y; Tel-Hashomer: Kalter-Leibovici O; and Zafat: Adawi F.

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Table 3—Attributes significantly associated with erectile dysfunction in multivariate analysis

Variable	P	Odds ratio (95% CI)
Patients' characteristics		
Age (10-year increments)	<0.0001	1.81 (1.57–2.09)
Physical activity (reference category: none)		
Work related	0.57	0.79 (0.54–1.16)
Leisure time	0.98	0.74 (0.53–1.03)
Both types	0.0009	0.50 (0.35–0.71)
Any alcohol consumption (reference category: none)	0.0326	0.70 (0.51–0.97)
Clinical characteristics		
Diabetes duration (5-year increments)	<0.0001	1.20 (1.10–1.31)
A1C (1% increment)	0.0368	1.09 (1.01–1.18)
Any microvascular complications	0.0199	1.39 (1.05–1.83)
Cardiovascular disease	0.0008	1.80 (1.28–2.54)
Diuretics	0.0135	1.87 (1.14–3.08)

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