Cost-Related Nonadherence to Medications Among Patients With Diabetes and Chronic Pain

Factors beyond finances

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OBJECTIVE — In the face of financial constraints, diabetic patients may forgo prescribed medications, causing negative health effects. This study examined how cost and noncost factors are associated with patterns of cost-related nonadherence to medications (CRN).

RESEARCH DESIGN AND METHODS — This was a cross-sectional survey of patients using medications for both diabetes and chronic pain ($n = 245$). Patients reported their income, out-of-pocket medication costs, education level, depressive symptoms, and medication-related beliefs and whether they cut back because of cost on *1*) both diabetes and pain medications, *2*) diabetes medications only, *3*) pain medications only, or *4*) neither. Multinomial logistic regression was used to model patients' adjusted odds ratios (AORs) of falling into these four possible categories.

RESULTS — Of the patients, 9% cut back on medications for both conditions, 13% cut back on diabetes medications alone, and 9% cut back on pain medications alone. Income <20,000 USD (AOR = 5.7, $P = 0.008$) and monthly medication costs >50 USD (AOR = 3.9, $P = 0.02$) increased patients' odds of CRN for both conditions versus neither. Low-income patients also were more likely to selectively forgo pain medications (AOR = 9.1, $P = 0.001$) but not diabetes medications (AOR = 2.1, $P = 0.12$). More depressive symptoms (AOR = 1.6, $P = 0.006$) and negative medication-related beliefs (AOR = 1.7, $P = 0.02$) increased patients' odds of cutting back selectively on medications for diabetes but not pain.

CONCLUSIONS — Patients who forgo medications for both diabetes and chronic pain appear to be influenced primarily by economic pressures, whereas patients who cut back selectively on their diabetes treatments are influenced by their mood and medication beliefs. Our findings point toward more targeted strategies to assist diabetic patients who experience CRN.

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Prescription drug spending in 2007 was >750 USD per capita in the U.S., of which patients must pay a growing share through medication copayments (1,2). Nine of 10 older adults use prescription medications, and those with Medicare Part D take five prescriptions per month on average (3). Even among low-income patients, most take their medications despite copayments (4); however, one-fifth or more of all patients may cut back because of cost concerns (5,6). Cost-related nonadherence to medications (CRN) has been associated with increased rates of serious adverse events, emergency department visits, hospitalizations, and poorer health (7,8).

Empirical studies have implicated financial, attitudinal, mood, and provider influences in CRN, although their relative effects are not well understood (4,9). Most of the variance in patients' reports of CRN remains unexplained by financial measures (10). Although economic pressures drive these decisions, noncost factors appear to modify the effect of medication cost at a given level of ability to pay (11).

Most survey-based studies of CRN have used a single global question to ascertain adherence and, therefore, could not discern whether patients cut back uniformly across their medications or selectively (6,7,12–14). Studies using administrative data indicate that patients vary in their adherence across medications, but these studies could not explore fully the influences of factors such as patients' mood and medication-related beliefs (15,16).

Building on our theoretical model of factors that influence patients' elasticity of demand for prescription drugs (9), in the present study we explored further how cost and noncost factors influence patients' adherence to prescription medications for two chronic conditions: type 2 diabetes and chronic pain. We hypothesized that although some patients would cut back on medications for both conditions, others would cut back selectively, and sought to understand the factors associated with these behaviors.

These analyses are important for clinical care because most efforts to address CRN have targeted patients' ability to pay exclusively, for example, through government assistance (e.g., Medicare Part D), pharmaceutical industry programs, and prescribing of less expensive therapeutic alternatives (10). Physicians are now called upon to incorporate discussions of medication cost pressures into their routine patient interactions (17). Because insufficient time may be the greatest barrier to such provider-initiated discussions (17), it is essential that we distinguish patients for whom ability to pay, as opposed

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to other factors, constitutes the dominant challenge to adherence.

RESEARCH DESIGN AND METHODS

The study was conducted in Flint, Michigan, an economically distressed, mid-sized city, as part of a larger study of medication cost problems among low-income patients with diabetes. Patients were identified through general medicine clinics of a large safety-net health system (17% of participants), its affiliated diabetes education center (58%), and the local network of federally qualified health centers (25%). Patients were eligible for the study if they had type 2 diabetes, used antihyperglycemia medication, had not been hospitalized in the prior 3 years for a serious psychiatric illness, and received most of their diabetes care in one of the participating clinical sites. Between July 2005 and December 2007, 3,800 patients (92%) were identified from medical records using diagnostic codes and contacted by phone, and 322 (8%) were identified at outpatient visits. Of this pool of 4,122 patients with an attempted contact, 2,516 could not be reached, 450 refused, and 1,116 were screened. A total of 841 screened patients were determined to be eligible, and of these, 806 (96%) completed an informed consent form and data collection via detailed in-person interviews with trained surveyors. The current study is based on a subset of 245 patients who reported using medications for chronic pain (arthritis, migraines, back pain, or sciatica) and diabetes (oral antihyperglycemia drugs or insulin). The study was approved by institutional review boards at all institutions involved.

Data collection and variable creation

Cost-related underuse of medications. Patients' CRN was measured using three items similar to those used in prior studies (5,11): "In the past 12 months, have you ever taken less of your [insert either "insulin," "diabetes pills," or "medication for chronic pain"] than prescribed because of the cost?" (yes/no for each). Patients were considered to have CRN for diabetes if they reported underuse of either diabetes pills or insulin. Based on their responses, patients were categorized into four groups: *1*) CRN for both chronic pain and diabetes medications, *2*) CRN for diabetes medications only, *3*) CRN for chronic pain medications only, or *4*) CRN for neither medication type.

Medication-related beliefs and information. Patients' beliefs about prescription medications were measured using a composite score based on items from the Beliefs about Medications Questionnaire (18). A factor analysis was performed on the eight items from the original scale, which showed one independent factor with eigenvalue >1. A subscale using the questions in which the rotated factor loadings exceeded 0.4 for the factor was created. To increase subscale reliability, individual items were sequentially dropped until the α value was maximized (0.68). The statements included in the resultant scale were, "Doctors use too many prescription medications," "Prescription medications do more harm than good," "Doctors place too much trust in prescription medications," and "If doctors had more time with patients they would prescribe fewer prescription medications." Patients indicated their level of agreement with each statement using a 3-point Likert scale of "agree," "unsure," and "disagree." To improve interpretability in regression models, this scale was standardized. In addition to these general beliefs items, the BMQ includes subscales addressing perceived necessity and concerns regarding specific medication types; these were not used in the current study because of the complexity of addressing these domains simultaneously for the two medication types in the context of the other predictors of interest.

Patients' satisfaction with the information they received about their medications was measured using a modified version of the Satisfaction with Information about Medications Scale (19). This 16-item scale asked patients to report the extent ("enough" versus "not enough") to which they are satisfied with the information they had received "from [their] doctors and other people working in the place where [they] get medical care" on topics such as "how [their] medications work" and "how to use [their] medications." The summary measure had an α of 0.96. Because 43% of patients indicated the highest level of satisfaction with medical information, the scale was dichotomized as complete versus incomplete satisfaction with medication information.

Other variables. Patients reported their age, sex, race/ethnicity, years of formal education, household income from all sources, monthly out-of-pocket cost for prescription medications, insurance status, and depression symptoms. Before-tax employment income and income from all other sources were reported separately using ordinal categories, and the midpoints within each of the two ranges were used to estimate patients' total income. Out-of-pocket medication costs were reported using ordinal categories that were dichotomized near the median to create an indicator of monthly out-of-pocket costs ≤50 vs. >50 USD. Depressive symptoms were measured using the Patient Health Questionnaire (PHQ-9) (20). A1C was measured at the time of survey via fingerstick and a point-of-care analyzer.

Statistical analysis

We examined unadjusted differences across groups defined by patients' sociodemographic characteristics, medication-related beliefs, and levels of depressive symptoms in the distribution of patients across the four categories of CRN using χ^2 tests. We then constructed a multinomial logistic regression model in two stages with the four-level CRN measure as the dependent variable. First we limited the model to factors related to patients' ability to pay for medications: income, out-of-pocket costs, and patient education. The second model included these measures as well as measures of potentially mutable factors: satisfaction with medical information, depressive symptoms, and beliefs about prescription medications. Demographic variables were not included in the models because they have previously been found to have little influence on CRN (4), a finding consistent with our bivariate results (Table 1). A1C and pain severity were excluded from the models because they are as likely to be a consequence as a cause of CRN. A likelihood-ratio test comparing the two models favored the second ($\chi^2 = 27.24$, d.f. = 9, $P = 0.001$), results of which are reported. Differences in the influence of a given predictor (as measured by the adjusted odds ratio [AOR]) between logit functions within the model were examined using Wald tests. The variance inflation factor was calculated for the final regression model and did not show significant multicollinearity (mean variance inflation factor = 1.09, range 1.02–1.21). The multinomial logistic regression model was repeated after CRN was defined for diabetes as underuse of diabetes pills, without consideration of insulin. There were no significant changes in the results. We also explored alternative models controlling for patients' overall number of medications and number of medications

Table 1—*Patient characteristics and association with adherence category*

	CRN for both	CRN for diabetes	CRN for pain	No CRN	*P*
	9.0	13.1	8.6	69.4	NA
Age					
<55 years	13.1	12.3	9.8	64.8	0.11
≥55 years	4.9	13.8	7.3	74.0	
Sex					
Female	7.3	14.7	7.3	70.6	0.22
Male	13.2	8.8	11.8	66.2	
Race					
Nonwhite	10.3	15.8	7.5	66.4	0.27
White	6.2	9.4	10.4	74.0	
Education					
≤12th grade	9.6	11.1	6.7	72.6	0.36
>12th grade	7.5	15.9	11.2	65.4	
A1C					
<7%	5.3	8.0	9.8	76.7	0.002
≥7%	12.1	17.4	6.8	63.6	
Annual income (USD)					
≤20,000	13.1	14.6	12.4	59.8	0.001
>20,000	3.7	11.1	3.7	81.5	
Medication costs (USD)					
≤50/month	7.5	12.1	8.7	71.7	0.46
>50/month	12.9	15.7	8.6	62.9	
Medical information satisfaction					
Incomplete	6.2	16.6	11.7	65.5	0.01
Complete	13.0	8.0	4.0	75.0	
PHQ-9 depression score					
<15	9.3	11.1	8.8	70.8	0.07
≥15	4.4	30.4	8.7	56.5	
Negative medication beliefs					
<Median	13.5	6.7	7.7	72.1	0.02
≥Median	5.7	17.9	9.3	67.1	

Data are row percents. $n = 245$. χ^2 tests were used to calculate *P* values. Satisfaction with information about medications was defined as complete if patients reported that they had enough information in every topic area listed in the modified Satisfaction with Information about Medications Scale. The depression scale used was the PHQ-9; ≥15 on the scale corresponds to at least moderately severe depression. Prescription medication beliefs were reported using a subscale generated from the Beliefs about Medications Questionnaire.

for specific comorbidities (hypertension and hyperlipidemia) as potential confounders. These medication variables had no statistically significant independent effects on CRN for diabetes or pain treatments and little discernible impact on other associations illustrated by the multivariate model. Here we present the more parsimonious model without these covariates.

Multinomial logistic regression simultaneously estimates multiple binary logistic regression models for outcomes of a nominal variable using one base category. The group without any CRN was used as the referent group.

To illustrate the impact of one key patient characteristic (i.e., depressive symptoms) on CRN behavior, we calculated the predicted probability distribution for two hypothetical groups of patients with minimal depression (PHQ-9 = 2) and severe depression (PHQ-9 = 25), holding all other covariates at their mean values (20). Analyses were performed using Stata 10.0 (StataCorp, College Station, TX).

RESULTS

Sample characteristics and associations with CRN categories

Patients were, on average, aged 55 years and predominantly women (72%) and African American (60%) with reasonably good glycemic control (46% with A1C <7%). Most had out-of-pocket medication costs ≤50 USD per month (71%), household income <20,000 USD (56%), and at most a high school education (56%). Roughly 3 of 5 patients (59%) were less than completely satisfied with information they had received about their medications, and 1 of 10 (10%) had at least moderately severe depression (PHQ-9 ≥15).

Roughly equal numbers of patients reported CRN for both diabetes and pain (8.6%) and for pain only (9%) (Table 1). Patients who cut back selectively on their diabetes medications were the largest underuse group (13.1%). Most patients did not report CRN for either condition (69.4%).

The age, sex, race, and educational achievement of patients across the four categories of CRN were roughly similar. Patients with higher A1Cs were more likely to underuse their diabetes medications, either alone or in combination with their pain treatment ($P = 0.002$). Patients' income was significantly associated with their adherence behavior ($P = 0.001$). Compared with higher-income patients, lower-income patients were three times as likely to cut back on both medication types (13.1%) and selectively on chronic pain medications (12.4%) but only slightly more likely to cut back only on their diabetes medications (14.6%).

Patients who were not completely satisfied with the information they had received about their medications were more likely to cut back selectively on their diabetes medications (16.6 vs. 8%) and on their pain medications only (11.7 vs. 4%) because of cost compared with patients who were completely satisfied. Among less depressed patients, 9.3% reported CRN for both medication types, 11.1% for diabetes only, and 8.8% for pain medications only. In contrast, patients with at least moderately severe depression were half as likely to report CRN for both conditions (4.4%), and nearly three times as likely to report underuse for diabetes medications only (30.4%). Patients who had more negative beliefs about prescription drugs were less likely to cut back on both types of medications (5.7 vs. 13.5%) and more likely to cut back on diabetes medications only (17.9 vs. 6.7%).

Multinomial logistic regression model

In the logistic model (Table 2), lower-income patients were more likely to report CRN for both conditions (AOR = 5.7, $P = 0.008$) and for pain only (AOR = 9.1, $P = 0.001$) but not to cut back selectively on diabetes medications (OR = 2.1, $P = 0.12$). Higher costs were associated with higher odds that patients would re-

Table 2—*Multinomial logistic regression results*

	CRN for both	CRN for diabetes	CRN for pain
Income <20,000 USD	5.74 (1.58–20.88)*	2.11 (0.82–5.47)	9.06 (2.44–33.60)*
Monthly medication costs >50 USD	3.90 (1.29–11.78)*	1.86 (0.71–4.83)	2.11 (0.67–6.64)
>12th grade education	1.15 (0.41–3.27)	1.42 (0.61–3.32)	2.44 (0.89–6.74)
Dissatisfaction with medical information	0.59 (0.22–1.61)†	1.97 (0.79–4.89)	3.41 (1.04–11.13)*
PHQ-9 depression score	1.29 (0.84–2.01)	1.65 (1.15–2.36)*	0.81 (0.50–1.31)‡
Negative medication beliefs	0.85 (0.52–1.40)‡	1.67 (1.08–2.57)*	1.12 (0.69–1.85)

Data are AORs (95% CI). Base category is the group of patients without CRN for either diabetes or chronic pain. Dissatisfaction with medical information is an indicator for whether the patient was above the median on the modified Satisfaction with Information about Medications Scale. AORs for the PHQ-9 depression score represent the effect of a 5-point increase in the PHQ-9. For negative prescription beliefs, AORs represent the effect of a 1-SD increase in the subscale created from the Beliefs about Medications Questionnaire. *$P < 0.05$ for the AOR relative to the base group (no CRN). †$P < 0.05$ for the difference between the AOR and the AOR for "CRN for pain." ‡$P < 0.05$ for the difference between the AOR and the AOR for "CRN for diabetes."

port underusing both medication types (OR = 3.9, $P = 0.02$) but did not increase patients' likelihood of cutting back selectively on one or the other medication type.

Depressive symptoms, negative medication-related beliefs, and dissatisfaction with information about medications were not significantly associated with cutting back on both treatment types. However, the odds that patients would selectively cut back on their pain medications was greater among patients reporting dissatisfaction with information about medications (AOR = 3.4, $P = 0.04$). A 5-point increase on the PHQ-9 depression scale increased the odds that patients would cut back selectively on their diabetes medications by a factor of 1.65 ($P = 0.006$). Patients with more depressive symptoms were more likely to cut back selectively on their diabetes medications than on their pain medications only ($P = 0.01$). A 1-SD increase on the scale of negative medication beliefs increased patients' likelihood of cutting back selectively on their diabetes treatment relative to not cutting back at all (AOR = 1.7, $P = 0.02$). Patients with more negative medication beliefs were more likely to cut back on their diabetes medications only than to cut back on both medication types (P value of the Wald test = 0.031).

Figure 1 shows the predicted probability distribution of patients across CRN categories within groups of nondepressed and depressed patients. The overall proportion of patients with some CRN is higher among those with more severe depressive symptoms (54 vs. 21%, $P < 0.05$). This difference reflects a greater number of depressed patients forgoing their diabetes medications only (42 vs. 7%, $P < 0.05$) rather than cutting back on their pain medications only or across the board.

CONCLUSIONS — In this study, lower income and higher out-of-pocket medication costs significantly increased the odds that diabetic patients would report CRN for both diabetes and chronic pain; lower income also increased patients' likelihood of cutting back on chronic pain medications alone. In contrast, neither of these indicators of patients' financial pressure was significantly associated with selective underuse of diabetes medications. Rather, selective underuse of diabetes medications due to "cost" was associated with depression and negative beliefs about pharmacotherapy. Dissatisfaction with information about medications—but not depressive symptoms—increased the likelihood that a patient would report selectively foregoing his or her pain treatment.

This is one of the first studies to investigate patient factors affecting CRN for multiple chronic conditions simultaneously (15). Most previous studies have treated CRN as a global patient-level behavior (14,17) or have used administrative data (4,13), with limited ability to link patients' adherence choices with possible determinants such as their depressive symptoms or medication-related beliefs. However, the results here are consistent with prior studies also suggesting that patients value their various medications differently, thereby differentially affecting the elasticity of demand for specific medications (21).

The current study adds to the evidence (6,16,21) that patients selectively forgo medications because of cost and are influenced in those decisions by noncost factors, such as beliefs, satisfaction with medication-related information, and depressed mood. Those who forgo medica-

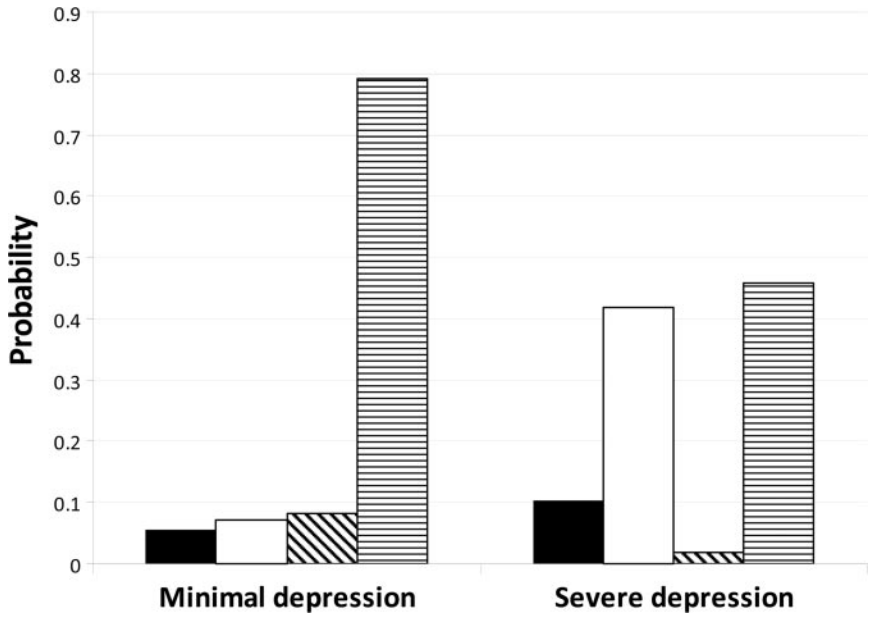

Figure 1—*Predicted probability of CRN among diabetic patients with chronic pain, with and without depressive symptoms. Predicted probabilities were generated using the multinomial logistic regression model shown in Table 2. For minimal depression, the PHQ-9 scale score was set at 2 and for severe depression was set at 25. All other covariates were held at their mean values. *□, diabetes; ▨, pain; ■, both; *▤, neither. *P < 0.05 for difference in probability between minimally and severely depressed patients.*

tions for both diabetes and chronic pain show the greatest sensitivity to factors related to ability to pay (e.g., income or out-of-pocket prescription costs).

Proposed measures to deal with financial pressures, such as prescribing less expensive medications and pharmaceutical company assistance programs, may be ineffective for patients whose predominant reasons for CRN are negative beliefs about medications or depressed mood. Physicians and other health care providers (e.g., pharmacists and care managers) should ask patients specifically about which of their medications they have difficulty paying for. For patients who report difficulty paying for only selected medications, providers need to further probe beliefs about prescription drugs, medication knowledge, medication-specific concerns, and mood. Clarifying the relative roles of these factors will help guide the best strategy for improving medication use and ultimately outcomes. Dissatisfaction with medication information is an important predictor of CRN for pain treatments, whereas negative medication beliefs are a predictor of CRN for diabetes therapies; these relationships underscore the important role of clinician-patient communication in CRN (22).

Our findings suggest that cost should be viewed as one of multiple potential causes for underuse, rather than a sole cause, because for some adherence problems, such as CRN for diabetes only, neither medication cost nor income was found to have significant effects. Indeed, a patient whose predominant reason for underuse of a medication is experiencing side effects but who also has concerns about the price might reasonably report CRN (9). Although CRN is a timely and important topic, further research is needed to clarify how best to isolate the effect of financial factors from that of other influences on adherence behavior.

We can only speculate as to the reasons for different patterns of medication underuse. Income may have only influenced selective CRN of pain but not of diabetes medications because patients may have felt that diabetes posed a greater threat to their long-term health, whereas pain medications provided "only" symptomatic benefit (6,16). Prior studies suggested that patients' cognitive and emotional representations of their illnesses may be among the most important independent predictors of their adherence (23). Unfortunately, these elements were only measured indirectly in the current study. In addition, patients may have opted to use cheaper, potentially suboptimal over-the-counter analgesics to treat their pain, whereas there were no similar nonprescription alternatives for their prescription diabetes medications (16). Individuals who were not completely satisfied with medication information may have had greater risk of CRN selectively for pain treatment because they may have less understanding of the intended use of their medications.

Our results build on findings of prior studies that depression increases risk of CRN (4). The effects of depression may be mediated by lower self-efficacy, pessimism about reducing long-term health risks, and increased cynicism about medication effectiveness. Depression is associated with disability and loss of income (24), which may contribute to CRN, but in our multivariate model, the effects of depression on CRN were independent of income. Patients with more negative beliefs about prescription medications in general may have higher rates of CRN because they perceive less value in their medications and are, therefore, less willing to pay for them.

This study has a number of limitations. First, as with all survey studies, there are risks of bias in self-reporting. Previous studies investigating the accuracy of self-reports of medication adherence compared with administrative data or biological assays have shown wide variation in their estimates (25). Both recall error and social desirability would tend to cause an overestimation of medication adherence, but what effect this would have on our results is unclear. We cannot make claims beyond association for the relation between CRN and other factors analyzed, in part because of difficulty asserting temporality. These findings may not be generalizable to underuse of medications for conditions other than diabetes and chronic pain. We could not investigate the impact of other important patient-level characteristics, such as trust in clinicians (11), because not all patients had primary care providers. Drug-specific medication copayments may influence patients' adherence choices but unfortunately were not available. Finally, the study had a low response rate; because of institutional review board restrictions, we could not gather data on study nonparticipants to determine the extent to which the sample represents the larger population.

With these caveats, we conclude that patients using both diabetes and chronic pain medications who cut back on both because of cost may be responding primarily to limited income and higher out-of-pocket costs. In contrast, patients prescribed both types of treatment who selectively forgo their diabetes medications may be affected more by factors such as depression and negative beliefs about prescription medications. More generally, patients' response to medication costs is not uniform: various patterns of underuse reflect different patient concerns. Greater attention by physicians to patients' particular reasons for underuse may lead to more effective interventions and ultimately better outcomes for diabetic patients who experience CRN.

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