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## Gender Differences in Clinical Outcomes Among Diabetics Hospitalized for Cardiovascular Disease (CVD)

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### Abstract

**BACKGROUND**—The risk of incident CVD has been shown to be greater among diabetic women than men but gender differences in clinical outcomes among diabetics hospitalized with CVD is not established. We aimed to determine if HbA<sub>1c</sub> was associated with 30-day and 1-year CVD rehospitalization, and total mortality among diabetics hospitalized for CVD, overall and by gender.

**METHODS**—This was a prospective analysis of diabetic patients hospitalized for CVD, enrolled in an NHLBI-sponsored observational clinical outcomes study (N=902, 39% female, 53% racial/ethnic minority, mean age 67±12 years). Laboratory, rehospitalization and mortality data were determined by hospital-based electronic medical record. Poor glycemic control was defined as HbA<sub>1c</sub> ≥7%. The association between HbA<sub>1c</sub> and clinical outcomes was evaluated using logistic regression; gender modification was evaluated by interaction terms and stratified models.

**RESULTS**—HbA<sub>1c</sub> ≥7% prevalence was 63% (n=566) and was similar by gender. HbA<sub>1c</sub> ≥7% vs. <7% was associated with increased 30-day CVD rehospitalization in univariate (OR=1.63;95%CI=1.05–2.54), and multivariable-adjusted models (OR=1.74;95%CI=1.06–2.84). There was an interaction between glycemic control and gender for 30-day CVD rehospitalization risk (p=0.005). In stratified univariate models, the association was significant among women (OR=4.83;95%CI=1.84–12.71), but not among men (OR=1.02;95%CI=0.60–1.71). The multivariate adjusted risk for HbA<sub>1c</sub> ≥7% vs. <7% among women was 8.50(95%CI=2.31–31.27) and 1.02(95%CI=0.57–1.80) for men. A trend toward increased 30-day/1-year mortality risk was observed for HbA<sub>1c</sub><6% vs. ≥6% for men and women.

**CONCLUSIONS**—Risk of 30-day CVD rehospitalization was 8.5-fold higher among diabetic women hospitalized for CVD with HbA<sub>1c</sub> ≥7% vs. <7%; no association was observed among men. A trend for increased 30-day/1-year mortality risk with HbA<sub>1c</sub><6% deserves further study.

### Keywords

Gender differences; rehospitalization; cardiovascular disease; diabetes; glycemic control; glycosylated hemoglobin A1c % (HbA<sub>1c</sub>); mortality

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Few studies in real world settings have examined gender differences in the association between glycemic control and clinical outcomes among diabetic patients hospitalized for CVD. There is debate about whether prognosis after CVD hospitalization is different by gender, as several studies have shown worse prognosis for women after acute coronary syndromes,<sup>1-3</sup> while others failed to show this disparity after MI, coronary artery bypass grafting and percutaneous coronary intervention.<sup>4-9</sup> Gender differences have not been adequately studied among diabetic populations in a post-statin era and during a time of heightened focus to reduce gender disparities. While there is evidence that poor glycemic control in patients with CVD is associated with worse outcomes and rehospitalization,<sup>10, 11</sup> others have failed to document an association,<sup>12-14</sup> and it is not established whether glycemic control impacts outcomes and rehospitalization equally in women and men. Barrett-Connor et al showed that diabetes was associated with a 3-fold increase in fatal CVD among women compared to a 2-fold increase among men in a population based longitudinal study.<sup>15</sup> A subsequent meta-analysis documented that diabetes was associated with a 50% increased risk for fatal CVD among women compared to men; the excess risk was largely explained by adverse risk profiles or possible treatment differences.<sup>16</sup> Given the increasing focus on reducing rehospitalization rates to improve overall quality of care and lower health care costs,<sup>17-19</sup> understanding risk factors for rehospitalization, such as glycemic control is important. Data is lacking from contemporary studies that examine gender differences in the association between glycemic control and rehospitalization and mortality in diabetic patients.

The purpose of this study was to evaluate the independent association between glycosylated hemoglobin A1c% (HbA<sub>1c</sub>) and 30-day CVD rehospitalization rates among diabetic patients hospitalized for CVD, and to determine if the association varied according to gender after adjustment for potential confounders. Additional aims were to evaluate the association between HbA<sub>1c</sub> and 1-year CVD rehospitalization and all-cause rehospitalization and all-cause mortality at 30 days and 1 year.

## RESEARCH DESIGN AND METHODS

### Study Design and Participants

This study was a prospective analysis of diabetic patients hospitalized for CVD (N=902) who participated in the National Heart, Lung and Blood Institute-sponsored Family Cardiac Caregiver Investigation To Evaluate Outcomes (FIT-O) study. The design and methods of FIT-O have been previously described.<sup>20</sup> Briefly, FIT-O was a prospective cohort study that evaluated patterns of caregiving and the relation to clinical outcomes of consecutively admitted patients to the cardiovascular service at an academic medical center (93% enrollment rate, N=4500). Patients who were unable to read or understand English or Spanish, lived in a full-time nursing facility, had a mental status that made them unable to participate, or refused to participate were excluded.

The current study included FIT-O participants with physician-documented diabetes (type 1 and type 2) who had a glycosylated hemoglobin A1c % (HbA<sub>1c</sub>) documented in the electronic medical record (EMR) within 12 months of the index admission. Among all patients with physician documented diabetes (n=1387), 485 (35%) had no HbA<sub>1c</sub> documented in the EMR within 12 months of the index admission and were thus excluded. The institutional review board of Columbia University Medical Center (CUMC) approved the study.

## Baseline Assessment

Participant baseline characteristics, medical history, admission primary diagnoses and prescribed medications were documented by standardized electronic chart review. Medical records were accessed using a secure and comprehensive electronic clinical information system at New York Presbyterian Hospital (NYPH)/CUMC. All research staff members were Health Insurance Portability and Accountability Act trained and certified in the use of this clinical information system. Current and previous medical conditions, including myocardial infarction (MI), congestive heart failure (CHF), stroke, renal disease, chronic obstructive pulmonary disease (COPD), peripheral vascular disease (PVD), smoker, dyslipidemia as well as type 1 or type 2 diabetes were collected from the EMR and were classified according to *International Classification of Disease, 9th Revision (ICD-9)* billing codes and physician or nurse practitioner notes. Insulin-dependent diabetes was defined as documented insulin prescription on discharge from the hospital. A trained research nurse collected medical history data. The admission diagnosis (CVD vs. non-CVD) was determined from ICD-9 billing codes for admission or primary diagnosis, and was validated in a sub-study by a blinded independent physician reviewer.<sup>21</sup>

A comorbidity index, Ghali, was calculated for all participants using the medical history data obtained through EMR review. The Ghali index ranges from 0 to 11 with 0 being lowest risk and weighs conditions such as MI, CHF, PVD and moderate or severe renal disease. Scores  $\geq 1$  are consistent with significant co-morbidities.<sup>22-24</sup> Admission type was classified as surgical (cardiac) vs. non-surgical. The names and/or types of prescribed medications were obtained from the EMR discharge notes and supplemented by ambulatory EMR, if needed. Caregiving status, which we have previously shown to be linked to rehospitalization and mortality, was assessed by standardized questionnaire administered to each participant at baseline.<sup>21, 25, 26</sup> A caregiver was defined as a paid professional (e.g., nurse/home aide) or an informal (nonpaid) person who assists the patient with medical and/or preventive care.

## Assessment of Glycemic Control

HbA<sub>1c</sub> level was documented from the EMR obtained in the central hospital laboratory and analyzed using Bio Variant 2. The HbA<sub>1c</sub> result obtained closest to the admission date (within 1 year) was used if no admission value available. Among hospitalized diabetics in this study, 89% had HbA<sub>1c</sub> documented within 3 months of admission. Poor glycemic control was defined as HbA<sub>1c</sub>  $\geq 7\%$ . Intensive glycemic control was defined as HbA<sub>1c</sub>  $< 6\%$ .

## Assessment of Clinical Outcomes

The primary clinical outcome was 30-day CVD rehospitalization. Other outcomes included CVD rehospitalization at 1 year and all-cause rehospitalization and all-cause mortality at 30 days and 1 year. Rehospitalization was systematically obtained from the NYPH/CUMC electronic clinical information system, which is updated daily. The participants' admitting date, admitting diagnoses and primary diagnoses for each hospitalization and rehospitalization were recorded. The readmission type was classified as CVD vs. non-CVD using ICD-9 billing codes. To supplement the outcome data collected by the clinical system, all participants were systematically contacted via mail or telephone 1 year after the index hospitalization/baseline survey date and were queried regarding rehospitalization in the past year (81% response rate). Rehospitalization was defined as rehospitalization at NYPH or elsewhere. Analyses using this definition have been similar to the analyses limited to readmission to NYPH only.<sup>21, 25</sup> Vital status was obtained from the clinical information system, which was updated monthly with National Death Index data. All mortality data were considered complete after a status update at a minimum of 18 months following

hospitalization for all participants to reduce misclassification of vital status due to delays in reporting.

### Data Management and Statistical Analysis

All data were double checked for errors and stored in a Microsoft Access database. Descriptive data are presented as frequencies and percentages. The univariate association between HbA<sub>1c</sub> and rehospitalization was evaluated by chi square analysis. Logistic regression was utilized to adjust for potential confounders including demographic (age, race/ethnicity, gender, health insurance, caregiving) and comorbidities (MI, CHF, stroke, renal disease, COPD, insulin-dependent diabetes, admission type (surgical [cardiac] vs. non-surgical) and prescription of evidenced-based medications on discharge (statin, Angiotensin-converting enzyme inhibitor (ACE-I)/Angiotensin receptor blockers (ARB), beta-blockers, antiplatelets) and to test for statistical interaction by gender using a using cross-product term (HbA<sub>1c</sub> X Gender). Stratified analyses were used to further evaluate interaction by gender. Analyses were conducted using SAS software (version 9.2; SAS Institute, Cary, North Carolina). Statistical significance was set at  $p < 0.05$ .

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## RESULTS

The baseline characteristics of the study population and differences among men and women are listed in Table 1. Among 902 hospitalized CVD diabetic patients, the mean age was  $67 \pm 12$  years. More than half of participants were racial/ethnic minorities and approximately one-third were women. More women vs. men were older than age 65 (64% vs. 55%,  $p = 0.01$ ), were racial/ethnic minorities (60% vs. 48%,  $p = 0.01$ ), and lacked health insurance (26% vs. 19%,  $p = 0.01$ ) compared to men.

The mean HbA<sub>1c</sub> was  $7.8\% \pm 1.8\%$ . Approximately two-thirds of participants had HbA<sub>1c</sub>  $\geq 7\%$  which did not significantly differ between women and men (61% vs. 64%,  $p = ns$ ). Forty-four percent of participants had insulin-dependent diabetes, which did not vary significantly between women and men (45% vs. 44%,  $p = ns$ ); 98% of participants were classified as type 2 based on physician documentation and ICD-9 billing codes.

The overall 30-day rehospitalization rate was 13% ( $n = 119$ ). Ninety-one percent of 30-day rehospitalizations were for CVD ( $n = 108$ ), and the rate was similar for women vs. men (11% vs. 13%,  $p = ns$ ). The overall 1-year rehospitalization rate was 57% ( $n = 511$ ). Eighty-five percent of 1-year rehospitalizations were for CVD ( $n = 434$ ), and the rate was not significantly different for women and men (52% vs. 46%,  $p = ns$ ).

Poor glycemic control (HbA<sub>1c</sub>  $\geq 7\%$  vs.  $< 7\%$ ) was associated with an increased risk of 30-day CVD rehospitalization (OR 1.63, 95% CI 1.05–2.54) (Table 2). There was a significant interaction between HbA<sub>1c</sub> and gender for risk of 30-day CVD rehospitalization ( $p = 0.005$ ). In gender stratified univariate analysis, the risk of 30-day CVD rehospitalization was significant among women with HbA<sub>1c</sub>  $\geq 7\%$  vs.  $< 7\%$  (OR 4.83, 95% CI 1.84–12.71); no significant association was observed among men (OR 1.02, 95% CI 0.60–1.71). This gender difference was observed across the following substrata: 1) demographic (e.g. age, race/ethnic group, health insurance, caregiving), 2) past medical history (e.g. previous MI, CHF,

Coronary Heart Disease [CHD]), 3) discharge diagnoses (e.g. CHD, CHF), 4) standard medical therapies (e.g. statin, ACE-I/ARB, beta-blocker, antiplatelets) and 5) reason for rehospitalization (e.g. CHD, CHF) (data not shown).

The association between potential confounders and 30-day CVD rehospitalization are presented in Table 2. Prior CHF (OR 1.64, 95% CI 1.09–2.48) and GHALI comorbidity index 1 (OR 1.61, 95% CI 1.05–2.46) were significant predictors of 30-day CVD rehospitalization. Discharge prescriptions of evidence-based medications were not a significant predictor of 30-day CVD rehospitalization, and notably the majority of patients were prescribed evidence-based therapies at discharge.

Table 3 shows the association between HbA<sub>1c</sub> 7% and increased risk of 30-day CVD rehospitalization remained significant after adjustment for demographics and comorbidities (OR 1.77, 95% CI 1.08–2.91). The multivariate adjusted association between HbA<sub>1c</sub> 7% and risk of 30-day CVD rehospitalization was observed among women (OR 8.50, 95% CI 2.31–31.27) but not among men (OR 1.02, 95% CI 0.57–1.80). The multivariate adjusted association between HbA<sub>1c</sub> 7% and risk of 30-day all-cause rehospitalization showed a similar relationship, (OR 1.55, 95% CI 0.97–2.49), and was observed among women (OR 6.51, 95% CI 2.04–20.79) but not among men (OR 0.91, 95% CI 0.52–1.57). The trend was similar but not statistically significant for 1) the 1-year CVD rehospitalization [whole study population (OR 1.24, 95% CI 0.91–1.70), among women (OR 1.38, 95% CI 0.81–2.35), among men (OR 1.09, 95% CI 0.73–1.63)] and 2) the 1-year all-cause rehospitalization [whole study population (OR 1.24, 95% CI 0.91–1.70), among women (OR 1.46, 95% CI 0.85–2.49), among men (OR 1.07, 95% CI 0.72–1.59)].

Intensive glycemic control (HbA<sub>1c</sub><6%) vs. HbA<sub>1c</sub> 6% was not associated with risk of 30-day CVD rehospitalization (OR 0.82, 95% CI 0.36–1.84) and was not significantly different between men and women. HbA<sub>1c</sub><6% vs. HbA<sub>1c</sub> 6% was not associated with risk of 30-day all-cause rehospitalization (OR 1.13, 95% CI 0.56–2.27), 1-year CVD rehospitalization (OR 0.87, 95% CI 0.53–1.43), or 1-year all-cause rehospitalization (OR 0.99, 95% CI 0.61–1.63) and no significant gender differences were observed.

The overall 30-day mortality rate was 3% (n=28) and did not differ by gender (women: n=9; men: n=19, p=ns). The 1-year mortality rate was 12% (n=109) and was similar for women (n=38) and men (n=71, p=ns). Intensive glycemic control (HbA<sub>1c</sub><6%) vs. HbA<sub>1c</sub> 6% was associated with a non-significant increase in 30-day mortality (OR 1.47, 95% CI 0.43–4.99) and 1-year mortality (OR 1.42 95% CI 0.72–2.80) and the trends were similar for women and men.

## CONCLUSIONS

### Discussion

Among diabetic patients hospitalized for CVD, HbA<sub>1c</sub> 7% vs.<7% was associated with a significant increased risk of 30-day CVD rehospitalization which varied significantly by gender. Notably, the increased risk associated with poor glycemic control was 8.5-fold among women in gender-stratified multivariable adjusted models; no association was observed among men. The gender disparity was not explained by differences in age or other measured confounders. The association between HbA<sub>1c</sub> 7% and 30-day all-cause rehospitalization and 1-year rehospitalization (all cause and CVD) followed similar trends. We also documented that intensive glycemic control (HbA<sub>1c</sub><6%) vs. 6% was associated with a non-significant increased 30-day and 1-year mortality risk but our ability to examine gender differences in mortality was limited due to the small number of deaths in this population.



The observed association between HbA<sub>1c</sub> 7% and the 63% increased risk of CVD rehospitalization in this study of consecutively hospitalized patients is consistent with Ueda et al who showed that in a registry of diabetic patients, increased HbA<sub>1c</sub> in diabetic patients was associated with a 40% increased risk of major adverse cardiovascular events after successful PCI, but the gender specific results were not reported.<sup>10</sup> Corpus et al showed a 2-fold increased risk of cardiac rehospitalization and 3-fold increased risk of revascularization of the targeted vessel within 12 months in diabetic patients with poor glycemic control who underwent PCI compared to those with HbA<sub>1c</sub><7%, but no gender differences were noted.<sup>11</sup> In contrast, Chan et al did not show a statistically significant association between poor glycemic control and major cardiovascular events, rehospitalization, or mortality in diabetic patients admitted with an acute coronary syndrome, but the study was limited by a small sample size.<sup>12</sup>

We observed an increased risk of rehospitalization among women but not among men, which is similar to studies that have shown greater adverse affects of diabetes in women compared to men with respect to risk of CVD.<sup>27, 28</sup> The majority of rehospitalizations in the current study were due to CVD and trends were similar for all-cause rehospitalization. Our study showed that the association between HbA<sub>1c</sub> 7% vs.<7% and 30-day CVD rehospitalization among women was independent of measured cofounders but likely there are unmeasured factors (e.g. social) that contribute to disparate CVD risk that we did not measure. Potential explanations for the increased risk of rehospitalization in diabetic women with elevated HbA<sub>1c</sub> may include traditional pathways in diabetic patients that elevate short term CVD risk such as inflammation and procoagulation,<sup>29, 30</sup> but may also be related to non-adherence to lifestyle and medication recommendations.<sup>31</sup> The possibility that gender differences in pathophysiology and risk factor control may influence the association between glycemic control and outcomes deserves further study.

We documented a non-significant association between intensive glycemic control (HbA<sub>1c</sub><6%) and increased 30-day and 1-year mortality risk. These results are consistent with what was observed in Action to Control Cardiovascular Risk in Diabetes (ACCORD), a randomized-controlled study designed to determine whether intensive glycemic control in diabetic patients could reduce CVD events, which documented that intensive glycemic control was associated with increased mortality.<sup>32</sup> Others have shown in a long-term follow-up that intensive glycemic control was associated with increased mortality for unclear reasons, and suggested that the difference may have been related to the effect of using multiple glucoselowering medications rather than hypoglycemia.<sup>33</sup> Furthermore, Aggarwal et al showed in a large cohort with long-term follow-up that in persons without diabetes, low HbA<sub>1c</sub> (<5%) was associated with an increased risk of mortality, perhaps suggesting that low HbA<sub>1c</sub> may be a marker of poor health.<sup>34</sup> The mechanisms associated with increased mortality could not be evaluated in this cohort, and the number of deaths was too few to evaluate by gender.

The present study had limitations that should be considered. There may have been misclassification of glycemic control due to measurements within one year of admission, however this was non-differential with respect to gender, and therefore unlikely to impact conclusions about the interaction of gender on the relationship between HbA<sub>1c</sub> and outcomes. Some participants may have been rehospitalized outside of NYPH/CUMC that were not captured, but our prior work evaluating outcomes at 1 year in this population showed that missing data were also non-differential with respect to gender and other baseline characteristics.<sup>21</sup> Our ability to evaluate mortality data according to subgroups such as age and gender was limited by the sample size due to low 30-day and 1-year mortality risk. There may be likely unmeasured cofounders that contribute to the association between glycemic control and outcomes not evaluated in this study.

## Implications

The finding that women with poorly controlled diabetes are at substantially higher risk for 30-day rehospitalization than their male counterparts has several implications for medical policy, reimbursement and prevention. Appropriate management of diabetes among women with CVD is critical given the risk of rehospitalization associated with poor glycemic control and the possibility of increased mortality associated with overly intensive control. Our data support the recommendation from the Institute of Medicine that gender-specific analyses should be conducted and reported.<sup>35</sup> These data also suggest that models of reimbursement related to 30-day rehospitalization risk may need to consider gender as well as diabetic status and glycemic control. Further research is needed to understand the etiology of gender differences in glycemic control and clinical outcomes, and to evaluate interventions to reduce gender differences in rehospitalization associated with poor glycemic control.

## REFERENCES

1. Vaccarino V, Krumholz HM, Berkman LF, et al. Sex differences in mortality after myocardial infarction. Is there evidence for an increased risk for women? *Circulation*. 1995; 91(6):1861–1871. [PubMed: 7882498]
2. Berger JS, Elliott L, Gallup D, et al. Sex differences in mortality following acute coronary syndromes. *JAMA*. 2009; 302(8):874–882. [PubMed: 19706861]
3. Hochman JS, Tamis JE, Thompson TD, et al. Sex, clinical presentation, and outcome in patients with acute coronary syndromes. Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes IIb Investigators. *N Engl J Med*. 1999; 341(4):226–232. [PubMed: 10413734]
4. Ahmed WA, Tully PJ, Knight JL, et al. Female sex as an independent predictor of morbidity and survival after isolated coronary artery bypass grafting. *Ann Thorac Surg*. 2011; 92(1):59–67. [PubMed: 21601828]
5. Kim C, Redberg RF, Pavlic T, et al. A systematic review of gender differences in mortality after coronary artery bypass graft surgery and percutaneous coronary interventions. *Clin Cardiol*. 2007; 30(10):491–495. [PubMed: 17880013]
6. D'Ascenzo F, Gonella A, Quadri G, et al. Comparison of mortality rates in women versus men presenting with ST-segment elevation myocardial infarction. *Am J Cardiol*. 2011; 107(5):651–654. [PubMed: 21195375]
7. Ogita M, Miyauchi K, Dohi T, et al. Gender-based outcomes among patients with diabetes mellitus after percutaneous coronary intervention in the drug-eluting stent era. *Int Heart J*. 2011; 52(6):348–352. [PubMed: 22188707]
8. Onuma Y, Kukreja N, Daemen J, et al. Impact of sex on 3-year outcome after percutaneous coronary intervention using bare-metal and drug-eluting stents in previously untreated coronary artery disease: insights from the RESEARCH (Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital) and T-SEARCH (Taxus-Stent Evaluated at Rotterdam Cardiology Hospital) Registries. *JACC Cardiovasc Interv*. 2009; 2(7):603–610. [PubMed: 19628181]
9. Saxena A, Poh CL, Dinh DT, et al. Does patient gender affect outcomes after concomitant coronary artery bypass graft and aortic valve replacement? An Australian Society of Cardiac and Thoracic Surgeons Database study. *Cardiology*. 2011; 119(2):116–123. [PubMed: 21912125]
10. Ueda H, Mitsusada N, Harimoto K, et al. Glycosylated hemoglobin is a predictor of major adverse cardiac events after drug-eluting stent implantation in patients with diabetes mellitus. *Cardiology*. 2010; 116(1):51–57. [PubMed: 20453503]
11. Corpus RA, George PB, House JA, et al. Optimal glycemic control is associated with a lower rate of target vessel revascularization in treated type II diabetic patients undergoing elective percutaneous coronary intervention. *J Am Coll Cardiol*. 2004; 43(1):8–14. [PubMed: 14715174]
12. Chan CY, Li R, Chan JY, et al. The value of admission HbA(1c) level in diabetic patients with acute coronary syndrome. *Clin Cardiol*. 2011; 34(8):507–512. [PubMed: 21717470]

13. Tsuruta R, Miyauchi K, Yamamoto T, et al. Effect of preoperative hemoglobin A1c levels on long-term outcomes for diabetic patients after off-pump coronary artery bypass grafting. *J Cardiol.* 2011; 57(2):181–186. [PubMed: 21185154]
14. Lemesle G, Bonello L, de Labriolle A, et al. Prognostic value of hemoglobin A1C levels in patients with diabetes mellitus undergoing percutaneous coronary intervention with stent implantation. *Am J Cardiol.* 2009; 104(1):41–45. [PubMed: 19576319]
15. Barrett-Connor EL, Cohn BA, Wingard DL, et al. Why is diabetes mellitus a stronger risk factor for fatal ischemic heart disease in women than in men? The Rancho Bernardo Study. *JAMA.* 1991; 265(5):627–631. [PubMed: 1987413]
16. Huxley R, Barzi F, Woodward M. Excess risk of fatal coronary heart disease associated with diabetes in men and women: meta-analysis of 37 prospective cohort studies. *BMJ.* 2006; 332(7533):73–78. [PubMed: 16371403]
17. Medicare program; hospital inpatient value-based purchasing program. Final rule. *Fed Regist.* 2011; 76(88):26490–26547.
18. Kocher RP, Adashi EY. Hospital readmissions and the Affordable Care Act: paying for coordinated quality care. *JAMA.* 2011; 306(16):1794–1795. [PubMed: 22028355]
19. Medicare program; hospital inpatient prospective payment systems for acute care hospitals and the long-term care hospital prospective payment system and FY 2012 rates; hospitals' FTE resident caps for graduate medical education payment. Final rules. *Fed Regist.* 2011; 76(160):51476–51846.
20. Mosca L, Mochari-Greenberger H, Aggarwal B, et al. Patterns of caregiving among patients hospitalized with cardiovascular disease. *J Cardiovasc Nurs.* 2011; 26(4):305–311. [PubMed: 21330929]
21. Mosca L, Aggarwal B, Mochari-Greenberger H, et al. Association between having a caregiver and clinical outcomes 1 year after hospitalization for cardiovascular disease. *Am J Cardiol.* 2012; 109(1):135–139. [PubMed: 21962999]
22. Ghali WA, Hall RE, Ash AS, et al. Evaluation of complication rates after coronary artery bypass surgery using administrative data. *Methods Inf Med.* 1998; 37(2):192–200. [PubMed: 9656664]
23. Ghali WA, Hall RE, Rosen AK, et al. Searching for an improved clinical comorbidity index for use with ICD-9-CM administrative data. *J Clin Epidemiol.* 1996; 49(3):273–278. [PubMed: 8676173]
24. Schneeweiss S, Maclure M. Use of comorbidity scores for control of confounding in studies using administrative databases. *Int J Epidemiol.* 2000; 29(5):891–898. [PubMed: 11034974]
25. Mochari-Greenberger HMM, Aggarwal B, Umann T, Mosca L. Caregiver Status. A Simple Marker to Identify Cardiac Surgery Patients at Risk for Longer Postoperative Length of Stay, Rehospitalization, or Death. *J Cardiac Nurs.* 2012 In Press.
26. Hammond G, Mochari-Greenberger H, Liao M, et al. Effect of gender, caregiver, on cholesterol control and statin use for secondary prevention among hospitalized patients with coronary heart disease. *Am J Cardiol.* 2012; 110(11):1613–1618. [PubMed: 22901971]
27. Howard BV, Cowan LD, Go O, et al. Adverse effects of diabetes on multiple cardiovascular disease risk factors in women. The Strong Heart Study. *Diabetes Care.* 1998; 21(8):1258–1265. [PubMed: 9702430]
28. Hunt KJ, Williams K, Hazuda HP, et al. The metabolic syndrome and the impact of diabetes on coronary heart disease mortality in women and men: the San Antonio Heart Study. *Ann Epidemiol.* 2007; 17(11):870–877. [PubMed: 17662617]
29. Chan P, Pan WH. Coagulation activation in type 2 diabetes mellitus: the higher coronary risk of female diabetic patients. *Diabet Med.* 1995; 12(6):504–507. [PubMed: 7648824]
30. Steinberg HO, Paradisi G, Cronin J, et al. Type II diabetes abrogates sex differences in endothelial function in premenopausal women. *Circulation.* 2000; 101(17):2040–2046. [PubMed: 10790344]
31. Sokol MC, McGuigan KA, Verbrugge RR, et al. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care.* 2005; 43(6):521–530. [PubMed: 15908846]
32. Gerstein HC, Miller ME, Byington RP, et al. Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med.* 2008; 358(24):2545–2559. [PubMed: 18539917]
33. Gerstein HC, Miller ME, Genuth S, et al. Long-term effects of intensive glucose lowering on cardiovascular outcomes. *N Engl J Med.* 2011; 364(9):818–828. [PubMed: 21366473]



34. Aggarwal V, Schneider AL, Selvin E. Low Hemoglobin A1c in Nondiabetic Adults: An elevated risk state? *Diabetes Care*. 2012; 35(10):2055–2060. [PubMed: 22855733]
35. Adler, NE.; Adashi, EY.; Aguilar-Gaxiola, S., et al. *Women's Health Research: Progress, Pitfalls, and Promise*. Washington DC: The National Academies Press; 2010. Institute of Medicine's (IOM) Committee on Women's Health Research.

**Table I**

## Baseline Characteristics of Diabetic Patients Admitted to the CVD Service

|   | ALL<br>N=902 | WOMEN<br>n=355 | MEN<br>n=547 | p value<br>(women vs. men) |
|---|--------------|----------------|--------------|----------------------------|
|   | n (%)        | n (%)          | n (%)        |                            |
| <b>Demographics</b>   |              |                |              |                            |
| Age ( ≥ 65 years vs. <65 years)                             | 527 (58%)    | 227 (64%)      | 300 (55%)    | <b>0.01</b>                |
| Race/ethnic group* (minority vs. white)                     | 437 (53%)    | 198 (60%)      | 239 (48%)    | <b>0.01</b>                |
| Gender (male vs. female)                                    | 547 (61%)    | -              | -            | -                          |
| Health insurance (none or self-pay vs. insured)             | 199 (22%)    | 94 (26%)       | 105 (19%)    | <b>0.01</b>                |
| Caregiving (paid or informal caregiver vs. none)            | 426 (47%)    | 183 (52%)      | 243 (44%)    | <b>0.04</b>                |
| <b>Glycemic Control</b>                                     |              |                |              |                            |
| Insulin-dependent diabetes (yes vs. no)                     | 397 (44%)    | 156 (45%)      | 241 (44%)    | 0.97                       |
| HbA <sub>1c</sub> ≥ 7%                                      | 566 (63%)    | 216 (61%)      | 350 (64%)    | 0.58                       |
| HbA <sub>1c</sub> 6.0%-<7%                                  | 267 (29%)    | 114 (32%)      | 153 (28%)    | 0.18                       |
| HbA <sub>1c</sub> <6.0%                                     | 69 (8%)      | 25 (7%)        | 44 (8%)      | 0.34                       |
| <b>Comorbidities</b>  |              |                |              |                            |
| Prior/Current MI (yes vs. no)                               | 340 (38%)    | 126 (35%)      | 214 (39%)    | 0.27                       |
| Prior/Current CHF (yes vs. no)                              | 293 (33%)    | 117 (33%)      | 176 (32%)    | 0.81                       |
| Prior/Current stroke (yes vs. no)                           | 125 (14%)    | 49 (14%)       | 76 (14%)     | 0.97                       |
| Prior/Current moderate to severe renal disease (yes vs. no) | 286 (32%)    | 106 (30%)      | 180 (33%)    | 0.34                       |
| Prior/Current COPD (yes vs. no)                             | 67 (7%)      | 22 (6%)        | 45 (8%)      | 0.26                       |
| Prior/Current PVD (yes vs. no)                              | 160 (18%)    | 62 (17%)       | 98 (18%)     | 0.86                       |
| Current smoker (current vs. prior or never)                 | 72 (8%)      | 24 (7%)        | 48 (9%)      | 0.28                       |
| Dyslipidemia history (yes vs. no)                           | 628 (70%)    | 247 (70%)      | 381 (70%)    | 0.98                       |
| Ghali Comorbidity Index ≥ 1 (yes vs. no)                    | 512 (57%)    | 193 (54%)      | 319 (58%)    | 0.24                       |
| Had cardiac surgery during admission (yes vs. no)           | 130 (14%)    | 47 (13%)       | 83 (15%)     | 0.42                       |
| <b>Prescribed medications on discharge</b>                  |              |                |              |                            |
| Statin (yes vs. no)   | 741 (82%)    | 292 (82%)      | 449 (82%)    | 0.95                       |
| ACE-I/ARB (yes vs. no)                                      | 482 (53%)    | 206 (58%)      | 276 (50%)    | <b>0.03</b>                |
| Beta-blocker (yes vs. no)                                   | 708 (78%)    | 276 (78%)      | 432 (79%)    | 0.66                       |
| Antiplatelet (yes vs. no)                                   | 774 (86%)    | 302 (85%)      | 472 (86%)    | 0.61                       |
| New insulin (yes vs. no)                                    | 87 (10%)     | 30 (8%)        | 57 (10%)     | 0.33                       |

\* 71 missing, n=831

**Table II**

Univariate Associations between HbA<sub>1c</sub> 7% vs. <7%, Comorbid Conditions, Medications and 30-day CVD Rehospitalization

|   | <b>30-day CVD Rehospitalization</b> |
|---|-------------------------------------|
|   | <b>OR (95%CI)</b>                   |
| <b>Main Outcome</b>   |                                     |
| HbA <sub>1c</sub> >7% vs.<7% (Overall)                      | <b>1.63 (1.05–2.54)</b>             |
| Female  | <b>4.83 (1.84–12.71)</b>            |
| Male  | 1.02 (0.60–1.71)                    |
| <b>Demographic Conditions</b>                               |                                     |
| Age (>65 years vs. <65 years)                               | 1.30 (0.86–1.97)                    |
| Race/ethnic group (minority vs. white)                      | 1.22 (0.80–1.87)                    |
| Gender (male vs. female)                                    | 1.22 (0.80–1.86)                    |
| Health insurance (none or self-pay vs. insured)             | 1.07 (0.67–1.73)                    |
| Caregiving (paid or informal caregiver vs. none)            | 1.29 (0.86–1.93)                    |
| <b>Comorbid Conditions</b>                                  |                                     |
| Insulin-dependent diabetes (yes vs. no)                     | 1.21 (0.81–1.81)                    |
| Prior/Current MI (yes vs. no)                               | 1.32 (0.88–1.98)                    |
| Prior/Current CHF (yes vs. no)                              | <b>1.64 (1.09–2.48)</b>             |
| Prior/Current stroke (yes vs. no)                           | 0.92 (0.50–1.66)                    |
| Prior/Current moderate to severe renal disease (yes vs. no) | 1.37 (0.90–2.08)                    |
| Prior/Current COPD (yes vs. no)                             | 1.49 (0.76–2.95)                    |
| Prior/Current PVD (yes vs. no)                              | 1.06 (0.63–1.78)                    |
| Smoking status (current vs. prior or never)                 | 1.05 (0.51–2.19)                    |
| Dyslipidemia history (yes vs. no)                           | 0.90 (0.58–1.38)                    |
| Ghali Comorbidity Index >1 (yes vs. no)                     | <b>1.61 (1.05–2.46)</b>             |
| Had cardiac surgery during admission (yes vs. no)           | 0.79 (0.43–1.46)                    |
| <b>Prescribed medications on discharge</b>                  |                                     |
| Statin (yes vs. no)   | 1.19 (0.69–2.05)                    |
| ACE-I/ARB (yes vs. no)                                      | 1.25 (0.83–1.88)                    |
| Beta-blocker (yes vs. no)                                   | 0.85 (0.53–1.36)                    |
| Antiplatelet (yes vs. no)                                   | 1.52 (0.79–2.93)                    |
| New insulin (yes vs. no)                                    | 0.72 (0.34–1.54)                    |

**Table III**

Multivariate Models: Association between HbA<sub>1c</sub> 7% vs.<7% and 30-day CVD Rehospitalization among Diabetic Patients Admitted for CVD

| Variable  | Overall                 | Gender Stratified        |                         |
|---|-------------------------|--------------------------|-------------------------|
|   | OR (95% CI)             | Women<br>OR (95% CI)     | Men<br>OR (95% CI)      |
| Main Outcome  |                         |                          |                         |
| HbA <sub>1c</sub> >7% vs.<7%                                | <b>1.77 (1.08–2.91)</b> | <b>8.50 (2.31–31.27)</b> | 1.02 (0.57–1.80)        |
| Demographic Conditions                                      |                         |                          |                         |
| Age (>65 years vs. <65 years)                               | 1.26 (0.80–2.01)        | <b>2.96 (1.08–8.12)</b>  | 0.90 (0.51–1.57)        |
| Race/ethnic group (minority vs. white)                      | 1.17 (0.74–1.85)        | 0.89 (0.38–2.10)         | 1.40 (0.79–2.48)        |
| Gender (male vs. female)                                    | 1.53 (0.96–2.44)        | -                        | -                       |
| Health insurance (none or self-pay vs. insured)             | 0.99 (0.57–1.71)        | 0.78 (0.28–2.16)         | 1.22 (0.61–2.42)        |
| Caregiving (paid or informal caregiver vs. none)            | 1.17 (0.75–1.82)        | 0.73 (0.31–1.74)         | 1.57 (0.90–2.72)        |
| Comorbid Conditions   |                         |                          |                         |
| Insulin-dependent diabetes (yes vs. no)                     | 0.89 (0.57–1.40)        | 0.49 (0.21–1.14)         | 1.00 (0.57–1.73)        |
| Prior/Current MI (yes vs. no)                               | 1.27 (0.82–1.98)        | 1.04 (0.44–2.46)         | 1.42 (0.82–2.44)        |
| Prior/Current CHF (yes vs. no)                              | <b>1.87 (1.18–2.95)</b> | <b>2.46 (1.05–5.76)</b>  | 1.74 (0.99–3.05)        |
| Prior/Current stroke (yes vs. no)                           | 0.79 (0.40–1.56)        | 0.37 (0.08–1.75)         | 0.99 (0.44–2.22)        |
| Prior/Current moderate to severe renal disease (yes vs. no) | 1.30 (0.81–2.09)        | 1.22 (0.47–3.16)         | 1.36 (0.76–2.43)        |
| Prior/Current COPD (yes vs. no)                             | 1.21 (0.57–2.56)        | 0.69 (0.12–3.79)         | 1.50 (0.62–3.61)        |
| Had cardiac surgery during admission (yes vs. no)           | 0.76 (0.38–1.55)        | 0.61 (0.12–3.19)         | 0.97 (0.43–2.18)        |
| Prescribed medications on discharge                         |                         |                          |                         |
| Statin (yes vs. no)   | 1.12 (0.60–2.10)        | 1.08 (0.31–3.76)         | 1.19 (0.56–2.53)        |
| ACE-I/ARB(yes vs. no)                                       | 1.30 (0.83–2.05)        | <b>3.14 (1.17–8.41)</b>  | 0.91 (0.53–1.58)        |
| Beta-blocker (yes vs. no)                                   | 0.66 (0.39–1.10)        | 0.92 (0.33–2.60)         | <b>0.52 (0.28–0.99)</b> |
| Antiplatelet (yes vs. no)                                   | 2.12 (0.97–4.63)        | 1.58 (0.39–6.51)         | 2.45 (0.94–6.40)        |