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Relationship Between Health Literacy and Unintentional and Intentional Medication Nonadherence in Medically Underserved Patients with Type 2 Diabetes

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Structured Abstract

Purpose—The purpose of this study was to investigate the relationship between health literacy and overall medication nonadherence, unintentional nonadherence, and intentional nonadherence. Limited health literacy may be associated with worse diabetes outcomes, but the literature shows mixed results and mechanisms remain unclear. Medication adherence is associated with diabetes outcomes and may be a mediating factor. Distinguishing between unintentional and intentional nonadherence may elucidate the relationship between health literacy and nonadherence in patients with type 2 diabetes.

Methods—Cross-sectional study of 208 patients with type 2 diabetes recruited from a primary care clinic in St. Louis, MO. Information was obtained from written questionnaire and patient medical records. Bivariate and multivariable regression were used to examine predictors of medication nonadherence.

Results—The majority of patients in the study were low-income, publicly insured, and African American, with limited health literacy and a high school/GED education or less. In multivariable models, limited health literacy was significantly associated with increased unintentional nonadherence, but not intentional nonadherence.

Conclusions—Results suggest differences in factors affecting intentional and unintentional nonadherence. The findings also suggest interventions are needed to decrease unintentional nonadherence among patients with type 2 diabetes and limited health literacy. Efforts to address

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unintentional medication nonadherence among patients with type 2 diabetes with limited health literacy may improve patient health.

Diabetes currently affects over 26 million US adults and 285 million adults worldwide.¹ Currently, patients with diabetes often access and utilize health care, but health outcomes such as glycemic control, obesity, and self-reported health status remain poor.² Health literacy, or the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions, may affect outcomes in diabetes. Limited health literacy has been associated with worse glycemic control and complications in patients with type 2 diabetes.^{3,4} Health literacy has become a priority for quality improvement in patient care.^{5–7} An estimated 36% of the US population has limited health literacy, and almost half of the US population struggles with understanding and using health information.^{4,8} Limited health literacy is associated with poorer patient-physician communication, health related skills, and health outcomes.^{5–7,9} Health literacy may also affect outcomes in type 2 diabetes. However, results in literature have been mixed, and factors that may mediate this pathway have not yet been identified.^{3,10–12}

One potential mediating mechanism may be diabetes medication adherence, which has been shown to improve patient outcomes in diabetes.^{13–15} Poor diabetes medication adherence has been associated with reduced glycemic control, higher blood pressure, and higher cholesterol.^{13,14} Additionally, poor diabetes medication adherence puts patients at increased risk for all-cause hospitalization and all-cause mortality.^{14,15} However, the relationship between health literacy and diabetes medication adherence has not yet been established.¹⁶ In patients with type 2 diabetes, limited health literacy has been linked to decreased primary adherence, or adherence to newly-prescribed medications.¹⁷ However, research on the relationship between health literacy and secondary diabetes medication adherence, or adherence to ongoing medications, yielded mixed results.¹⁷

A potential reason behind the inconsistent results in the literature regarding the relationship between health literacy and medication adherence is that studies may not distinguish between unintentional and intentional nonadherence. Unintentional nonadherence includes having trouble remembering or forgetting to take medication, while intentional nonadherence reflects a decision, such as stopping medication when feeling better or worse.¹⁸ Prior literature has shown that increased concern about adverse effects of medications, decreased cognitive ability in recognition or planning, and higher patient-physician discordance on beliefs about patient well-being may lead to increased unintentional nonadherence in other disease contexts.^{19,20} Those with limited health literacy may have poorer patient-physician communication, leading to miscommunication regarding adverse effects, medication regimen planning, or patient well-being.⁶ We hypothesized that this could lead to increased unintentional medication nonadherence in patients with limited health literacy. A previous study showed that limited health literacy is not related to overall medication adherence, but is related to increased likelihood of forgetting to take medications in underserved patients with type 2 diabetes.²¹ However, this study did not distinguish between unintentional and intentional nonadherence. Another study in an elderly patient population showed that patients with limited health literacy were more likely to be

unintentionally nonadherent to medications, and less likely to be intentionally nonadherent.¹⁸ However, this study was not conducted specifically in a patient population with type 2 diabetes. Thus, to our knowledge, prior studies have not systematically examined how health literacy might differently relate to unintentional and intentional medication nonadherence in patients with type 2 diabetes.

The purpose of this study is to investigate the relationship between health literacy and unintentional and intentional diabetes medication nonadherence in a diverse, medically underserved patient population. This study therefore lays the groundwork for whether and the ways in which focused educational interventions might mitigate the effects of limited health literacy on diabetes medication nonadherence, and potentially improve outcomes in patients with type 2 diabetes.

Methods

Setting and Study Participants

From July 2013 to April 2014, research assistants attempted to enroll 4243 visitors in the waiting room of Barnes-Jewish Center for Outpatient Health primary care clinic in St. Louis, MO. Patients who were 18 years of age or older and spoke English were eligible. As shown in Figure 1, patients were ineligible (n=1111, 26%) because they were not a patient at the clinic (n=492), unable to speak English fluently (n=122), or had already taken the survey (n=374). Common reasons for refusal to participate in the study (n=1752, 41%) included lack of interest (n=543), lack of time (n=93), and not feeling well (n=57); most people did not offer a reason for refusal. Those that refused were slightly less likely to be African-American in comparison to those included in our study (73% vs. 74%), and less likely to be female in comparison to those included in our study (60% vs. 71%).

Written consent was obtained from patients before enrollment. Patients completed a written questionnaire that collected demographic information, self-reported health literacy and self-reported medication adherence (n=1010). The questionnaire was verbally administered for 27 patients upon their request in a designated room in the clinic. Data were also collected from patient medical records regarding insurance status, medication regimen, and depressive symptoms for patients who consented to release private health information for research purposes. The majority of patients who completed the survey consented to release their private health information (n=767, 75.9%). Survey participants received a small incentive. The protocol was approved by the Institutional Review Board at Washington University in St. Louis.

Of the 1010 patients that completed the survey, 284 had a diagnosis of type 2 diabetes and were prescribed diabetes medications based on their medical records; 223 of these patients completed both the health literacy and medication nonadherence measures on the survey. Of these patients, 15 self-identified as other race/ethnicity and were excluded from the analysis due to small sample size. 208 patients that self-identified as non-Hispanic White or African American were included in the data analysis.

Measures

Health literacy was assessed using the Brief Health Literacy Screen (BHLS) which consists of 3 Single Item Screeners (SILS), single items that assess self-reported health literacy.^{22,23} The 3 SILS were questions regarding patients' difficulty learning about their medical condition, confidence filling out medical forms, and difficulty reading hospital materials. Each SILS was scored on a 4 point scale, with 0 points meaning no difficulty and 4 points meaning most difficulty. For example, "How confident are you filling out medical forms by yourself" was answered on a scale from "not at all confident" (4 points) to "extremely confident" (0 points). The three SILS scores were added together to create the 12-point BHLS index. BHLS scores from 0–2 were categorized as adequate health literacy, and BHLS scores from 3–12 were categorized as limited health literacy. These cutoffs were established in prior work as values that were sensitive and specific for the patient population.²⁴

Medication nonadherence was assessed in a questionnaire format using the Morisky Medication Adherence Scale (MMAS-4), a validated 4-item instrument.^{25–27} A score of 0 was the lowest possible nonadherence score and a score of 4 was the highest possible nonadherence score.

Each of the subscales of the MMAS-4, unintentional and intentional nonadherence, consists of two items from the Morisky Medication Adherence Scale and were coded as dichotomous (yes/no) variables.²⁸

Covariates included factors that have previously been found to have an effect on medication adherence, including age, gender, race, insurance, diagnosis of depression, and medication regimen complexity.^{29–34} To measure depressive symptoms, diagnosis of depression or major depressive disorder was extracted from medical records. To assess complexity of medication regimen, information was abstracted from medical records to identify the dosage form, dosage frequency, and special instructions on the bottle. This information was then used to calculate the Medication Regimen Complexity Index (MRCI), a previously validated measurement of medication regimen complexity.³⁵ More complex dosage forms, increased dosage frequency, and increased additional instructions on the prescription label increase the score for each medication. The final MRCI score is the sum of the scores for all of the patient's current medications.

Statistical Analysis

Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC). Health literacy, demographics, and other covariates were analyzed against medication nonadherence using bivariate regressions. Covariates tested for entry into the model were factors that have been found to be related to medication adherence in prior literature. These covariates included age, gender, race, insurance, medication regimen complexity, and depression. Variables with bivariate relationships $p < 0.20$ were then included in the multivariable model. For bivariate and multivariable analysis, linear regressions were performed for overall medication nonadherence, and logistic regressions were performed for unintentional and intentional nonadherence. In the models, those of other races than

Caucasian or African American were excluded due to small sample size (n=15). Statistical significance was assessed as $p < 0.05$. Participants with missing data were excluded from each model.

Results

Characteristics of study participants are shown in Table 1. Of the 208 patients, 55 (26%) were white and 153 (74%) were black. The mean age of patients was 53.0 years (SD = 10.9). The majority (n=145, 78%) had an income less than \$20,000. About 36% (n=73) of patients had a diagnosis of depression. With respect to educational attainment, 39 (19%) had less than a high school education, 75 (37%) had a high school degree or GED, 62 (31%) had completed some college, and 27 (13%) had completed a college or graduate degree. The majority (64%; n=132) had limited health literacy based on the BHLS.

Bivariate analyses between health literacy or other possible correlates and the outcomes of overall medication nonadherence, unintentional nonadherence, and intentional nonadherence are shown in Table 2. In bivariate analysis, limited health literacy, the primary predictor variable, was associated with increased overall nonadherence ($\beta = 0.39$, SE=0.19, $p = 0.037$). Other covariates that were significant included increased age, which was associated with decreased overall medication nonadherence ($\beta = -0.03$, SE=0.01, $p = 0.002$). Older age was also associated with increased unintentional nonadherence (OR=1.03, 95% CI: [1.01, 1.06], $p = 0.018$). Patients diagnosed with depression had increased unintentional nonadherence (OR=1.81, 95% CI: [1.00, 3.26], $p = 0.049$). Patients who had an income less than \$20,000 were more likely to be intentionally nonadherent to their medications (OR=2.29, 95% CI: [1.07, 4.91], $p = 0.033$).

Multivariable analyses of medication nonadherence, unintentional nonadherence and intentional nonadherence are shown in Table 3. In multivariable analysis of overall medication nonadherence, the primary predictor of health literacy was not significant, but age was a significant covariate. Older patients were less likely to be nonadherent ($\beta = -0.02$, SE=0.01, $p = 0.027$). Patients with limited health literacy were more likely to be unintentionally nonadherent (OR=1.87, 95% CI: [1.01, 3.49], $p = 0.048$). In this model, older age was also a significant covariate; older age predicted lower unintentional nonadherence in the multivariable model (OR=0.97, 95% CI: [0.95, 1.00], $p = 0.038$). In the model predicting intentional nonadherence, health literacy was not a significant predictor, but income was a significant covariate. Patients with an income less than \$20,000 were more likely to be intentionally nonadherent than those with an income more than \$20,000 (OR=2.32, 95% CI: [1.03, 5.21], $p = 0.042$).

Among other tested covariates, gender, race, educational attainment, insurance status, depression, and medication regimen complexity were not significantly associated with overall medication nonadherence, unintentional nonadherence, or intentional nonadherence.

Conclusions/Discussion

Our study examined the relationship of health literacy with unintentional and intentional medication nonadherence in a diverse sample of patients with type 2 diabetes. Different

factors were found to influence unintentional vs. intentional nonadherence. Limited health literacy was associated with increased unintentional nonadherence, such as forgetting or having trouble remembering to take medications. However, health literacy was not found to be related to intentional nonadherence, which includes stopping medications when feeling better or worse. These findings indicate that the distinction between unintentional and intentional medication nonadherence may play a role in the mixed results found in previous literature regarding the relationship between health literacy and medication adherence.

Evidence for a relationship between health literacy and medication adherence in patients with type 2 diabetes has been mixed.¹⁷ Bains and Egede (2011) did not find a relationship between health literacy and medication adherence in patients with type 2 diabetes.¹⁰ However, Osborn et al. (2011) found that health literacy explained racial disparities in adherence in patients with type 2 diabetes.³⁶ These mixed results may be clarified by differentiating between different types of medication adherence. Thurston et al. (2015) found that limited health literacy was not associated with overall medication nonadherence, but was associated with increased likelihood of forgetting to take medications in underserved patients with type 2 diabetes.²¹ Forgetting to take medications is encompassed in unintentional nonadherence, and our study similarly found that limited health literacy was associated with increased unintentional nonadherence. Lindquist et al. (2012) found that health literacy was associated with increased unintentional medication nonadherence and decreased intentional nonadherence in an elderly patient population.¹⁸ Our study found a similar association with unintentional medication nonadherence, but not with intentional nonadherence in patients with type 2 diabetes. The differences between the results of prior studies may stem from differences in the study populations and different variables included in the statistical models.

Additionally, our study adds to the understanding of how other variables are related to medication nonadherence in this population. Our results are consistent with findings from other studies that younger patients with type 2 diabetes are more likely to be nonadherent to medications.^{37,38} Our study also found a relationship between income and intentional nonadherence. Prior studies have not found a relationship between income and medication adherence in patients with type 2 diabetes. However, socioeconomic status has been linked to medication adherence in other patient populations, including the elderly and patients with HIV or cardiovascular disease.^{29,30,39} Additionally, decreasing the co-pay of medications in a patient population with private insurance was shown to improve diabetes medication adherence, which suggests that cost plays a role in adherence.³² The relationship between income and medication adherence may thus be confounded by health insurance coverage. However, to examine this effect, our model included insurance status, which was not found to be related to medication nonadherence. The relationship of income with intentional medication nonadherence observed in our study suggests that low-income patients may be less likely to spend money on medications when feeling better or worse.

There were several limitations to our study. First, our study is cross-sectional and thus cannot lead to conclusions about causal relationships. Secondly, the validated adherence questionnaire used here did not account for how often patients missed medication, or how much medication was missed overall. The adherence questionnaire also did not assess

diabetes medication specifically, but rather overall adherence to medications, which may have included other medications if the patient had comorbidities. Although we did not directly adjust for comorbidities, the MRCI for each patient includes the total number of medications and dosages which would be increased in a patient with multiple comorbidities. We were unable to include year of diabetes diagnosis or previous glycemic control as covariates in the study. Additionally, health literacy and medication adherence were measured by self-report. However, we used validated self-report measures to assess both constructs.^{22–27} Furthermore, the sample was drawn from the primary care clinic of a large, urban hospital serving a medically underserved patient population and findings therefore may not generalize to other populations. Our patient population had a mean age of 53 and was predominantly low-income and African American with limited health literacy, and thus findings may not be generalizable to other patient populations. Also, the objective measure used for depression obtained from the EMR only assessed a diagnosis of depression, and does not indicate the degree to which the depression is being treated or controlled.

Overall, our results show that health literacy is related to unintentional medication nonadherence, potentially affecting a large number of adults with limited health literacy. Health literacy may be associated with increased unintentional nonadherence due to the importance of health literacy in patient-physician communication. These findings therefore suggest that health literacy must be addressed between patients and providers as a way to improve medication adherence and, potentially, patient outcomes. Cost burdens for diabetes patients must also be considered, particularly as patients with low income may be more likely to have limited health literacy.⁸ In addition, distinguishing between different types of nonadherence in studies when investigating predictors of diabetes medication nonadherence is imperative. A further area for investigation may be patient beliefs and emotional well-being in relationship to different types of diabetes medication nonadherence among patients with limited health literacy, as these variables are associated with diabetes medication adherence in prior studies.^{34,40,41}

Implications for Diabetes Education

These findings suggest that it will be critical to develop and implement educational interventions that decrease medication nonadherence and are suitable for patients with limited health literacy. Diabetes education programs that focus on self-care and risk factor control have been shown to improve self-care and A1C in patients with limited health literacy.¹⁷ Computerized diabetes education programs have also been shown to improve diabetes knowledge among patients with limited health literacy.¹⁷ Because these types of educational interventions have shown promise in patients with limited health literacy, they can be further evaluated for their effect on medication nonadherence, in particular, unintentional medication nonadherence. Pharmacist involvement in patient education regarding medications and lifestyle management has been effective in increasing adherence and A1C, but should be further studied in patients with limited health literacy.⁴² Additionally, our findings suggest that patient education that helps those with limited health literacy remember to take their medications may be important in improving medication adherence overall. Interventions such as bi-weekly automated telephone assessment, self-care education calls with nurse follow-up, or SMS reminders with Real Time Medication

Monitoring, may be useful in reducing unintentional nonadherence in patients with type 2 diabetes and should be further evaluated in patients with limited health literacy.^{42,43}

Beyond health literacy, assessing other predictors of medication nonadherence in the clinic may be useful in tailoring patient education towards specific reasons behind medication nonadherence, and in developing interventions to support adherence to medications in patients with diabetes. Poor medication adherence has been associated with reduced glycemic control, increased macrovascular complications, and increased all-cause hospitalization and mortality in patients with type 2 diabetes.^{13–15} Thus, developing interventions suitable for those with all levels of health literacy will be important in improving health outcomes in patients with diabetes.

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Figure 1. Flowchart of Study Recruitment from Primary Care Clinic in St. Louis, MO from July 2013 to April 2014.

Table 1

Characteristics of Study Participants

Characteristic	N (%)
Health Literacy (BHLS)^a (n=208)	
Adequate health literacy	76 (36.5)
Limited health literacy	132 (63.5)
Unintentional Nonadherence^b (n=208)	115 (55.3)
Intentional Nonadherence^b (n=208)	83 (39.9)
Gender (n=206)	
Female	146 (70.9)
Male	60 (29.1)
Race (n=208)	
Caucasian	55 (26.4)
African-American	153 (73.6)
Income (n=187)	
<\$20,000	145 (77.5)
\$20,000	42 (22.5)
Educational Attainment (n=203)	
Less than high school	39 (19.2)
High school/GED	75 (37.0)
Some college	62 (30.5)
College degree or more	27 (13.3)
Insurance (n=206)	
Private insurance	22 (10.7)
Public insurance	143 (69.4)
Uninsured	41 (19.9)
Diagnosis of depression (n=203)	
No depression	130 (64.0)
Depression	73 (36.0)
Characteristic	Mean (SD)
Overall Medication Nonadherence (MMAS-4)^b (n=208)	1.4 (1.3)
Age (n=200)	53.0 (10.9)
MRCI^c (n=195)	32.1 (15.4)

N = number of study participants, % = percentage of study participants, SD = standard deviation, BHLS = Brief Health Literacy Screen, MMAS-4 = Morisky Medication Adherence Scale-4, MRCI = Medication Regimen Complexity Index.

^aBrief Health Literacy Screen, validated measure of health literacy.^{22–23}

^bMorisky Medication Adherence Scale-4, validated measure of medication adherence. Use of the ©MMAS-4 is protected by US copyright laws. Permission for use is required. A Licensure agreement is available from: Donald E. Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA School of Public Health, 650 Charles E. Young Drive South, Los Angeles, CA 90095-1772.^{24–26}

^cMedication Regimen Complexity Index, validated measure of medication regimen complexity.³⁴

Table 2

Bivariate Analyses of Health Literacy and Possible Covariates with Overall Nonadherence, Unintentional Nonadherence, and Intentional Nonadherence

	Overall Nonadherence ^a Parameter Estimate (SE)	Unintentional Nonadherence ^a Odds Ratio (95% CI)	Intentional Nonadherence ^a Odds Ratio (95% CI)
Health Literacy (BHLS)^b (n=208)			
Adequate health literacy	Reference	Reference	Reference
Limited health literacy	0.39 (0.19) ^c	1.66 (0.94, 2.93)	1.60 (0.89, 2.88)
Age (n=200)	-0.03 (0.01) ^c	1.03 (1.01, 1.06) ^c	1.02 (0.99, 1.05)
Gender (n=206)			
Male	Reference	Reference	Reference
Female	0.14 (0.20)	1.32 (0.72, 2.41)	1.06 (0.57, 1.97)
Race (n=208)			
Caucasian	Reference	Reference	Reference
African-American	-0.19 (0.20)	0.96 (0.52, 1.78)	0.73 (0.39, 1.40)
Income (n=187)			
\$20,000	Reference	Reference	Reference
<\$20,000	0.19 (0.23)	0.92 (0.46, 1.85)	2.29 (1.07, 4.91) ^c
Educational Attainment (n=203)			
Less than high school	0.61 (0.32)	0.87 (0.32, 2.34)	0.48 (0.17, 1.31)
High school diploma/GED	0.11 (0.29)	1.22 (0.50, 2.95)	0.89 (0.35, 2.25)
Some college	0.25 (0.30)	0.96 (0.39, 2.40)	0.79 (0.31, 2.05)
College degree or more	Reference	Reference	Reference
Insurance (n=206)			
Private insurance	Reference	Reference	Reference
Public insurance	-0.06 (0.35)	1.68 (0.57, 4.98)	0.54 (0.18, 1.60)
Uninsured	-0.14 (0.30)	1.84 (0.71, 4.78)	0.75 (0.29, 1.95)
Diagnosis of depression (n=203)			
No depression	Reference	Reference	Reference
Depression	0.35 (0.19)	1.81 (1.00, 3.26) ^c	1.14 (0.64, 2.05)
MRCI^d (n=195)	0.00 (0.01)	0.99 (0.97, 1.01)	1.00 (0.98, 1.02)

SE = standard error, CI = confidence interval, BHLS = Brief Health Literacy Screen, MRCI = Medication Regimen Complexity Index.

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^bBrief Health Literacy Screen, validated measure of health literacy.²²⁻²³

^cp<0.05

^dMedication Regimen Complexity Index, validated measure of medication regimen complexity.³⁴

Table 3

Multivariate Models of the Relationship Between Health Literacy and Overall Nonadherence, Unintentional Nonadherence, and Intentional Nonadherence

	Overall Nonadherence ^a (n=174) Parameter Estimate (SE)	Unintentional Nonadherence ^a (n=193) Odds Ratio (95% CI)	Intentional Nonadherence ^a (n=182) Odds Ratio (95% CI)
Health Literacy (BHLS)^b			
Adequate health literacy	Reference	Reference	Reference
Limited health literacy	0.33 (0.22)	1.87 (1.01, 3.49) ^c	1.20 (0.61, 2.34)
Age	-0.02 (0.01) ^c	0.97 (0.95, 1.00) ^c	
Gender			
Male	Reference	Reference	
Female	0.01 (0.23)	1.39 (0.70, 2.76)	
Income			
\$20,000	Reference		Reference
<\$20,000	0.10 (0.24)		2.32 (1.03, 5.21) ^c
Educational Attainment			
Less than high school	0.44 (0.36)		2.28 (0.74, 7.02)
High school diploma/GED	0.03 (0.31)		1.11 (0.41, 3.02)
Some college	0.26 (0.31)		1.19 (0.43, 3.26)
College degree or more	Reference		Reference
Diagnosis of Depression			
No depression	Reference	Reference	
Depression	0.34 (0.22)	1.80 (0.92, 3.51)	

SE = standard error, CI = confidence interval, BHLS = Brief Health Literacy Screen.

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^bBrief Health Literacy Screen, validated measure of health literacy.^{22–23}

^cp<0.05