Title

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Journal

Diabetes Care, 31(1)

ISSN

1066-9442

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Publication Date

2008

DOI

10.2337/dc07-1244

Peer reviewed

Sex Disparities in Control and Treatment of Modifiable Cardiovascular Disease Risk Factors Among Patients With Diabetes

Translating Research Into Action for Diabetes (TRIAD) Study

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OBJECTIVE — Cardiovascular disease (CVD) mortality has decreased in men but not in women with diabetes. We investigated whether sex differences in control and treatment of CVD risk factors might underlie this disparity.

RESEARCH DESIGN AND METHODS — We performed cross-sectional analyses from a cohort of patients with diabetes sampled from 10 U.S. managed care health plans. Study end points included not being in control for CVD risk factors (≥140 mmHg for systolic blood pressure [SBP], ≥3.35 mmol/l for LDL cholesterol, and ≥8.0% for A1C) and the intensity of medication management (number of medication classes) for patients not in control. Logistic regression models with random intercepts were used to adjust probabilities of control and management for demographics, clinical characteristics, and clustering within health plans.

RESULTS — There were 1,315 women and 1,575 men with a history of CVD and 3,415 women and 2,516 men without a history of CVD. Among patients with CVD, adjusted estimated probabilities for not being in control and risk differences varied significantly between men and women for SBP (men 41.2%, women 46.6%; risk difference −5.4% [95% CI −9.5 to −1.3]) and LDL cholesterol (men 22.4%, women 28.3%; risk difference −5.9% [−9.9 to −1.8]). There were no significant sex differences in intensity of medication management for patients not in control. In patients without CVD there were no significant differences in control or intensity of medication management.

CONCLUSIONS — In diabetic patients with CVD, poorer control of SBP and LDL cholesterol for women may contribute to the sex disparity in CVD mortality trends.

Diabetes Care **31:69–74, 2008**

During the last 25 years in the U.S., cardiovascular disease (CVD)-related mortality has declined among men with and without diabetes (1). Among women, however, a decrease in CVD-related mortality has been observed only for those without diabetes (1,2). A recent analysis (2) of a series of independent samples of the U.S. population who participated in the National Health and Nutrition Surveys has shown that among men with diabetes, the CVD mortality rate decreased from 26.4 annual deaths per 1,000 persons in 1971–1986 to 12.8 annual deaths per 1,000 persons in 1998–2000. Among women with diabetes the CVD mortality rate did not decline between 1971–1986 (10.5 annual deaths per 1,000 persons) and 1998–2000 (9.4 annual deaths per 1,000 persons) (2). Diabetes is a substantial risk factor for CVD and is a greater risk factor for CVD in women than in men (3,4). CVD-related mortality rates are 3–7 times higher among women with diabetes than among women without diabetes (4). Among men, these rates are 2–4 times higher among those with diabetes than among those without the disease (4).

The reason for these sex differences is not known, but they may be attributable to a combination of biological (5) and behavioral (6) factors or, possibly, to differences in the quality of health care that patients receive (7). Several studies (7–10) have reported that women with diabetes are less likely than men to receive the recommended processes of care for CVD prevention, such as lipid screening, foot examination, and aspirin use. It is less clear whether levels of modifiable CVD risk factors are managed differently in women than in men.

We investigated sex disparities regarding the levels of control and the degree of medication treatment of CVD risk factors such as levels of systolic blood pressure (SBP), LDL cholesterol, and A1C in a population-based cohort of managed care patients with diabetes as part of the

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Received for publication 29 June 2007 and accepted in revised form 9 October 2007.

Published ahead of print at http://care.diabetesjournals.org on 12 October 2007. DOI: 10.2337/dc07-1244.

*A complete list of the TRIAD Study Group members can be found in the APPENDIX.

Abbreviations: CVD, cardiovascular disease; TRIAD, Translating Research into Action for Diabetes; SPB, systolic blood pressure.

The contents of this article solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention and the National Institute of Diabetes and Digestive and Kidney Diseases.

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

Translating Research into Action for Diabetes (TRIAD) Study (11).

RESEARCH DESIGN AND METHODS

— The TRIAD Study methods have been described previously (11). The primary objective of the TRIAD Study is to determine how the structural and organizational characteristics of health systems and health care provider groups influence processes and outcomes of diabetes care (12). Six translational research centers collaborate with 10 health plans and 68 provider groups, which serve ~180,000 patients with diabetes. Health plans from Hawaii, California, Texas, Indiana, Michigan, New Jersey, and Pennsylvania are represented and include a racially and ethnically diverse membership. The study protocol was approved by the institutional review boards at all six translational research centers.

The TRIAD Study population consisted of a random sample of adult enrollees with diabetes from the participating health plans. Patients were eligible for the TRIAD Study if they were aged ≥18 years, were community dwelling, were English or Spanish speaking, were not pregnant, had diabetes for at least 1 year, were continuously enrolled in the health plan for at least 18 months, and used services during that time.

Diabetes diagnosis was based on data from the year before enrollment and included one or more of the following criteria: at least two outpatient visits or one inpatient stay with a diagnostic code for diabetes (ICD-9 250.xx) or laboratory tests or values suggesting diabetes (at least two A1C tests ordered or a diagnostic A1C or fasting blood glucose level) or a prescription for medications for diabetes (for example, insulin or an oral antidiabetic agent). At the time of the survey, patients who met these initial criteria were included only if they verified that they had diabetes and received most of their diabetes care through the participating TRIAD health plan. All of the participants provided informed consent.

Data sources

Recruitment was completed in September 2001. Patient surveys included questions on health status, diabetes duration, current diabetes treatment, and demographic characteristics. Of the 13,086 individuals who were contacted and eligible, 11,927 (91%) completed the survey (56.6% by computer-assisted telephone interview and 43.4% by written survey). If we assume that the individuals whom we could not contact had the same rate of eligibility as those whom we contacted, the response rate as endorsed by the Council of American Survey Research Organizations (13) was 69%.

Of the patients completing a survey, 73% consented to medical record review and subsequently had charts available for review; the participants whose charts were reviewed were similar to the overall study population (14). Centrally trained reviewers used standardized data collection software to abstract levels of modifiable CVD risk factors (see below) and medications during the 12 months before the survey date. Five percent of records were abstracted in a double-blind fashion; that is, reviewers were not aware of which subjects were selected for double abstraction. Inter-rater reliability (κ) for the main quality measures derived from medical record data ranged from 0.86 to 0.94.

Study end points included levels of modifiable CVD risk factors such as the most recent levels of SBP, LDL cholesterol, and A1C. These outcomes were analyzed as binary variables (≥140 vs. <140 mm Hg for SBP, ≥3.35 vs. < 3.35 mmol/l for LDL cholesterol, and ≥8.0 vs. < 8.0% for A1C) according to the levels considered to be not in control and that therefore require more action as recommended at that time by the American Diabetes Association (15). We defined a second set of end points to reflect the intensity of medication management strategies of the three outcomes for individuals with risk factor values at or above these cut points. For each CVD risk factor, we calculated the sex-specific proportion of the patients with levels not in control who were currently receiving more intensive medication management, presumably reflecting a greater effort to manage the outcome (16). More intense medication management was operationalized as the use of two or more drug classes of antihypertensive agents for hypertension, of one or more lipid-lowering agents for hypercholesterolemia, and of two or more oral agents or insulin for diabetes.

The covariates were obtained from the patient survey: age, sex, race/ethnicity, education, income, BMI, smoking, duration of diabetes, and a four-level treatment variable (diet-controlled, oral agents only, oral agents and insulin, or insulin alone). History of CVD was defined according to self-reported myocardial infarction, stroke, coronary artery bypass, or angioplasty.

Statistical methods

We used hierarchical logistic regression models (SAS GLIMMIX Macro with penalized quasi-likelihood-estimation method) with random intercepts for health plan to account for the multilevel study design (health plan, provider group, and patient levels). Our goal was to estimate population-level differences in the levels and treatment of CVD risk factors by sex. We used hierarchical logistic regression to model the probability of having CVD risk factors not in control or of receiving more intense medication treatment for those with poorly controlled CVD risk factors. We then modeled the risk differences between men and women and their 95% CIs. A1C, LDL cholesterol, and SBP values were unavailable for 8, 24, and 5% of the patients, respectively; these patients were excluded only from analyses of the missing end point. We first present the unadjusted estimated probabilities of having modifiable CVD risk factors not in control or receiving more intense medication treatment because management of CVD risk factors in patients with diabetes are normative standards of quality of care that are relevant for all of the patients, regardless of demographics or clinical characteristics (15,17). We also explored whether demographic and clinical characteristics (such as age, race/ethnicity, education, income, BMI, time since diabetes diagnosis, hypoglycemic therapy, and current smoking) explained observed sex differences. Because women were much less likely than men to have a history of CVD (27.8 vs. 38.5%), therefore resulting in possible confounding between sex and history of CVD, the analyses were stratified by history of CVD.

RESULTS

— There were 1,314 women and 1,575 men with a history of CVD and 3,415 women and 2,516 men without a history of CVD. Within each stratum, women were older than men and were more likely to come from U.S. minority racial/ethnic groups, to report lower education and income levels, to have a longer diabetes duration, to use insulin alone or in combination with hypoglycemic oral agents, and to have a higher BMI (Table 1).

Among patients with a history of CVD, women were significantly more likely than men to have SBP ≥140 mmHg

Table 1—*Characteristics among men and women by history of CVD*

	With CVD		Without CVD	
	Men	Women	Men	Women
n	1,575	1,314	2,516	3,415
Age				
20–44 years	5.0	5.1	14.9	15.1
45–64 years	43.5	39.9	54.1	48.5
≥65 years	51.5	55.0	31.0	36.4
Race/ethnicity				
Non-Hispanic white	49.0	43.2	42.4	38.1
Non-Hispanic black	12.8	21.9	12.2	20.2
Hispanic	14.9	13.8	16.5	17.2
Asian/Pacific Islander	14.6	12.8	19.5	15.5
Other	8.7	8.3	9.4	9.0
Educational level				
Less than high school	25.0	33.3	17.7	24.6
Graduated high school	28.1	31.7	25.2	31.8
More than high school	46.9	35.0	57.1	43.6
Income				
<$15,000/year	25.7	51.1	17.3	37.3
$15,000–40,000/year	35.3	31.2	27.9	30.9
$41,000–75,000/year	24.3	11.6	30.5	20.2
≥$75,000/year	14.7	6.1	24.3	11.7
Diabetes treatment				
Diet only	5.9	6.4	9.5	7.7
Oral agents only	60.4	52.1	66.2	61.6
Oral agents and insulin	20.6	26.3	15.3	17.6
Insulin only	13.0	15.2	9.0	13.1
Time since diabetes diagnosis				
<1 year	0.6	0.9	1.2	1.2
1–4 years	23.5	17.4	32.2	27.8
5–9 years	23.5	21.8	28.4	26.3
≥10 year	52.4	60.0	38.2	44.7
Current cigarette smoking	17.6	16.4	19.6	18.8
BMI (kg/m^2)	29.8 ± 6.1	31.6 ± 7.5	30.2 ± 6.4	32.3 ± 8.0

Data are % or means ± SD.

and LDL cholesterol ≥3.35 mmol/l in both unadjusted models and models adjusted for covariates (all P values < 0.01). No differences in the estimated probability of having A1C levels not in control were observed between men and women with a history of CVD (Table 2).

Among patients without a history of CVD, women were significantly more likely to have SBP ≥140 mmHg than men in unadjusted analysis (P = 0.04); this observed sex difference in SBP control was largely reduced and no longer significant after adjustment for covariates. Men and women without a history of CVD had similar estimated probabilities for having LDL cholesterol or A1C levels not in control (Table 2).

Table 3 reports the intensity of medication management among patients with levels of CVD risk factors not in control. Among those with a history of CVD, the estimated probabilities of receiving lipid-lowering medication if LDL cholesterol levels were ≥3.35 mmol/l were lower in women than in men, although the risk differences between men and women were not significant in either the unadjusted analysis (risk difference = 6.7%; P = 0.12) or the adjusted analysis (risk difference = 9.1%; P = 0.06). The estimated probabilities of receiving two or more antihypertensive medications if SBP was ≥140 mmHg or two or more diabetes medications if A1C was ≥8.0% were similar in men and women with a history of CVD.

Among patients without a history of CVD, women were significantly more

Table 2—*Estimated probabilities and risk differences between men and women for CVD risk factors not in control: the TRIAD Study, 2000–2001*

	With CVD				Without CVD			
	Estimated probability				Estimated probability			
	Men	Women	Risk difference	95% CI	Men	Women	Risk difference	95% CI
Unadjusted*								
SBP ≥140 mmHg	39.8	47.3	−7.5	−11.2 to −3.7	40.1	42.8	−2.7	−5.3 to −0.1
LDL ≥3.35 mmol/l	20.8	28.1	−7.3	10.9 to −3.6	27.7	29.8	−2.1	−4.8 to 0.7
A1C ≥8%	40.3	40.4	0.1	−3.9 to 3.7	41.6	41.8	−0.3	−3.0 to 2.4
Multiple adjusted†								
SBP ≥140 mmHg	41.2	46.6	−5.4	−9.5 to −1.3	41.9	41.7	0.2	−2.7 to 3.0
LDL ≥3.35 mmol/l	22.4	28.3	−5.9	9.9 to −1.8	28.3	30.2	−1.9	−4.8 to 1.0
A1C ≥8%	40.7	39.3	1.4	−2.8 to 5.6	43.0	41.9	1.1	−1.9 to 4.0

Data are % unless otherwise indicated. History of CVD is defined by self-reported myocardial infarction, stroke, coronary artery bypass, or angioplasty. SBP data were available for 1,504 men and 1,279 women with a history of CVD and for 2,372 men and 3,265 women without a history CVD. LDL data were available for 1,267 men and 999 women with a history of CVD and for 1,934 men and 2,473 women without a history of CVD. A1C data were available for 1,454 men and 1,195 women with a history of CVD and for 2,294 men and 3,150 women without a history of CVD. *Data are generated from a hierarchical logistic regression model, accounting for clustering within the health plan and controlled for the proportion of men in the health plans. †Data are generated from a hierarchical logistic regression model accounting for clustering within the health plan, controlled for the proportion of men in the health plans, and adjusted for age, race/ethnicity, income, educational level, hypoglycemic therapy (for SBP and LDL only), time since diabetes diagnosis, current smoking, and BMI.

Table 3—*Estimated probabilities and risk differences between men and women for intensity of medication management for each CVD risk factor among patients with levels not in control: the TRIAD Study, 2000–2001*

Intensity of medication management	With CVD				Without CVD			
	Estimated probability				Estimated probability			
	Men	Women (%)	Risk difference	95% CI	Men	Women	Risk difference	95% CI
Unadjusted*								
SBP	67.1	65.1	2.0	−3.5 to 7.5	46.3	54.4	−8.1	−12.3 to −3.8
LDL cholesterol	61.9	55.2	6.7	−1.8 to 15.3	45.0	44.6	0.4	−5.4 to 6.3
A1C	72.7	76.3	−3.7	−9.0 to 1.7	72.7	74.1	−1.4	−5.1 to 2.2
Multiple adjusted†								
SBP	69.3	65.2	4.1	−1.6 to 9.8	49.2	53.0	−3.8	−8.3 to 0.8
LDL cholesterol	63.0	53.9	9.1	−0.3 to 18.5	45.9	44.1	1.9	−4.2 to 8.0
A1C	71.6	74.7	−3.1	−9.0 to 2.8	72.2	72.6	−0.4	−4.3 to 3.6

Data are % unless otherwise indicated. History of CVD is defined by self-reported myocardial infarction, stroke, coronary artery bypass. or angioplasty. SBP indicates more intense medication management if treated with ≥2 antihypertensive drugs among patients with SBP ≥140 mmHg (612 men and 626 women with CVD and 954 men and 1,429 women without a history of CVD). LDL cholesterol indicates more intense medication management if treated with ≥1 lipid-lowering medication among patients with LDL ≥3.35 mmol/l (260 men and 276 women with CVD and 525 men and 731 women without a history of CVD). A1C indicates more intense medication management if treated with insulin or ≥2 oral agents among patients with A1C ≥8% (593 men and 499 women with CVD and 982 men and 1,355 women without a history of CVD). *Data are generated from a hierarchical logistic regression model accounting for clustering within the health plan and controlled for the proportion of men in the health plans. †Data are generated from a hierarchical logistic regression model accounting for clustering within the health plan, controlled for the proportion of men in the health plans, and adjusted for age, race/ethnicity, income, educational level, hypoglycemic therapy (for SBP and LDL only), time since diabetes diagnosis, current smoking, and BMI.

likely to receive two or more antihypertensive medications than men if SBP was ≥140 mmHg ($P < 0.01$), although this difference was no longer significant after adjustment for covariates ($P = 0.10$). Medication management intensities for LDL cholesterol levels ≥3.35 mmol/l and A1C levels ≥8.0% were similar in men and women without a history of CVD (Table 3). Of note, both men and women with a history of CVD were more likely to receive more intense medication management for hypertension or hypercholesterolemia than men and women without a history of CVD, whereas intensity of medication management for diabetes was similar in patients with and without a history of CVD (Table 3).

CONCLUSIONS — In this insured population of patients with diabetes from several managed care organizations in the U.S., we saw several sex differences in risk factor control and management. In patients with a history of CVD, women were more likely than men to have uncontrolled levels of both SBP and LDL cholesterol; they were also somewhat less likely than men to be receiving more intensive medication management when LDL cholesterol levels were not in control. These differences among patients with a history of CVD were not explained by sex differences in sociodemographic and clinical characteristics. It is possible that the clinicians perceive women's CVD risk as being lower than that of men, despite their history of a prior CVD event. Sex disparities in the levels and treatment of modifiable CVD risk factors may also reflect patient differences in knowledge and risk perception. In a large survey conducted in 2003 (18), 46% of the women were aware that heart disease is the leading killer of women, although only 31% cited high cholesterol and only 19% reported hypertension as causes of CVD. In another study of individuals who had experienced similar types of acute coronary syndrome events (19), women perceived their cardiac disease as less severe than did men. In addition, women with diabetes and their health care providers may not discuss cardiovascular risk and may place a higher priority on treating hyperglycemia and diabetes-related symptoms, as reflected by the observed lack of sex differences in A1C levels or management.

Our findings are consistent with previous reports concerning lipid control and management. We have reported previously (7) that women with diabetes in the TRIAD sample were significantly less likely than men with diabetes to receive lipid testing and lipid-lowering medications when all the patients, regardless of lipid levels, were considered. Others have reported similar results (8,9). Another study (20) has reported that 85% of the men and 82% of the women ($P = 0.08$) had either LDL cholesterol <3.35 mmol/l or received appropriate management (lipid medication initiation and intensification) if LDL cholesterol levels were ≥3.35 mmol/l. Because it has been reported that the use of a more detailed lipid-quality measure reduces the number of patients who appear to be receiving "suboptimal" care (16), we evaluated medication management of LDL cholesterol among the patients whose values were not in control. This measure gives credit for greater effort to manage this CVD risk factor and may reduce the effect of possible biological differences on quality assessment, such as diabetes having a greater adverse effect on lipids in women than in men (5). Nevertheless, we observed an ~9% difference between men and women in the estimated probability of being treated with lipid-lowering medications.

The possibility of sex differences in management of blood pressure among patients with diabetes has received less attention. A study reported that among patients with a history of CVD who were treated with antihypertensive agents, the proportion of the patients with blood pressure levels ≥140/90 mmHg was somewhat higher in women than in men (unadjusted proportions 34 vs. 29%, $P = 0.25$) (9).

This study has several limitations. Given the limited time during which values of CVD risk factors and medications were abstracted, we used number of medication classes from the medical record at the time of risk factor measurements as a surrogate for intensity of care. We were

not able to determine more doses or whether providers changed therapy in response to suboptimal control of a CVD risk factor. Second, medical records could not be obtained for ~30% of the TRIAD sample because some patients did not provide consent. It is possible that quality of care might have been different for these patients. However, survey data indicated that patients with missing medical records were quite similar to the other participants in terms of sex distribution, sociodemographic characteristics, duration of diabetes, and self-reported health status (14). The strengths of this study include the large and demographically diverse sample of men and women with diabetes from several health plans and provider groups across the U.S., the objective measures of CVD risk factor levels and medication prescribed, and the availability of several sociodemographic and clinical characteristics.

It has been reported that an 8% improvement in cholesterol control for cardiac patients translates to an additional 7,200 people having their cholesterol effectively controlled and an estimated 250 lives saved (21). The unadjusted risk difference between men and women with history of CVD in the estimated probabilities of having LDL cholesterol in poor control reported here was 7.3%. These sex disparities might help to explain the sex disparities in CVD mortality observed in women with diabetes in a national sample (1,2). Given the proven effectiveness and cost-effectiveness of intensified lipid and blood pressure control in patients with diabetes in reducing CVD events and deaths (22–25), more intense treatment in women with diabetes offers the opportunity to reduce the observed gap between men and women with diabetes in the reduction of CVD mortality.

Acknowledgments— This study was funded jointly by Program Announcement no. 04005 from the Centers for Disease Control and Prevention (Division of Diabetes Translation) and the National Institute of Diabetes and Digestive and Kidney Diseases.

Significant contributions to this study were made by members of the Translating Research into Action for Diabetes (TRIAD) Study Group. The authors acknowledge the participation of our health plan partners.

APPENDIX

Translating Research Into Action for Diabetes (TRIAD) Study Group

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