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Citation
Gouni-Berthold, Ioanna, Heiner K. Berthold, Christos S. Mantzoros, Michael Bohm, and Wilhelm Krone. 2008. Sex disparities in the treatment and control of cardiovascular risk factors in type 2 diabetes. Diabetes Care 31(7): 1389-1391.

Published Version
doi:10.2337/dc08-0194

Permanent link
http://nrs.harvard.edu/urn-3:HUL.InstRepos:5025223

Sex Disparities in the Treatment and Control of Cardiovascular Risk Factors in Type 2 Diabetes

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OBJECTIVE — To assess whether sex differences exist in the effective control and medication treatment intensity of cardiovascular disease (CVD) risk factors.

RESEARCH DESIGN AND METHODS — We performed a cross-sectional analysis including 44,893 patients with type 2 diabetes (51% women). End points included uncontrolled CVD risk factors (LDL cholesterol ≥130 mg/dl, systolic blood pressure [SBP] ≥140 mmHg, and A1C ≥8%) and the intensity of medical management in patients with uncontrolled CVD risk factors. Multiple-adjusted odds ratios were calculated after stratification for the presence of CVD (present in 39% of the patients).

RESULTS — Women with CVD were less likely to have SBP, LDL cholesterol, and A1C controlled and less likely to receive intensive lipid-lowering treatment. Women without CVD were less likely than men to have LDL cholesterol controlled with no differences in SBP or A1C control.

CONCLUSIONS — Women with diabetes and CVD have poorer control of important modifiable risk factors than men and receive less intensified lipid-lowering treatment.

Diabetes Care 31:1389–1391, 2008

Mortality rates from cardiovascular disease (CVD) have been declining during recent years in both men and women in the U.S. and Europe (1,2). However, in patients with diabetes, a decrease has been observed only in men (2). Furthermore, the relative risk for fatal diabetes-associated coronary heart disease is 50% higher in women than in men (3). More adverse cardiovascular risk profiles among women with diabetes has been postulated as a possible explanation, as well as potential disparities in treatment that favor men (3–5). A study from U.S. managed care health plans found poorer control of blood pressure and LDL cholesterol in female compared with male patients and suggested that these findings may contribute to the sex disparity in CVD mortality trends (6). No study in Europe has investigated sex disparities in the main cardiovascular risk factors in patients with diabetes and/or has put them into perspective with treatment intensity.

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Received 29 January 2008 and accepted 25 March 2008.
Published ahead of print at http://care.diabetesjournals.org on 28 March 2008. DOI: 10.2337/dc08-0194.
I.G.-B. and H.K.B. contributed equally to this work.
I.G.-B. has received honoraria for speaking engagements from Pfizer and Eli Lilly. M.B. has received speakers' honoraria from AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, MSD Sharp & Dohme, Essex Pharma, Pfizer, Servier, and sanofi-aventis and has been on advisory panels for AstraZeneca, Boehringer Ingelheim, MSD Sharp & Dohme, Essex Pharma, Pfizer, Servier, and sanofi-aventis. W.K. has received grant/research support from MSD Sharp & Dohme and speakers' honoraria from AstraZeneca, MSD Sharp & Dohme, Essex Pharma, Pfizer, and sanofi-aventis and has been on advisory panels for MSD Sharp & Dohme and Essex Pharma.

RESEARCH DESIGN AND METHODS — This study is a cross-sectional trial in outpatients with type 2 diabetes using data from the DUTY registry (7). Data of 44,893 patients were obtained from 3,096 office-based physicians. End points included levels of modifiable CVD risk factors, i.e., most recent levels of systolic blood pressure (SBP), LDL cholesterol, and A1C (intermediate outcomes). These outcomes were analyzed as binary variables according to levels considered not in control and therefore requiring more action, as recommended by the American Diabetes Association (8). A second set of end points was defined to reflect the intensity of medication management strategies of the three outcomes for subjects 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, presumably reflecting a greater effort to manage the outcome.

Stratified by the presence or absence of CVD, we used logistic regression models to estimate differences in the levels and treatment of CVD risk factors by sex. We estimated the probability of having CVD risk factors not under control or of receiving more intense medication for those with poorly controlled risk factors and modeled the risk differences between men and women and their confidence intervals (CIs). The main explanatory variable was patient sex. The covariates included age, BMI, duration of diabetes, and current smoking.

RESULTS — Subject characteristics are shown in supplemental Table 1 (available in an online appendix at http://dx.doi.org/10.2337/dc08-0194). Approximately 63% of the patients had SBP ≥140 mmHg, 48% had LDL cholesterol ≥130 mg/dl, and 24% had A1C levels ≥8.0%. Intensive treatment with antihypertensive agents was done in 39% of the patients, with lipid-lowering drugs in 32% and antihyperglycemic agents in 39%. Unadjusted risk differences were

Table 1—*Odds ratios (ORs) and 95% CIs between diabetic men and women for CVD risk factors not under control, as well as for intensity of medication management* for each CVD risk factor among patients with levels not under control (unadjusted and adjusted estimates using male sex as the referent)*

	With CVD (n = 9,521 men and 8,050 women)			Without CVD (n = 12,417 men and 14,905 women)		
	OR	95% CI	*P*	OR	95% CI	*P*
CVD risk factors not in control (unadjusted)						
SBP ≥140 mmHg	1.20	1.12–1.27	<0.0001	1.08	1.03–1.13	0.003
LDL cholesterol ≥130 mg/dl	1.33	1.25–1.42	<0.0001	1.21	1.15–1.28	<0.0001
A1C ≥ 8%	1.04	0.97–1.11	0.32	1.01	0.95–1.07	0.82
CVD risk factors not in control (multiple adjusted)						
SBP ≥140 mmHg	1.19	1.11–1.29	<0.0001	1.0	0.95–1.06	0.99
LDL cholesterol ≥130 mg/dl	1.44	1.33–1.55	<0.0001	1.25	1.18–1.32	<0.0001
A1C ≥8%	1.15	1.06–1.25	0.0009	1.04	0.97–1.1	0.29
Intensity of medication management (unadjusted)						
≥2 antihypertensive agents	1.09	1.02–1.16	0.014	1.19	1.12–1.26	<0.0001
≥1 lipid-lowering drug	0.76	0.72–0.81	<0.0001	0.99	0.93–1.04	0.62
≥2 oral antihyperglycemic agents or insulin	1.11	1.03–1.18	0.003	1.05	0.995–1.11	0.073
Intensity of medication management (multiple adjusted)						
≥2 antihypertensive agents	0.998	0.92–1.08	0.97	1.01	0.95–1.08	0.71
≥1 lipid-lowering drug	0.85	0.79–0.91	<0.0001	0.99	0.93–1.05	0.65
≥2 oral antihyperglycemic agents or insulin	1.04	0.95–1.13	0.40	0.96	0.9–1.03	0.25

*Outcomes analyzed as binary variables (≥140 vs. <140 mmHg for SBP, ≥130 vs. <130 mg/dl for LDL cholesterol, and ≥8.0 vs. <8.0% for A1C) according to the levels considered not in control and therefore requiring more action, as recommended by the American Diabetes Association. More intense medication management was defined as the use of two or more drug classes of antihypertensive agents for hypertension, of one or more lipid-lowering agents for lipid management, and of two or more oral agents or insulin for antihyperglycemic treatment.

larger in women than in men throughout (online appendix, supplemental Table 2).

The upper part of Table 1 shows the calculated odds ratios for risk factors not under control. After multiple adjustments, among patients with a CVD history, women were significantly more likely than men to have SBP ≥140 mmHg, LDL cholesterol ≥130 mg/dl, and A1C levels ≥8.0%. The largest differences observed between men and women were regarding LDL cholesterol control. Among patients without a history of CVD, women were significantly more likely than men to have LDL cholesterol ≥130 mg/dl, while there was no difference in SBP or A1C.

The lower part of Table 1 reports the estimated probabilities of the intensity of medication management. In adjusted models, among those with a history of CVD, the medication intensity was similar in men and women with respect to antihypertensive and antihyperglycemic medications, but women received significantly less lipid-lowering medications. Among patients without a history of CVD, there were no significant differences.

CONCLUSIONS — In this large German population of patients with type 2 diabetes, women with a history of CVD were more likely to have all three risk factors uncontrolled, with differences in lipid control being the most pronounced. Women were also less likely to receive lipid-lowering medications. Among patients without a history of CVD, women were more likely to have uncontrolled LDL cholesterol. These results are of particular interest, since it has been shown that the stronger effect of type 2 diabetes on the risk of coronary heart disease in women is in part explained by a greater effect of atherogenic dyslipidemia and blood pressure in diabetic women (9). Our findings are consistent with previous reports (5,10), albeit supported by a much larger data source. A cross-sectional analysis in American patients with diabetes found that women were less likely than men to have A1C <7%, less likely to be treated with lipid-lowering medications, and, when treated, less likely to have LDL cholesterol <100 mg/dl (4). We extend the above data by showing that lack of control is even more pronounced among patients with CVD, a finding with obvious clinical implications.

We have recently shown that among patients with diabetes, physicians focus more on antihyperglycemic treatment, although blood pressure and lipid control are more effective in affecting patient-related end points (7).

A limitation of the study is its cross-sectional design. The strengths include its large size: >10 times higher than previously published studies in this field. It has been shown that a target-driven, long-term, intensified intervention aimed at multiple risk factors in patients with type 2 diabetes reduces the risk of cardiovascular events (11). The present study shows that diabetic women have poorer control of important modifiable risk factors than diabetic men and receive less intensified lipid-lowering therapy. More intensive treatment of diabetic women may improve the sex disparity in CVD mortality.

Acknowledgments— Establishment of the DUTY registry was supported by an unrestricted research grant by MSD Sharp & Dohme, Haar, Germany. Data collection was executed by contract research organization (CRO) Kendle GmbH & Co. GMI KG, Munich, Germany.

C.S.M. is a recipient of an award from the Alexander von Humboldt Foundation.

Employees of the sponsor contributed to the design of the registry. The three primary authors had no participation in the planning or conduct of the study. After the study had

been concluded, they had full access to all of the data. Neither the sponsor nor the CRO had a role in the evaluation and interpretation of the data or in writing the manuscript.

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