Sex Disparities in Treatment of Cardiac Risk Factors in Patients With Type 2 Diabetes

DEBORAH J. WEXLER, MD, MSC[1]
RICHARD W. GRANT, MD, MPH[2]
JAMES B. MEIGS, MD, MPH[2]

DAVID M. NATHAN, MD[1]
ENRICO CAGLIERO, MD[1]

OBJECTIVE — Diabetes eliminates the protective effect of female sex on the risk of coronary heart disease (CHD). We assessed sex differences in the treatment of CHD risk factors among patients with diabetes.

RESEARCH DESIGN AND METHODS — A cross-sectional analysis included 3,849 patients with diabetes treated in five academic internal medicine practices from 2000 to 2003. Outcomes were stratified by the presence of CHD and included adjusted odds ratios (AORs) that women (relative to men) were treated with hypoglycemic, antihypertensive, lipid-lowering medications or aspirin (if indicated) and AORs of reaching target HbA_{1c}, blood pressure, or lipid levels.

RESULTS — Women were less likely than men to have HbA_{1c} <7% (without CHD: AOR 0.84 [95% CI 0.75–0.95], $P = 0.005$; with CHD: 0.63 [0.53–0.75], $P < 0.0001$). Women without CHD were less likely than men to be treated with lipid-lowering medication (0.82 [0.71–0.96], $P = 0.01$) or, when treated, to have LDL cholesterol levels <100 mg/dl (0.75 [0.62–0.93], $P = 0.004$) and were less likely than men to be prescribed aspirin (0.63 [0.55–0.72], $P < 0.0001$). Women with diabetes and CHD were less likely than men to be prescribed aspirin (0.70 [0.60–0.83], $P < 0.0001$) or, when treated for hypertension or hyperlipidemia, were less likely to have blood pressure levels <130/80 mmHg (0.75 [0.69–0.82], $P < 0.0001$) or LDL cholesterol levels <100 mg/dl (0.80 [0.68–0.94], $P = 0.006$).

CONCLUSIONS — Women with diabetes received less treatment for many modifiable CHD risk factors than diabetic men. More aggressive treatment of CHD risk factors in this population offers a specific target for improvement in diabetes care.

D iabetes confers a markedly increased risk of coronary heart disease (CHD) events in both women and men (1) and eliminates the protective effect of female sex on the risk of CHD. In women with and without diagnosed heart disease, diabetes raises the relative risk of heart disease mortality 3- to 10-fold relative to that of women without diabetes (2–6). Despite declining CHD mortality over the last 30 years in the U.S. population overall and in men with diabetes, women with diabetes appear to have experienced an increase in age-adjusted CHD mortality (7).

Several pathophysiological mecha-nisms may contribute to the increased risk of CHD mortality in men and women with diabetes. Patients with type 2 diabetes have an increased incidence of conventional and unconventional CHD risk factors (8,9). Women with diabetes may be subject to even more adverse changes in coagulation, vascular function, and CHD risk factor levels than diabetic men (10–13).

In addition to sex-based physiologic differences, there may also be differences in treatment of CHD risk factors that contribute to increased risk in women with diabetes. Several studies of patients without diabetes have demonstrated disparities in treatment of heart disease and CHD risk factors among women and men in primary care (14,15) and hospital settings (16,17). Treatment disparities have been shown to be related to differences in patient risk factors (18) and physician behavior (19). These differences may persist even after a problem is identified: when women receive treatment, they are often treated less aggressively (20).

Treating modifiable CHD risk factors (such as blood pressure and lipids) and using ACE inhibitors and aspirin reduce mortality in diabetes (21–25), which is now considered a CHD equivalent (26). The Heart Protection Study showed an ~25% reduction in vascular event rates in all subgroups treated with simvastatin, including patients with diabetes and women, regardless of initial levels of LDL and HDL cholesterol (27). In 2000, the American Diabetes Association (ADA) recommended statin therapy for patients with LDL cholesterol >100 mg/dl if CHD or multiple risk factors were present, as well as prophylactic use of aspirin and blood pressure control with an ACE inhibitor to delay progression to microalbuminuria (28). Subsequent recommendations are more stringent (29). The American Heart Association, concordant with the latest ADA guidelines, has endorsed an HDL target of >50 mg/dl and recommends that statins be initiated in women with diabetes, even if LDL is <100 mg/dl (30).

In light of these recommendations and the possibility of sex disparities in CHD risk factor control in the high-risk diabetic state, we sought to determine whether there were differences in the treatment of CHD risk factors in women compared with men in a large primary care cohort of patients with diabetes, stratified by presence of diagnosed CHD.

RESEARCH DESIGN AND METHODS

We conducted a cross-sectional observational study of outpatients with diabetes in five internal medicine practices—two hospital based and three community based—affiliated with an academic medical center between 1 January 2000 and 31 July 2003. Data were collected from the hospital Central Data Repository (laboratory test dates and results), billing claims (hospitalizations and hospital discharge diagnoses), administrative records (patient demographics and insurance status), and directly from the electronic medical record or written medical record (problem lists and prescribed medications at the end of the study period). In addition, we performed manual chart reviews at one community-based health center and one hospital-based clinic to assess changes in blood pressure and medication prescription.

We generated lists of potentially eligible patients using billing claims for nongestational diabetes (ICD-9 codes 250.00–250.90) over a 3-year period. For the two clinics that underwent manual chart review, trained research nurses created diabetes registries. Diabetes was defined based on the diagnosis being listed in the problem list, diabetes-specific medicine listed in the medication list (e.g., sulfonylurea, metformin, insulin, or equipment for insulin injection or home glucose monitoring), or diabetes diagnosis discussed in a progress note. Using these registries as a gold standard, we developed an automated algorithm to identify patients with diabetes using billing claims, laboratory testing, and problem lists and medications from the electronic medical record. Compared with the gold standard chart review, the algorithm had a sensitivity of 98% and specificity of 98% for diabetes. We then used this validated algorithm to develop diabetes registries for the additional clinics. Determination of the type of diabetes was not possible in ~50% of the sample;

in the remainder, 97% of patients were recorded as having type 2 diabetes. We limited our analysis to patients who had at least one visit early (1 January 2000 to 31 August 2001) and one visit late (1 December 2001 to 31 July 2003) in the observation period to capture a population of patients who were attending regular follow-up visits at the practices.

Forty-four percent of the patients in the study cohort were treated at hospital-based primary care practices; the rest were treated at health centers located in different neighborhoods in and around Boston. The population represented a broad sociodemographic sample of outpatients with type 2 diabetes.

Patients with missing values for HbA$_{1c}$, total cholesterol, HDL, or LDL ($n = 382$) were excluded from the original sample of 4,231, leaving a population of 3,849 for analysis (91%). The excluded patients were of similar age, sex, and race as the included patients, but fewer spoke English (81 vs. 87%, $P = 0.002$).

Demographic variables examined included age, race (white, African American, Hispanic, or other) and whether the patient spoke English (yes/no). All comorbidity and treatment variables were determined at the end of the study period. Active treatment for diabetes and CHD risk factors was defined as follows: treatment for hyperglycemia (prescription of α-glucosidase inhibitors, biguanides, insulin, glitinides, sulfonylureas, or thiazolidinediones); treatment for hypertension (ACE inhibitors, angiotensin receptor blocker [ARB], α-blocker, β-blocker, calcium-channel blocker, or thiazide); and treatment for hyperlipidemia (hydroxymethylglutaryl-CoA reductase inhibitors, cholestyramine, colestipol, fenofibrate, gemfibrozil, or niacin). We also determined whether the nonprescription medications aspirin, acetaminophen, and ibuprofen were listed in the medical record.

Hypertension was present if listed on the problem list or if an antihypertensive medication was listed on the medication list. CHD was defined by having CHD (or synonyms) on the problem list or CHD-specific medications such as sublingual nitroglycerin on the medication list. Dyslipidemia was defined as present if listed on the problem list, if a lipid-lowering drug had been prescribed, or if the subject was not taking a lipid-lowering drug and LDL was >100 mg/dl and HDL was <40 mg/dl in men and <50 mg/dl in women.

Over 80% of patients identified using these algorithms had hypertension, CHD, or dyslipidemia recorded in the problem list. Current smoking was determined by inclusion on the problem list.

We stratified all analyses by the presence or absence of diagnosed CHD as indicated by CHD entry in the medical record, but we present some collapsed results for analyses where results did not differ by CHD status. Descriptive statistics included t tests for means and the χ^2 test for proportions comparing differences between women and men. We used logistic regression models to estimate adjusted odds ratios (AORs) and 95% CIs that women, using treatment in men as the referent, were prescribed specific treatments. The models were adjusted for sociodemographic variables that differed by sex in the bivariate analysis including age, racial/ethnic group, language, and smoking status and included a term for clinic site as a random effect to account for possible within-site correlation of treatment patterns.

Evaluation of treatment appropriateness included use of hypoglycemic medicines in all patients and those with HbA$_{1c}$ >7%, an ACE inhibitor or ARB in all patients, antihypertensive medication in patients with hypertension, lipid-lowering therapy in patients with dyslipidemia, and aspirin in all patients. Using the same modeling strategy, we also estimated the odds of treatment effectiveness in patients who were prescribed medications for hyperglycemia, hypertension, and hyperlipidemia. Treatment effectiveness was defined as meeting recommended risk factor treatment goals defined by the ADA, the National Cholesterol Education Program, and the American Heart Association guidelines or quality-of-care benchmarks established by the National Committee on Quality Assurance (NCQA) (31). Analysis of antihypertensive treatment effectiveness was limited to the subset of patients ($n = 1,817$, 47% of cohort) for whom blood pressure data were available. All analyses were conducted using the SAS System for Windows, version 8.2 (32). Statistical significance was defined as a two-tailed P value <0.05.

RESULTS

Of 3,849 patients with diabetes in our analysis cohort, about one-half were women. Thirty percent

Table 1—Population characteristics

Characteristic	Patients without CHD			Patients with CHD		
	Male	Female	P^*	Male	Female	P^*
n		2,699 total			1,150 total	
Sociodemographic						
n (%)	1,240 (46)	1,459 (54)	<0.0001	656 (57)	494 (43)	<0.0001
Age (years)	60 ± 13	64 ± 13	<0.0001	69 ± 10	71 ± 11	0.01
Practice site (%)			0.003			0.01
CHC 1	8	8		7	9	
CHC 2	26	32		18	25	
CHC 3	20	21		20	22	
HPB 1	18	15		21	15	
HPB 2	28	24		33	29	
Race (%)			0.001			0.03
White	70	63		83	80	
Hispanic	15	20		4	7	
Black	9	10		6	8	
Other	6	8		6	4	
English-speaking (%)	88	82	<0.0001	93	91	0.24
CHD risk factors (%)†						
Hypertension	83	83	0.85	98	97	0.54
Hyperlipidemia‡	91	92	0.49	96	97	0.52
Current smoking	17	13	0.001	13	12	0.69

Data are means ± SD, unless otherwise noted. Columns may not sum to 100% due to rounding error. *Men versus women by t test for continuous variables and χ^2 for categorical variables; †identified by problem list or condition-specific medication; ‡identified by problem list, condition-specific medication, or LDL >100 and HDL <40 in men, <50 in women. CHC, community health center; HBP, hospital-based practice.

(1,150) of the cohort had diagnosed CHD. Table 1 shows the baseline characteristics for men and women, stratified by CHD status. In general, women were more likely than men to be older, non-white, and non-English speaking and to be treated at a community health center. Women with CHD had significantly higher systolic blood pressure than their male counterparts. Women with and without CHD had higher total HDL and LDL levels than the men.

Compared with national benchmarks established by the NCQA (31), this cohort received high-quality care on most measures (Table 2). Over 60% of the entire population had an HbA$_{1c}$ <8.0%, compared with the NCQA goal of 55%, although fewer women than men with CHD achieved this goal (62 vs. 69%, P = 0.01). In the subset of the cohort with data on blood pressure, >65% of patients had blood pressure <140/90 mmHg (the NCQA target) with no differences by sex. Lipid levels were also well controlled compared with national standards but were less well controlled in women compared with men. Eighty-one percent of women and 87% of men without CHD (P = 0.002) and 88% of women and 92% of men with CHD (P = 0.02) had LDL levels <130 mg/dl, compared with the NCQA benchmark of 63%. Still, unadjusted measures of HbA$_{1c}$, blood pressure, and lipid control in patients prescribed medications for those conditions revealed several differences in levels by sex. In patients without CHD, women had lower diastolic blood pressure and higher levels of total cholesterol and its subfractions; in patients with CHD, women had higher levels of systolic blood pressure, HbA$_{1c}$, and cholesterol and its subfractions.

Men and women were equally likely to be treated with hypoglycemic medication (Table 3). Men and women without diagnosed CHD who were treated with hypoglycemic medications had equivalent glycemic control, with about one-third meeting an HbA$_{1c}$ target of <7% and about two-thirds <8%. Women with diagnosed CHD who were taking hypoglycemic medications had worse glycemic control than their male counterparts. In multivariable analysis adjusted for age, sociodemographic variables, and clinic site, women were less likely than men to have HbA$_{1c}$ controlled to <7% (AOR 0.84 [95% CI 0.75–0.95], P = 0.005, n = 2,310; Fig. 1B).

In unadjusted analyses stratified for the presence or absence of CHD, about one-half of all patients without CHD and four-fifths of patients with CHD were treated with lipid-lowering medication (Table 3). In general, among patients receiving lipid-lowering therapy, men were more likely than women to have lower LDL and total cholesterol levels, whereas women had higher HDL cholesterol levels. These differences persisted after stratification for the presence of diagnosed CHD. After controlling for age, socio-

Table 2—Levels of blood pressure, HbA$_{1c}$, and cholesterol

	Patients without CHD			Patients with CHD		
	Male	Female	P^*	Male	Female	P^*
BP (n)†		1,230 total			587 total	
Systolic BP (mmHg)	129 ± 16	131 ± 17	0.37	129 ± 18	133 ± 19	0.01
Diastolic BP (mmHg)	77 ± 10	74 ± 10	<0.0001	72 ± 10	71 ± 11	0.11
BP <130/80 (%)	28	31	0.18	40	34	0.12
BP <140/90 (%)	66	65	0.65	71	66	0.24
HbA$_{1c}$ (n)		2,699 total			1,150 total	
HbA$_{1c}$ (%)	7.6 ± 1.7	7.6 ± 1.6	0.62	7.5 ± 1.5	7.7 ± 1.5	0.05
HbA$_{1c}$ <7.0% (%)	41	40	0.44	41	34	0.03
HbA$_{1c}$ <8.0% (%)	67	69	0.25	69	62	0.01
Cholesterol						
Total (mg/dl)	174 ± 39	186 ± 37	<0.0001	157 ± 37	174 ± 41	<0.0001
Total <200 mg/dl (%)	78	68	<0.0001	87	78	0.0002
HDL (mg/dl)	43 ± 11	50 ± 15	<0.0001	40 ± 11	46 ± 13	<0.0001
LDL (mg/dl)	98 ± 32	104 ± 32	<0.0001	85 ± 29	92 ± 34	<0.0001
LDL <100 mg/dl (%)	56	50	0.006	73	65	0.002
LDL <130 mg/dl (%)	85	82	0.01	92	88	0.02

Data are means ± SD, unless otherwise noted. Columns may not sum to 100% due to rounding error. *Men versus women by t test for continuous variables and χ^2 for categorical variables; †blood pressure (BP) data for community health center 3 and hospital-based practice 2 only (n = 1,817).

Table 3—*Comparison of diabetes and CHD treatments in men and women*

	Patients without CHD			Patients with CHD		
	Male	Female	P*	Male	Female	P*
Medications (*n*)†		2,699 total			1,150 total	
Aspirin (%)	46	37	<0.0001	79	72	0.01
Acetaminophen (%)	6	9	0.002	8	11	0.18
Ibuprofen (%)	10	15	0.0002	7	8	0.26
Glycemic management (*n*)		2,699 total			1,150 total	
Any hypoglycemic medication (%)†	87	85	0.16	89	88	0.79
HbA$_{1c}$ of patients taking hypoglycemic medication (*n*)		2,310 total			1,016 total	
HbA$_{1c}$ (%)	7.8 ± 1.7	7.8 ± 1.6	0.82	7.6 ± 1.6	7.9 ± 1.4	0.01
HbA$_{1c}$ <7.0% (%)	35	32	0.11	36	26	0.005
HbA$_{1c}$ <8.0% (%)	63	64	0.48	66	57	0.005
Lipid management (*n*)		2,699 total			1,150 total	
Any lipid-lowering medication	54	51	0.09	80	77	0.1
Levels of patients on lipid lowering therapy (*n*)		1,419 total			1,113 total	
Total cholesterol (mg/dl)	171 ± 41	184 ± 39	<0.0001	158 ± 37	174 ± 41	<0.0001
Total cholesterol <200 mg/dl (%)	81	70	<0.0001	87	78	0.0002
HDL (mg/dl)	42 ± 11	50 ± 14	<0.0001	40 ± 11	46 ± 13	<0.0001
LDL (mg/dl)	94 ± 33	101 ± 34	0.0003	86 ± 29	93 ± 35	<0.0001
LDL <100 mg/dl (%)	62	56	0.02	75	70	0.14
LDL <130 mg/dl (%)	87	81	0.002	92	88	0.02
Cardiac risk ratio <5 (%)‡	75	83	0.0004	80	82	0.3
BP management (*n*)†		2,699 total			1,150 total	
Any antihypertensive medication (%)	78	78	0.9	97	95	0.11
ACE inhibitor or ARB (%)	68	67	0.8	77	77	0.96
BP for patients taking antihypertensive medication (*n*)		995 total			576 total	
Systolic BP (mmHg)	132 ± 17	133 ± 16	0.13	129 ± 18	133 ± 19	0.01
Diastolic BP (mmHg)	77 ± 11	74 ± 11	<0.0001	72 ± 10	71 ± 11	0.12
BP <130/80 (%)	27	27	0.75	41	34	0.1
BP <140/90 (%)§	62	61	0.56	71	66	0.25

Data are means ± SD unless otherwise noted. *Men versus women by *t* test for continuous variables and χ^2 for categorical variables; †as listed in the medical record; ‡blood pressure (BP) data for community health center 3 and hospital-based practice 2 only, *n* = 1817; §cardiac risk ratio = total cholesterol/HDL cholesterol.

demographic variables, and clinic site, women with hyperlipidemia appeared less likely than men to be prescribed lipid-lowering medications (AOR 0.82 [95% CI 0.71–0.96], *P* = 0.01, *n* = 2,464; Fig. 1*A*). When they were treated, women remained less likely than men to have LDL <100 mg/dl (0.75 [0.62–0.93], *P* = 0.007, *n* = 1,419) or <130 mg/dl (0.58 [0.46–0.70], *P* < 0.0001, *n* = 1,419, Fig. 1*B*).

In both unadjusted and adjusted analyses, women were as likely as men to be treated with antihypertensive medications, including ACE inhibitors or ARBs (Table 3 and Fig. 1*A*). Among patients without diagnosed CHD, men and women were equally likely to have blood pressure <140/90 mmHg (Table 3 and Fig. 1*B*). Among patients with CHD, nearly all of whom were treated with antihypertensive agents, women had a higher mean systolic blood pressure than men in unadjusted analysis (133 vs. 129 mmHg, *P* = 0.01, Table 3) and were less likely to have blood pressure controlled to

<140/90 mmHg (AOR 0.88 [95% CI 0.85–0.91], *P* < 0.0001, *n* = 587, Fig. 1*B*).

In unadjusted analyses of patients with diabetes, aspirin was listed less frequently in the medication lists of women than men without CHD (37 vs. 46%, *P* < 0.0001) and of women than men with CHD (72 vs. 79%, *P* < 0.01). In contrast, two other nonprescription medicines, acetaminophen and ibuprofen, were listed with equal frequency for women and men with diagnosed CHD and more frequently for women without CHD (Table 3). In multivariable analyses adjusted for age, sociodemographic variables, and clinic site (Fig. 1*A*), women without CHD were less likely to have aspirin on their medication list than men (AOR 0.63 [0.55–0.72], *P* < 0.0001, *n* = 2,699). The results among patients with diagnosed CHD were similar to those for patients without diagnosed CHD: women with diagnosed CHD were 30% less likely than men to have aspirin listed in their medical records.

CONCLUSIONS — In this large cohort of patients with diabetes seen in five academically affiliated primary care clinics, one-third of whom had diagnosed CHD, women were significantly less likely than men to receive recommended treatments for several major modifiable CHD risk factors and, when treated, were less likely to achieve recommended goals of therapy. Even though all of the patients received, on the whole, above-average quality of care by NCQA standards, women did not uniformly receive as good care as men in unadjusted analyses and after adjusting for differences in age, race, clinic site, and other variables. Among patients without CHD, women were less likely than men to be prescribed lipid-lowering medications and aspirin and were less likely to have HbA$_{1c}$ and LDL at goal levels. Among patients with CHD (and likely to reap the greatest benefits from treatment of CHD risk factors), women were less likely than men to be taking aspirin or to have their HbA$_{1c}$,
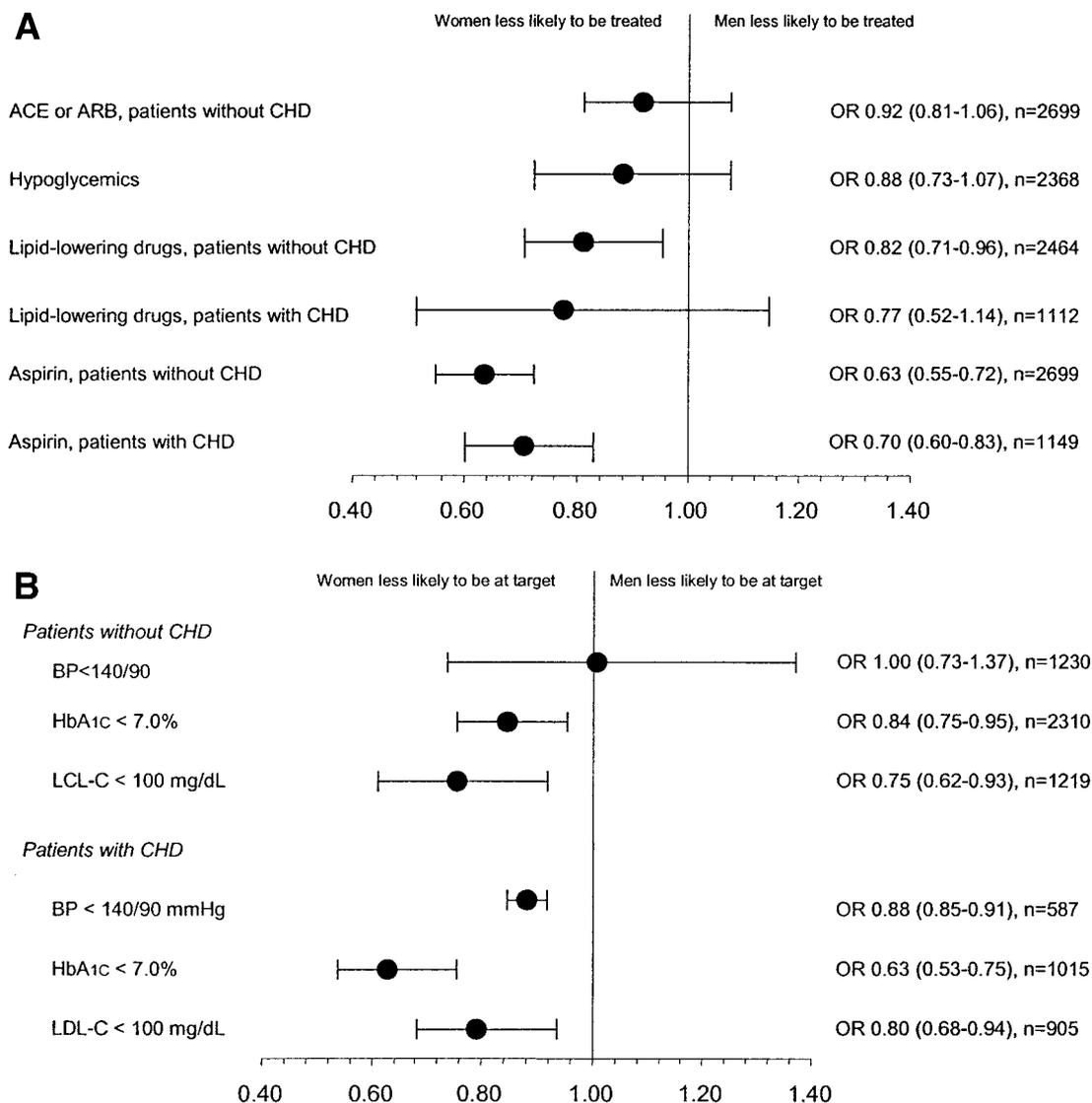
A

Women less likely to be treated | Men less likely to be treated

ACE or ARB, patients without CHD — OR 0.92 (0.81-1.06), n=2699

Hypoglycemics — OR 0.88 (0.73-1.07), n=2368

Lipid-lowering drugs, patients without CHD — OR 0.82 (0.71-0.96), n=2464

Lipid-lowering drugs, patients with CHD — OR 0.77 (0.52-1.14), n=1112

Aspirin, patients without CHD — OR 0.63 (0.55-0.72), n=2699

Aspirin, patients with CHD — OR 0.70 (0.60-0.83), n=1149

0.40   0.60   0.80   1.00   1.20   1.40

B

Women less likely to be at target | Men less likely to be at target

Patients without CHD

BP<140/90 — OR 1.00 (0.73-1.37), n=1230

HbA1c < 7.0% — OR 0.84 (0.75-0.95), n=2310

LCL-C < 100 mg/dL — OR 0.75 (0.62-0.93), n=1219

Patients with CHD

BP < 140/90 mmHg — OR 0.88 (0.85-0.91), n=587

HbA1c < 7.0% — OR 0.63 (0.53-0.75), n=1015

LDL-C < 100 mg/dL — OR 0.80 (0.68-0.94), n=905

0.40   0.60   0.80   1.00   1.20   1.40

Figure 1—A: *Odds of receiving treatment, if indicated, for women relative to men. Indicated treatment: ACE or ARB for all patients, hypoglycemics for all patients on treatment or with HbA_{1c} >7.0%, lipid-lowering for patients diagnosed with hyperlipidemia or LDL cholesterol >100 mg/dl and HDL cholesterol <40 mg/dl in men or <50 mg/dl in women, and aspirin for all patients. B: Effectiveness of therapy on treatment. Odds ratio, women versus men, of achieving recommended goals of therapy for patients receiving antihypertensive, glucose-lowering, and lipid-lowering medications, stratified by presence of diagnosed CHD. BP, blood pressure; LDL-C, LDL cholesterol.*

blood pressure, or lipids controlled to recommended levels.

Women with diabetes have not experienced the same improvement in CHD events and mortality as men with diabetes and as women and men without diabetes over the last 30 years (7). Although there are probably biological and other reasons for these differences, our results suggest that differences in clinical treatment may also contribute to the excess burden of CHD in women with diabetes.

Increasingly, the medical profession and the public have been paying particular attention to heart disease in women

(33). The American Heart Association recently launched its "Go Red for Women" campaign, published clinical guidelines focused on women (30), and prioritized sex-specific research goals to improve understanding of the diagnosis and treatment of heart disease in women (34). Women are increasingly aware of their own risk of cardiovascular death (35).

However, differences in treatment patterns persist. Lower adherence to treatment guidelines has been demonstrated in patients with diabetes who are older and whose conditions are more medically complicated, but sex-based dif-

ferences were not examined (36,37). A Swedish study from 2004 examined the treatment of 9,375 patients with diabetes in the primary care setting and found that men had lower blood pressure, HbA_{1c}, and LDL levels (38), but there have been few other studies of this disparity in diabetes. Although the women in our study were older and less likely to be white than the men (differences for which the models adjusted), they had a similar prevalence of CHD risk factors.

Other studies of patients without diabetes have also found that women with dyslipidemia are less likely than men to be

treated with lipid-lowering agents (39). This may be explained by the fact that women frequently have higher HDL levels. Health care providers in general may disregard elevated LDL levels, assuming a protective effect of elevated HDL levels. Emphasis on the protective effects of elevated levels of HDL in patients with diabetes may be misplaced, as some evidence shows that HDL in patients with diabetes may not be as protective as in patients without diabetes (40). Furthermore, results from the Scandinavian Simvastatin Survival Study, the Cholesterol and Recurrent Events (Investigators) Trial (CARE), and the Heart Protection Study have consistently shown a 25–35% reduction in the relative risk of cardiovascular events in patients with diabetes who were treated with statins at all levels of baseline cholesterol. Finally, the consensus recommendations for treating elevated LDL levels are identical for men and women.

No obvious justification can be given to explain the marked differences we observed in aspirin recommendations between diabetic women and men with and without CHD. We have shown in a similar population that hypertension and hyperlipidemia are managed less aggressively than hyperglycemia (41). In this cohort, it appears that female sex may additionally decrease attention to treatment of cardiac risk factors, possibly related to patient preferences or physician perceptions of risk.

Several potential limitations must be addressed. First, the possibility of differential record-keeping by sex cannot be completely eliminated, but the fact that the prevalence of many risk factors and treatments were equal between sexes whereas many of the sex differences were relatively large suggests that differential reporting is unlikely to have confounded our analysis. Similarly, nonprescription medications such as aspirin may have been undercounted and could have been recorded differentially by sex. But because acetaminophen and ibuprofen were listed more frequently for women, it seems that records of nonprescription medication are likely to reflect patient use rather than biased reporting by sex. (Although more women were taking ibuprofen, the additional number taking ibuprofen was not enough to account for the decrement in those taking aspirin.) Another concern is the timing of diag-

noses and treatments, which cannot be determined in a cross-sectional study. This cohort of patients with diabetes was seen in follow-up over a 3-year period, and their hypertension, hyperlipidemia, and risk for CHD were long-standing problems. Over 85% were receiving treatment for hypertension and hyperglycemia, and more than half were treated for hyperlipidemia; data were collected at the end of the study period. Consequently, the cohort is likely to reflect patients who were actively being treated rather than those who were about to have medications initiated for newly diagnosed problems. Finally, the five different internal medicine practices, although socioeconomically diverse, were all affiliated with one urban academic health center, limiting the generalizability of this study to other settings.

In summary, this large, clinic-based cohort of patients with diabetes received generally high-quality diabetes care, yet women were less likely than men to be treated with aspirin and lipid-lowering therapy; also, their lipids, blood pressure, and hyperglycemia tended to be treated less effectively. Sex differences in CHD risk reduction may partially explain the persistent increased risk of CHD events in women with diabetes observed in national surveys. More aggressive treatment of CHD risk in women with diabetes appears to offer a specific target for improvement in diabetes care.

References

1. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M: Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 339:229–234, 1998
2. Hu G, Group DS: Gender difference in all-cause and cardiovascular mortality related to hyperglycaemia and newly-diagnosed diabetes. *Diabetologia* 46:608–617, 2003
3. Hu FB, Stampfer MJ, Solomon CG, Liu S, Willett WC, Speizer FE, Nathan DM, Manson JE: The impact of diabetes melli-

tus on mortality from all causes and coronary heart disease in women: 20 years of follow-up. *Arch Intern Med* 161:1717–1723, 2001
4. Kanaya AM, Grady D, Barrett-Connor E: Explaining the sex difference in coronary heart disease mortality among patients with type 2 diabetes mellitus: a meta-analysis. *Arch Intern Med* 162:1737–1745, 2002
5. Liao Y, Cooper RS, Ghali JK, Lansky D, Cao G, Lee J: Sex differences in the impact of coexistent diabetes on survival in patients with coronary heart disease. *Diabetes Care* 16:708–713, 1993
6. Natarajan S, Liao Y, Cao G, Lipsitz SR, McGee DL: Sex differences in risk for coronary heart disease mortality associated with diabetes and established coronary heart disease. *Arch Intern Med* 163:1735–1740, 2003
7. Gu K, Cowie CC, Harris MI: Diabetes and decline in heart disease mortality in US adults. *JAMA* 281:1291–1297, 1999
8. Beckman JA, Creager MA, Libby P: Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. *JAMA* 287:2570–2581, 2002
9. Hurst RT, Lee RW: Increased incidence of coronary atherosclerosis in type 2 diabetes mellitus: mechanisms and management. *Ann Intern Med* 139:824–834, 2003
10. Ossei-Gerning N, Wilson IJ, Grant PJ: Sex differences in coagulation and fibrinolysis in subjects with coronary artery disease. *Thromb Haemost* 79:736–740, 1998
11. Walden C, Knopp R, Wahl P, Beach K, Strandness E: Sex differences in the effect of diabetes mellitus on lipoprotein triglyceride and cholesterol concentrations. *N Engl J Med* 311:953–959, 1984
12. Steinberg HO, Paradisi G, Cronin J, Crowde K, Hempfling A, Hook G, Baron AD: Type II diabetes abrogates sex differences in endothelial function in premenopausal women. *Circulation* 101:2040–2046, 2000
13. Howard B, Cowan L, Go O, Welty T, Robbins D, Lee E: Adverse effects of diabetes on multiple cardiovascular disease risk factors in women: the Strong Heart Study. *Diabetes Care* 21:1258–1265, 1998
14. Williams D, Bennett K, Feely J: Evidence for an age and gender bias in the secondary prevention of ischaemic heart disease in primary care. *Br J Clin Pharmacol* 55:604–608, 2003
15. Di Cecco R, Patel U, Upshur RE: Is there a clinically significant gender bias in post-myocardial infarction pharmacological management in the older (>60) population of a primary care practice? *BMC Fam Pract* 3:8, 2002
16. Chandra NC, Ziegelstein RC, Rogers WJ, Tiefenbrunn AJ, Gore JM, French WJ, Rubison M: Observations of the treatment of women in the United States with myo-

cardial infarction: a report from the National Registry of Myocardial Infarction-I. *Arch Intern Med* 158:981–988, 1998

17. Rathore SS, Chen J, Wang Y, Radford MJ, Vaccarino V, Krumholz HM: Sex differences in cardiac catheterization: the role of physician gender. *JAMA* 286:2849–2856, 2001

18. Ghali WA, Faris PD, Galbraith PD, Norris CM, Curtis MJ, Saunders LD, Dzavik V, Mitchell LB, Knudtson ML: Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) Investigators: sex differences in access to coronary revascularization after cardiac catheterization: importance of detailed clinical data. *Ann Intern Med* 136:723–732, 2002

19. Schulman KA, Berlin JA, Harless W, Kerner JF, Sistrunk S, Gersh BJ, Dube R, Taleghani CK, Burke JE, Williams S, Eisenberg JM, Escarce JJ: The effect of race and sex on physicians' recommendations for cardiac catheterization. *N Engl J Med* 340:618–626, 1999

20. Corbelli JA, Corbelli JC, Bullano MF, Willey VJ, Cziraky MJ, Banks LD, Cooke BE, Galla AM, Berchou KA, Drury CJ: Gender bias in lipid assessment and treatment following percutaneous coronary intervention. *J Gend Specif Med* 6:21–26, 2003

21. Pyorala K, Pedersen T, Kjekshus J, Faergeman O, Olsson A, Thorgeirsson G: Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease: a subgroup analysis of the Scandinavian Simvastatin Survival Study (4S). *Diabetes Care* 20:614–620, 1997

22. Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG, Brown L, Warnica JW, Arnold JM, Wun CC, Davis BR, Braunwald E: The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels: Cholesterol and Recurrent Events Trial investigators. *N Engl J Med* 335:1001–1009, 1996

23. The Heart Outcomes Prevention Evaluation Study Investigators: Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 342:145–153, 2000

24. Collaborative overview of randomised trials of antiplatelet therapy: prevention of

death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *BMJ* 308:81–106, 1994

25. ETDRS Investigators: Aspirin effects on mortality and morbidity in patients with diabetes mellitus: Early Treatment Diabetic Retinopathy Study report 14. *JAMA* 268:1292–1300, 1992

26. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive summary of the 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). *JAMA* 285:2486–2497, 2001

27. Heart Protection Study Collaborative Group: MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 360:7–22, 2002

28. American Diabetes Association: Standards of medical care for patients with diabetes mellitus (Position Statement). *Diabetes Care* 23:S32–S63, 2000

29. American Diabetes Association: Hypertension management in adults with diabetes (Position Statement). *Diabetes Care* 27: S65–S75, 2004

30. Mosca L, Appel LJ, Benjamin EJ, Berra K, Chandra-Strobos N, Fabunmi RP, Grady D, Haan CK, Hayes SN, Judelson DR, Keenan NL, McBride P, Oparil S, Ouyang P, Oz MC, Mendelsohn ME, Pasternak RC, Pinn VW, Robertson RM, Schenck-Gustafsson K, Sila CA, Smith SC Jr, Sopko G, Taylor AL, Walsh BW, Wenger NK, Williams CL: American Heart Association: evidence-based guidelines for cardiovascular disease prevention in women. *Circulation* 109:672–693, 2004

31. National Committee on Quality Assurance: Diabetes Physician Recognition Program [Internet]. Available from www.ncqa.org/DPRP/dprpfaq.html. Accessed 14 January 2005

32. *SAS Version 8.2.* Cary, NC, SAS Institute.

33. Barrett-Connor E, Giardina E-GV, Gitt AK, Gudat U, Steinberg HO, Tschoepe D: Women and heart disease: the role of diabetes and hyperglycemia. *Arch Intern Med* 164:934–942, 2004

34. Shaw LJ, Lewis JF, Hlatky MA, Hsueh

WA, Kelsey SF, Klein R, Manolio TA, Sharrett AR, Tracy RP: National Heart, Lung and Blood Institute; American College of Cardiology Foundation: Women's ischemic syndrome evaluation: current status and future research directions: report of the National Heart, Lung and Blood Institute Workshop: 2–4 October 2002: Section 5: gender-related risk factors for ischemic heart disease. *Circulation* 109:E56–E58, 2004

35. Mosca L, Ferris A, Fabunmi R, Robertson RM: Tracking women's awareness of heart disease: an American Heart Association national study. *Circulation* 109:573–579, 2004

36. Massing MW, Foley KA, Sueta CA, Chowdhury M, Biggs DP, Alexander CM, Simpson RJ Jr.: Trends in lipid management among patients with coronary artery disease: has diabetes received the attention it deserves? *Diabetes Care* 26:991–997, 2003

37. Massing MW, Henley NS, Carter-Edwards L, Schenck AP, Simpson RJ Jr.: Lipid testing among patients with diabetes who receive diabetes care from primary care physicians. *Diabetes Care* 26: 1369–1373, 2003

38. Nilsson PM, Theobald H, Journath G, Fritz T: Gender differences in risk factor control and treatment profile in diabetes: a study in 229 Swedish primary health care centres. *Scand J Prim Health Care* 22: 27–31, 2004

39. O'Meara JG, Kardia SL, Armon JJ, Brown CA, Boerwinkle E, Turner ST: Ethnic and sex differences in the prevalence, treatment, and control of dyslipidemia among hypertensive adults in the GENOA study. *Arch Intern Med* 164:1313–1318, 2004

40. Gowri MS, Van der Westhuyzen DR, Bridges SR, Anderson JW: Decreased protection by HDL from poorly controlled type 2 diabetic subjects against LDL oxidation may be due to the abnormal composition of HDL. *Arterioscler Thromb Vasc Biol* 19:2226–2233, 1999

41. Grant RW, Cagliero E, Murphy-Sheehy P, Singer DE, Nathan DM, Meigs JB: Comparison of hyperglycemia, hypertension, and hypercholesterolemia management in patients with type 2 diabetes. *Am J Med* 112:603–609, 2002