Effects of Gender and Depression on Oral Medication Adherence in Persons with Type 2 Diabetes Mellitus

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ABSTRACT

Background: In a range of chronic conditions including diabetes, it has been observed that depressive symptoms may be associated with nonadherence to medications.

Objective: The objective of the study was to determine the main effects, and interactive effect, of depression and gender on patients' adherence to oral diabetes medications.

Methods: A cross-sectional design was employed, in which persons with type 2 diabetes mellitus completed a questionnaire regarding medication-use behaviors, depressive symptoms (measured by the 8-item Patient Health Questionnaire [PHQ-8]), health beliefs, and demographics. A 2 × 2 factorial analysis of variance was used to determine the effects of gender and depression on medication adherence after adjusting for age, education, self-efficacy, social support, and number of doses of diabetes medications.

Results: Of the 391 respondents who completed the questionnaire, 73 (18.7%) were categorized as having depression (ie, PHQ-8 score >10). Overall, women (n = 196) had a mean (SD) score of 6.10 (6.19) on the PHQ-8, and men (n = 195) had a lower score of 4.62 (5.28) (t = 2.75; P < 0.01). There was a significant main effect of depression, but not gender, on patients' adherence to diabetes medications in that those who were categorized as depressed had significantly worse adherence to diabetes medications (F = 4.82; P = 0.03). Additionally, there was a significant “gender × depression” interaction effect on adherence (F = 5.93; P = 0.01). Men with depression had mean adherence scores that indicated more nonadherence than did men without depression (9.44 [3.45] vs 7.47 [2.50], respectively), but adherence varied little between women with depression and women without depression (7.83 [2.69] vs 7.55 [2.58], respectively).

Conclusions: The association between depression and medication adherence appears to be stronger in men than in women. Clinicians should be cognizant of the potential effect of depression on self-care for diabetes, particularly in men with depressive symptoms. (Gend Med. 2007;4:205–213)

Key words: gender, depression, self-efficacy, social support, diabetes.
INTRODUCTION
The United Kingdom Prospective Diabetes Study demonstrated that intensive treatment with medications is one of the most important tools to achieve glycemic control in patients with type 2 diabetes mellitus (DM). However, suboptimal adherence to diabetes medication has been frequently reported in the literature. In a systematic review of studies regarding adherence to diabetes medication regimens, Cramer found that adherence to oral antihyperglycemic regimens ranged from 36% to 93%. Nonadherence to diabetes medication is a major contributor to poor glycemic control and is also associated with higher cost of medical care.

Several studies across a range of chronic conditions including diabetes have observed that depressive symptoms may be associated with nonadherence to medication. Understanding the impact of depression on diabetes self-care behaviors is important: in a meta-analysis of the prevalence of comorbid depression in adults with diabetes, major depression and elevated depressive symptoms affected 11% and 31%, respectively, of diabetic individuals.

Numerous mechanisms for the effect of depression on medication adherence have been proposed. Poor motivation, lack of social support, or a decrease in attention or memory, which all accompany depression, could contribute to nonadherence to medication. Depression is also associated with several health beliefs that, in turn, may affect medication adherence. For example, depression-related pessimism and hopelessness may make it more difficult for patients to perceive treatment benefits and may amplify their perceptions of treatment barriers. In persons with diabetes, greater depressive symptoms have been associated with higher perceived severity of diabetes, greater perceived susceptibility to diabetes complications, higher perceived barriers to self-care, and lower self-efficacy for diabetes self-care.

Women with diabetes are more likely to have depression recognized by a health care provider, and are more likely to be prescribed antidepressants. In general, women receive better quality of care for depression, compared with men. A recent study by Katon et al found that diabetic men are more likely to suffer adverse consequences of depression, compared with their female counterparts. In the same study, diabetic men with depression had a significantly higher rate of diabetes-related complications (≥3) than did diabetic men without depression (33.6% vs 17.4%, respectively). However, there was no significant difference in the complication rate between diabetic women with depression and diabetic women without depression (17.7% vs 15.1%, respectively). Thus, gender appeared to moderate the effect of depression on the complications of diabetes.

Although it is clear that glycemic control is affected by self-care behaviors, it is not clear whether men and women experience similar effects of depression on self-care behaviors. If women are better than men at maintaining their diabetes self-care while experiencing depression, this may partially explain the differences in diabetes complications for men and women who experience depression. Because medication use is an important component of self-care for diabetes, we focused our analyses on the impact of depression on diabetes medication use. Thus, our objective was to determine the main effects, and interactive effect, of gender and depression on patients' adherence to oral diabetes medication.

METHODS
Subjects
After the study was approved by a University of Michigan Institutional Review Board, the sample was drawn from the members of a managed care organization in the midwestern United States. More than 6000 adults (aged ≥18 years) who were likely to have diabetes were identified from medical and pharmacy claims data using Health Plan Employer Data and Information Set technical specifications. Based on these specifications, the identified subjects had ≥1 claim for a diabetes medication as well as diagnosis codes for diabetes. These 6000+ adults, serving
as the sampling frame, were stratified by age in 10-year increments. Approximately equal numbers of male and female subjects were randomly selected from each age category to create a final sample of 1700 people. A 74-item questionnaire and cover letter were mailed to the subjects in October 2003, along with reminder postcards the following week. One month after the postcards, a follow-up survey was sent to nonrespondents. Subjects were asked to return their completed questionnaires in the stamped, addressed envelope provided.

The questionnaire listed all potential diabetes medications and asked the subjects to indicate which drugs they took for diabetes. Patients who used oral diabetes medications were included in the study; patients who used only insulin were excluded to increase the likelihood that patients had type 2 DM and to enhance the validity of adherence measurement. Physicians frequently encourage patients to adjust their dose of insulin based on blood glucose readings or symptom experience. Including insulin-using patients within this set of analyses would vastly complicate adherence measurement, because adherence measures ask patients if they skip or adjust doses. For patients using only insulin, self-adjustment of doses may indicate good adherence rather than poor adherence.

**Measures**

**Respondent Characteristics**

The demographic information collected in the questionnaire included age, gender, education, and family income. Comorbidity data were collected by asking respondents to check a box listed next to 7 health problems commonly found in people with diabetes, and an option to write in additional disease states was provided as well. To estimate the duration of disease, respondents were also asked to indicate the age at which they received a diagnosis of diabetes.

**Depressive Symptoms**

Depressive symptoms were measured by the 8-item Patient Health Questionnaire (PHQ-8), which was derived from the 9-item Patient Health Questionnaire (PHQ-9). The PHQ-9 has demonstrated good specificity and sensitivity in diagnosing major depressive disorders and also provides a continuous severity score that has shown excellent construct validity. The PHQ-8 differs from the PHQ-9 in that the item assessing suicidality has been deleted; however, a recent study noted similar sensitivity and specificity between the PHQ-8 and the PHQ-9 in screening for depression. In addition, suicidality is primarily present in severe depression.

The depressive symptom score was obtained by summing responses to each of the 8 individual items. Thus, the scores for the PHQ-8 ranged from 0 to 24, with higher scores representing more-severe depressive symptoms. Scores of 5, 10, 15, and ≥20 represented mild, moderate, moderately severe, and severe depression, respectively, on the PHQ-9. Respondents with PHQ-8 scores ≥10 were categorized as depressed.

**Social Support**

Social support was measured by a summed scale consisting of 2 items. The first item required the respondent to indicate the level of support received from friends or family regarding diabetes, whereas the second item referred to support from a physician or health care team. Responses to both items were measured on a 5-point scale ranging from 1 = “not supportive at all” to 5 = “extremely supportive.” The 2 items were summed to obtain an overall assessment of social support (range, 2–10). These items were similar to those in the diabetes social support measure developed by Connell et al.

**Self-Efficacy**

Medication-related self-efficacy was defined as the confidence a person has about adhering to diabetes medications. A single item, “How confident are you in your ability to take your diabetes medications exactly as directed by your doctor?” was used to measure medication-
specific self-efficacy. Response was measured on a 5-point Likert scale ranging from 1 = “not at all confident” to 5 = “extremely confident.” The validity of this 1-item measure has been demonstrated in a previous study.31

Diabetes Medication Adherence
Diabetes medication-use behavior was measured with a 4-item scale similar to a measure developed by Horne et al.32 The first 2 items asked respondents about their agreement (on a 5-point scale ranging from “strongly agree” to “strongly disagree”) with the statements “I sometimes forget to take my diabetes medications,” and “I sometimes alter the dose of my diabetes medication to suit my own needs.” The second 2 items asked respondents to indicate the frequency with which they purposefully altered the dose from that recommended by their physician, as well as their frequency of forgetting to take diabetes medications. Responses were scored on a 5-point scale that ranged from “never” to “very often.”

A total medication nonadherence score was obtained by summing responses to each of the 4 individual items. Scores ranged from 4 to 20, with higher scores indicating greater reported nonadherence. The validity of this measure has been reported in other studies.31,32

Analysis
Analysis of the data was performed using SPSS version 14.0 (SPSS Inc., Chicago, Illinois). To examine the pattern of mean scores for the demographic variables, social support, self-efficacy, and medication adherence across gender and depression subgroups, subjects were placed into 1 of 4 groups: men without depression, women without depression, men with depression, and women with depression. To test the interactive effects of gender and depression on medication adherence, a 2 × 2 factorial analysis of variance model was constructed. The following covariates were entered in each analysis: age, education level (no college vs college), family income (annual family income <$25,000 vs ≥$25,000), self-efficacy, social support, and number of daily doses of diabetes medication. The F score was reported for the main effects of gender and depression, along with the gender × depression interaction term. P values of <0.05 were considered significant.

RESULTS
Respondent Characteristics
Of the initial mailing to 1700 subjects, 254 questionnaires were undeliverable, resulting in 1446 potential responses. There were 694 usable questionnaires returned, resulting in a net response rate of 48%; however, only 599 respondents answered all of the items necessary for our analyses. Persons with diabetes who used only insulin were also excluded, resulting in a total of 391 respondents for subsequent analysis. An analysis of nonresponse bias was conducted and no significant bias was found. The respondent characteristics were consistent with the known characteristics of the original sample (eg, age, gender, comorbidity).

The mean (SD) age of respondents taking oral diabetes medication was 56.0 (11.1) years, with almost equal numbers of men and women (50.1% vs 49.9%, respectively). Most of the respondents (306 [78.3%]) were white, approximately two thirds (256 [65.5%]) reported some college or higher level of education, and 83 (21.2%) had an annual family income of <$25,000. The mean number of daily doses of diabetes medication was 2.4, and the mean duration of diabetes was 7.3 years. The vast majority (339 [86.7%]) reported having at least 1 complication of diabetes, which included heart disease, high cholesterol, kidney disease, neurological disorder, failing eyesight, high blood pressure, or amputation.

Gender and Depression
Seventy-three (18.7%) of the 391 respondents were categorized as having depression (ie, PHQ-8 scores ≥10). Overall, women (n = 196) had a mean (SD) score of 6.10 (6.19) on the PHQ-8, and men (n = 195) had a lower mean score of 4.62 (5.28). This difference was statistically significant (t = 2.75; P < 0.01). The distribution of the respondents' characteristics across
Gender, Depression, and Nonadherence

Depression had a significant main effect on medication nonadherence ($F = 4.82; P = 0.03$): persons categorized as depressed were less adherent. There was no significant relationship between gender and adherence ($F = 3.01; P = 0.08$). However, the gender × depression interaction effect was significant ($F = 5.93; P = 0.01$); that is, men with depression self-reported significantly worse medication adherence than did men without depression, whereas women were relatively adherent regardless of depressive symptom severity (Figure). The covariates of age, education, income, self-efficacy, social support, and the number of daily doses of diabetes medications were included in this analysis. Only social support ($F = 35.97; P < 0.001$) and number of daily doses ($F = 6.05; P = 0.01$) were statistically significant covariates. The adjusted model $R^2$ was 0.17.

DISCUSSION

Previous studies have shown a significant relationship between depression and diabetes self-care behaviors.7-9 Across these studies, diabetic patients with depression had worse adherence to diabetes medication regimens than did diabetic patients without depression. However, these studies did not examine the potential interactive effect of gender and depression in shaping diabetes medication-use behaviors. Our study found that adherence to the diabetes medication regimen was affected by depression in men, whereas adherence was affected very little by depression in women. This may partially explain the findings of Katon et al.,22 in which diabetic men with depression had a significantly higher rate of diabetes-related complications than did diabetic men without depression, and there was no significant difference in the complication rate between diabetic women with or without depression. Perhaps the interactive effect of gender and depression on diabetes self-care behaviors leads to a higher complication rate for diabetic men with depression.

Women with chronic illnesses such as diabetes and coronary heart disease generally face greater obstacles in self-care compared with men.33,34 An important obstacle to self-care is depression, and studies have shown a higher prevalence of depression in women.35,36 However, women with depressive symptoms are more likely than their male counterparts to be diagnosed with depression and be prescribed an antidepressant.19-21 One can reason that if women are more likely to receive treatment for depression, they may be more likely to achieve control of depressive symptoms. If this is true, then women may be better able to maintain self-care behaviors for diabetes. However, the women in this study had slightly higher levels of self-reported depressive symptoms, and thus the differences in diabetes medication adherence are unlikely due to differences in the remission of depressive symptoms.

Empirical studies in the domains of social support and self-efficacy offer insight into gender differences in depression and self-care for chronic diseases. Social support can ameliorate the negative impact of chronic disease on depression.29 The effect of social support on depression can be either direct or indirect. The level of support one has directly affects the severity of depression,37,38 and social support structures can facilitate self-management behaviors, such as diabetes self-care. In the current study, the women with depression received less social support; however, their self-efficacy for medication-taking was slightly higher than that of the men with depression. Perhaps women are more resilient in the face of depression and low social support because they have always relied on themselves to manage their health. Recent evidence presented at the annual meeting of the American Diabetes Association indicates that adolescent girls tend to take on more responsibility for self-management of diabetes than do adolescent boys.39 This appears to build the self-efficacy of young women for diabetes self-management at a young age, whereas young
Table. Distribution of variables across gender x depression categories. *

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Nonadherence ±</th>
<th>Self-Efficacy ±</th>
<th>Social Support ±</th>
<th>Daily Dose ±</th>
<th>Age</th>
<th>% Low Income</th>
<th>% No College</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men without depression</td>
<td>168</td>
<td>7.47 (2.50)</td>
<td>4.62 (0.64)</td>
<td>8.07 (1.59)</td>
<td>2.44 (1.31)</td>
<td>56.04 (10.60)</td>
<td>9.7</td>
<td>24.6</td>
</tr>
<tr>
<td>Women without depression</td>
<td>150</td>
<td>7.55 (2.58)</td>
<td>4.57 (0.75)</td>
<td>8.08 (1.67)</td>
<td>2.51 (1.34)</td>
<td>57.55 (11.35)</td>
<td>35.3</td>
<td>46.0</td>
</tr>
<tr>
<td>Men with depression</td>
<td>27</td>
<td>9.44 (3.45)</td>
<td>4.12 (1.09)</td>
<td>7.60 (2.12)</td>
<td>2.42 (1.24)</td>
<td>54.31 (10.25)</td>
<td>20.0</td>
<td>26.9</td>
</tr>
<tr>
<td>Women with depression</td>
<td>46</td>
<td>7.83 (2.69)</td>
<td>4.49 (0.98)</td>
<td>7.15 (2.09)</td>
<td>2.21 (1.24)</td>
<td>51.73 (11.57)</td>
<td>36.4</td>
<td>34.1</td>
</tr>
<tr>
<td>Total</td>
<td>391</td>
<td>7.68 (2.66)</td>
<td>4.57 (0.80)</td>
<td>7.94 (1.74)</td>
<td>2.44 (1.31)</td>
<td>56.00 (11.10)</td>
<td>23.30</td>
<td>34.1</td>
</tr>
</tbody>
</table>

*For continuous variables, the mean (SD) is presented; for categorical data, the percentage is presented.
†Higher scores indicate worse medication adherence (range, 4–20).
‡Higher scores indicate more medication-related self-efficacy (range, 1–5).
§Higher scores indicate more diabetes-related social support (range, 2–10).
men tend to rely more on their parents and do not build self-care skills. If men are socialized to rely on others (eg, parent or spouse) for help in managing their health, they may be less able to cope with health problems in later life.

It is also important to note that depression may heighten the perceived threat of diabetes complications. Recent evidence suggests that women may be less likely than men to perceive some chronic diseases as threatening. A study of persons who had experienced acute coronary syndrome (ie, recent myocardial infarction or unstable angina) found that women rated their cardiac disease as being less severe than did men when clinical severity of the disease was controlled. Despite lower health status, more cardiac symptoms, and worse clinical status, women still perceived their disease severity as no worse than that of their male counterparts. This is also consistent with a study of older adults in which women were found to be more passive about their health than were men. Perhaps, this apparent lack of concern stems from women being accustomed to self-managing health problems throughout their lives, and thus the development of a new health problem in later life is less stressful.

**Limitations**

This study is limited in that it represents a cross-sectional examination of depression and medication-use behaviors, and the conclusions are also limited to diabetic patients who take oral medications. Furthermore, measurement of all variables was accomplished through self-report and thus may be imperfect for some constructs. Although medication adherence based on response to a 4-item scale may be an imperfect measure, questionnaire-based self-reports have been shown to be concordant with other measures of medication adherence. In addition, the demarcation between depression and "no depression" was based solely on the PHQ-8 score. Clinical assessment would allow for more valid categorization of patients. Differences in clinical variables such as where and how often the patient was seen might have influenced the results of this study. For example, if women are seen more often by a physician, they will have more opportunities for careful monitoring, which may lead to improved glycemic control and better management of their diabetes and depression. Women may be protected by the simple fact that they receive more medical care. Clearly, further exploration is needed to discern why patient self-care behaviors are altered between the sexes in the face of depression.

**CONCLUSIONS**

Gender moderated the relationship of depression and medication adherence. Medication adherence is significantly associated with depression in men but not in women. The factors contributing to this difference are unclear but may be related to differences in how men and women cope with the burden of self-managing a chronic disease. Clinicians should be cognizant of the potential effect of depression on self-care for diabetes, particularly in men with depressive symptoms.

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