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The Relationship between Depressive Symptoms and Medication Non-Adherence in Type 2 Diabetes: The Role of Social Support

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Abstract

Objective—Medication adherence promotion interventions are needed that target modifiable behavioral factors contributing to the link between depressive symptoms and poor adherence to diabetes self-care behaviors. In an effort to identify what factors contribute to this link, we examined the role of social support as a mediator of the relationship between depressive symptoms and medication non-adherence.

Method—We recruited 139 subjects with type 2 diabetes. Using an indirect effect test with bias corrected bootstrapping, we tested whether depressive symptoms had an indirect effect on medication non-adherence through a lack of social support.

Results—More depressive symptoms were associated with medication non-adherence (total effect =.06, $p < .001$), more depressive symptoms were associated with less social support (direct effect of the predictor on the mediator = −.96, $p = .02$), and less social support was associated with medication non-adherence (direct effect of the mediator on the outcome = −.01, $p < .01$). While the relationship between more depressive symptoms and medication non-adherence persisted with social support in the predicted pathway, the degree of this relationship was partially explained by a

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relationship between more depressive symptoms and less social support (indirect effect = .01, 95% BC bootstrapped CI of .0005 to .0325).

Conclusion—Providing social support to patients with diabetes who have symptoms of depression may ameliorate some of the deleterious effects of depressive symptoms on medication non-adherence, but social support alone is not enough.

INTRODUCTION

Adherence to hypoglycemic agents is important for glycemic control [1], decreases hospitalizations and, in turn, reduces healthcare costs [2]. However, medication adherence is often suboptimal and varies between oral agent-only (36%-87%) versus concomitant or insulin-only (54%-81%) regimens [2]. There are several barriers to medication adherence, including cost, forgetting, difficulty reading prescription drug labels and obtaining refills [3], and a diagnosis of depression [4].

Diabetes and co-morbid depression are associated with poor adherence to self-care behaviors, including medication adherence, as well as a reduction in quality of life, poor metabolic control, and an increased risk of mortality [5, 6]. Antidepressant agents effectively minimize depressive symptoms [7], but do not effectively improve diabetes self-care behaviors [8] or glycemic control [7], and adherence to oral hypoglycemic agents may actually get worse overtime [8]. Thus, non-pharmacological, medication adherence promotion interventions are needed that target modifiable behavioral factors contributing to the link between depressive symptoms or a clinical diagnosis of depression and poor adherence to hypoglycemic agents.

Medication adherence promotion interventions in other chronic disease contexts (e.g., HIV, hypertension) often target social support (i.e., help patients identify sources of social support networks and/or serve as a source of support for the patient) in an effort to overcome patient deficits in this domain [9, 10]. While there has been mixed evidence regarding a relationship between a lack of social support and medication non-adherence or vice versa (i.e., a relationship between social support and medication adherence), most studies sin this literature have found support for this relationship [10-13]. In contrast, depression is consistently associated with both a lack of social support [14, 15] and medication non-adherence [6, 16], but there is minimal evidence suggesting the relationship between depression and medication non-adherence persists after adjustment for social support [17]. Further, there is no evidence, to our knowledge, that a lack of social support *explains* the relationship between depression and medication-non-adherence in diabetes or in other chronic health conditions.

Thus, our study objective was to examine the role of social support, or the lack thereof, on the relationship between depressive symptoms and non-adherence to diabetes medications. We specifically tested the hypothesis that the relationship between depressive symptoms and medication non-adherence would be either fully or partially explained by a lack of social support after controlling for relevant covariates. Evidence in support of this hypothesis would imply that providing social support to patients with diabetes and depressive symptoms might counteract the negative effect of these symptoms on medication non-adherence.

RESEARCH DESIGN AND METHODS

Participants

We recruited consecutive patients with diagnosed type 2 diabetes mellitus (T2DM) and scheduled appointments at the internal medicine clinic of an academic medical center in the Southeastern United States. The institutional review board at our institution approved all procedures prior to study enrollment. Eligible participants were clinic patients, age 18 years or older with a diagnosis of T2DM in the medical record, and a clinic appointment between June-August 2008. We approached consecutive patients with a clinical diagnosis of T2DM over a 10 week period. The response rate was approximately 75%. We did not capture data on non-participants, so we are unable to describe differences between participants and non-participants. Patients were ineligible if they did not speak English, or if the research assistants determined (by interaction or chart documentation) they were too ill or cognitively impaired to participate. Patients were considered cognitively impaired if they could not provide coherent answers to the demographic questions. Patients were defined as too ill to participate if they had severe medical or psychiatric illness that made it impossible to complete the study assessments in one sitting, if the patient requested to terminate the interview for medical reasons, or if the research assistant perceived that the patient was too sick to participate.

Data and procedure

Research assistants reviewed the electronic clinic roster daily to identify eligible patients. Eligible patients were approached in the clinic waiting room, and were provided with a description of the study. Those interested and eligible were consented. Participants completed the assessment in a private area before or after their scheduled clinic appointments, depending on clinic flow.

Data collected included self-reported age, gender, race/ethnicity, education, income, health insurance status, and valid and reliable measures of depressive symptoms, social support, and medication non-adherence. Hemoglobin A1C values were extracted from participants' electronic medical record.

Depressive symptoms—Depressive symptoms were assessed with the Patient Health Questionnaire (PHQ-9) [18]. The PHQ-9 has demonstrated usefulness as a screening tool for depression with acceptable reliability, validity, sensitivity, and specificity [19]. The PHQ-9 is a 9-item self-report questionnaire corresponding to the nine DSM-IV signs and symptoms of major depression [18]. Participants are asked to rate how they felt in the previous 2 weeks. Each question is scored 0 to 3 (0 = not at all, 1 = several days, 2 = more than half the days and 3 = nearly every day) and summed to produce a composite score ranging from 0-27, with higher scores representing more depressive symptomology. Depressive symptoms was treated as a continuous variable, but was also categorized according to established guidelines as no depressive symptoms (PHQ-9 score <5), mild depressive symptoms (PHQ-9 score 5-9) and major depressive symptoms (PHQ-9 score ≥10) [18].

Social support—Social support was assessed with the 19-item Medical Outcomes Study (MOS) Social Support Survey [20]. The MOS is a valid and reliable measure of social support that has demonstrated test-retest reliability, and internal consistency reliabilities greater 0.91 [20]. The MOS measures perceived general functional support in multiple domains, including emotional, informational, tangible, positive social interaction, and affectionate support. Emotional support contains 4 items: measuring the expression of positive affect, empathetic understanding, and encouragement feeling expressions. Information support contains 4 items measuring the provisions of advice, information,

guidance or feedback. Tangible support contains 4 items measuring the offering of material aid or behavioral assistance. Positive social interaction contains 4 items measuring the availability of other persons to do fun things with you. Affectionate support contains 3 items measuring the expressions of love and affection. For each item, participants are asked to indicate how often each type of support is available to them if they needed it. Response options are in Likert format, ranging from 1 = none of the time to 5= all of the time. The scores are summed, rescaled on a 100-pont scale, and then averaged to determine a total score for social support. Higher scores on the MOS Social Support Survey indicate a greater perception of social support.

Medication non-adherence—Medication non-adherence was assessed with the 4-item Morisky adherence scale; a commonly used self-report tool that has good reliability and validity [21, 22]. The theory underlying this measure is that medication non-adherence occurs because of forgetting, carelessness, stopping a drug when feeling better, or starting a drug when feeling worse. Each item corresponds to one of these domains and responses are in a “yes” or “no” format. A positive response to any question indicates a problem with adherence. Thus, items are summed to produce scores ranging from 0-4, with higher scores indicating more medication non-adherence.

Data analyses

Analyses were performed using SPSS 19.0. First, we tested medication adherence group differences (i.e., adherent versus non-adherent) by demographic characteristics, self-reported health status, depressive symptoms, and social support using chi-square tests for categorical variables and independent sample’s t-tests for continuous variables.

At least a dozen methods for testing hypotheses about mediation have been proposed [23, 24].Of these approaches, bootstrapping [23, 25] is the currently recommended approach because it does not require a significant effect of the predictor on the outcome for mediation to occur; it has more power, maintains reasonable control over the Type 1 error rate; and, for multiple meditator models or when adjusting for covariates, it provides the most powerful and reasonable methods of obtaining confidence limits for all indirect effects (i.e., mediators) – in particular, bias corrected (BC) bootstrapping [26]. Thus, we conducted an indirect effect test with BC bootstrapped (5000 cases) estimation to examine whether depressive symptoms have an indirect effect on medication non-adherence through a lack of social support after adjustment for relevant covariates (i.e., age, gender, race/ethnicity, education, income, and insurance status).

RESULTS

A total of 139 participants completed all measures noted above. Mean (SD) age was 62.7 (11.9) years. The majority were female (71.9%), African American (71.4%), not employed (78.3%), and had a high school education or greater (65.9%), an annual income >$15K (64.2%), and had health insurance (96.4%); 61.9% were categorized as having no depressive symptoms, 23.8% as having mild depressive symptoms, and 14.3% as having major depressive symptoms. Sample characteristics by medication adherence groups (i.e., adherent versus non-adherent) are presented in Table 1.

Table 2 presents the indirect effect of depressive symptoms (as a continuous variable) on medication non-adherence (as a continuous variable) via social support (as a continuous variable) adjusted for patient age, gender, race/ethnicity, education, income, and insurance status. The BC bootstrap results indicated that more depressive symptoms were associated with medication non-adherence (total effect =.06, $p < .001$), more depressive symptoms were associated with less social support (direct effect of the predictor on the mediator = −.

96, $p = .02$), and less social support was associated with medication non-adherence (direct effect of the mediator on the outcome = −.01, $p < .01$). The relationship between more depressive symptoms and medication non-adherence persisted with social support in the predicted pathway (direct effect of depressive symptoms on medication non-adherence =.05, $p < .01$). However, the degree of this relationship was partially explained by depressive symptoms being associated with less social support (indirect effect = .01, 95% BC bootstrapped CI of .0005 to .0325).

CONCLUSION

Our findings suggest more depressive symptoms have an indirect effect on medication non-adherence through a lack of social support (i.e., part of the direct effect of more depressive symptoms on medication non-adherence is due to a relationship between having more depressive symptoms and, in turn, less social support), but social support does *explain* depression's direct effect on medication non-adherence. Hence, providing social support to patients with diabetes and co-morbid depression will *help* ameliorate some of the deleterious effects of depressive symptoms on medication non-adherence, but social support alone is not enough. This finding is a critical step towards both developing a comprehensive framework to inform diabetes medication adherence promotion efforts [32], particularly for individuals at highest risk for medication non-adherence (i.e., persons with diabetes and co-morbid depression).

We previously reported that, among adults with diabetes, depressive symptoms were associated with less frequent performance of recommended self-care behaviors (including physical activity, appropriate dietary behavior, and appropriate self-monitoring of blood glucose behavior), and this was largely due to depressive symptoms being associated with patients' having less social motivation and specifically less social support [33]. In the current study, we found a relationship between depressive symptoms and medication non-adherence that was partially due to depressive symptoms being associated with a lack of social support. While more evidence is needed to support these relationships and account for other behavioral factors in the predicted pathway between depressive symptoms and medication non-adherence, results from our current and former analyses suggest that interventions to optimize diabetes care among adults with diabetes and depressive symptoms may need to address patients' lack of social motivation by helping them identify sources of social support and/or serving as a source of social support (e.g., providing support resources for diabetes management [34], or offering peer-based interventions [35]).

There are study limitations to acknowledge. The findings are based on a small sample of indigent patients who completed a cross-sectional survey and provided self-reported medication non-adherence. As a result, we were unable to perform subgroup analysis (i.e., by gender, race/ethnicity, or health literacy status) to identify moderators of the relationship between depressive symptoms, social support, and medication non-adherence; there may be limited generalizability; and causality cannot be assumed. We also used the PHQ-9 to quantify depressive symptoms, and this instrument has been associated with an overestimation of the prevalence of major depression among samples with diabetes and other comorbidities that produce somatic symptoms similar to depression. However, the 14.3% rate of major depression in this sample is fairly comparable to depression rates reported in other diabetes studies [39]. Finally, although patients may under-report medication non-adherence, recent studies suggest self-report measures are viable and accurate measures of this behavior [40].

A multi-faceted approach to depression management in adults with diabetes and comorbid depression is particularly important [41], given findings from multiple studies showing that

depression treatment improves depressive symptomatology, but has a minimal effect, if any, on diabetes self-care behaviors and glycemic control [36-38, 41]. While intervention efforts that successfully enhance patients' social support might partially ameliorate the relationship between depressive symptoms and medication non-adherence, more research is needed to identify a comprehensive set of behavioral factors to target that would completely ameliorate the negative effects of depressive symptomatology on medication non-adherence. Such research should include multiple measures of adherence (e.g., refill adherence, electronic monitoring assessments, and self-reports), larger, more socioeconomically diverse samples, and investigate whether depressive symptoms are associated with medication non-adherence through other modifiable determinants of behavioral performance (e.g., medication adherence-related knowledge, beliefs, attitudes, or self-efficacy).

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Table 1

Participant characteristics by medication adherence versus non-adherence.

	Medication Adherence	
	Adherent	**Non-adherent**
Characteristics	**Mean ± SD, or %**	**Mean ± SD, or %**
N=139 (n)	60	79
Mean Age (Years)	64.5 ± 12.1	61.3 ± 11.6
Age Categories		
18-49 years	15.0	14.1
50-64 years	26.7	43.6
65+ years	58.3	42.3
Females	67.8	75.9
Race/Ethnicity		
Non-Hispanic White	29.1	28.2
Non-Hispanic Black	70.9	71.8
Mean Education (Years)	12.4 ± 6.9	12.4 ± 3.5
Education Categories		
<High school graduate	43.9	27.0
High school graduate	28.1	37.8
>High school graduate	28.1	35.1
Employed	21.7	21.8
Annual Household Income		
<$10,000	43.9	26.7
<$15,000	28.1	38.7
$15,000+	29.1	34.7
Insured	98.3	94.9
Health Status		
Better than last year	20.0	19.2
Worse than last year	18.3	32.1
Same as last year	61.7	48.7
Depressive Symptoms (PHQ-9, $p < .01$)	3.2 ± 3.5	5.4 ± 5.4
Depression Categories ($p < .05$)		
No depression	72.7	53.5
Minor depression	21.8	25.4
Major depression	5.5	21.1
Social Support (MOS, $p < .05$)	87.9 ± 16.0	81.4 ± 22.0

Note. SD = standard deviation; PHQ-9 = Patient Health Questionnaire; MOS = Medical Outcomes Study Social Support Survey. Chi-square test for categorical variables and independent sample's t-tests for continuous variables.

Table 2

Total, direct, and indirect effects of depressive symptoms on medication non-adherence.

	Social Support	Medication Non-Adherence
Total effect		
Depressive Symptoms	---	.06***
Direct effects		
Depressive Symptoms	−.96*	.05**
Social Support	---	−.01*
Indirect effect		
Social Support	---	.01‡
Partial effect of covariates		
Age	---	−.06
Gender	---	.26
Race/ethnicity	---	.23
Education	---	.23
Income	---	−.02
Insurance Status	---	−.10

Note. Total, direct, and indirect effects are adjusted for age, gender, race/ethnicity, education, income, and insurance status.

* $p < 0.05$,

** $p < 0.01$,

*** $p < 0.001$,

‡ statistically significant (i.e., the 95% bias-corrected bootstrapped Confidence Interval is .0005 to .0325).