

Factors Influencing Cost-Related Nonadherence to Medication in Older Adults: A Conceptually Based Approach

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ABSTRACT

Objective: Although multiple noncost factors likely influence a patient's propensity to forego treatment in the face of cost pressures, little is known about how patients' sociodemographic characteristics, physical and behavioral health comorbidities, and prescription regimens influence cost-related nonadherence (CRN) to medications. We sought to determine both financial and nonfinancial factors associated with CRN in a nationally representative sample of older adults.

Methods: We used a conceptual model developed by Piette and colleagues that describes financial and nonfinancial factors that could increase someone's risk of CRN, including income, comorbidities, and medication regimen complexity. We used data from the 2004 wave of the Health and Retirement Study and the 2005 HRS Prescription Drug Study to examine the influence of factors within each of these domains on measures of CRN (including not filling, stopping, or skipping doses) in a nationally representative sample of Americans age 65+ in 2005.

Results: Of the 3071 respondents who met study criteria, 20% reported some form of CRN in 2005. As in prior studies, indicators of financial stress such as higher out-of-pocket payments for medications and lower net worth were significantly associated with CRN in multivariable analyses. Controlling for these economic pressures, relatively younger respondents (ages 65–74) and depressive symptoms were consistent independent risk factors for CRN.

Conclusions: Noncost factors influenced patients' propensity to forego treatment even in the context of cost concerns. Future research encompassing clinician and health system factors should identify additional determinants of CRN beyond patients' cost pressures.

Keywords: cost-related medication nonadherence, depressive symptoms, financial, older adults.

Introduction

Out-of-pocket (OOP) prescription medication costs are increasing for many Americans, and a substantial number of patients experience cost-related medication nonadherence (CRN) [1–4]. This nonadherence can lead to serious adverse health events [5–9]. Financial risk factors associated with CRN are well documented, including low income, lack of drug coverage, and high copayment burden [8,10–15].

Financial pressures alone, however, explain only a minority of the variance in patients' risk for CRN [16], and nonfinancial predictors of patients' adherence in the context of cost pressures are poorly understood [6]. Identifying potentially modifiable factors influencing nonadherence [17] could benefit patient health and well being by providing clinicians and health systems information about who might benefit from targeted adherence counseling or changes in their treatment plan to promote more effective pharmacotherapy. Most studies that explore predictors or correlates of CRN are not theoretically grounded [6,18], and examining a variety of factors simultaneously that have been shown to be associated with CRN could highlight the relative importance of various domains such as patients' ability to pay, medical comorbidities, and mental health.

The current study takes advantage of a large nationally representative sample of older adults to concurrently examine cor-

relates of CRN using a conceptual model developed by Piette et al. [16], which posits an approach to understanding the influence of patient, medication, clinician, and health system factors on individuals' responses to medication costs [18]. While previous studies have either explored predictors of CRN [8,10,12–14,16,19–23] or have reviewed the literature on factors associated with CRN [6,18], our study is the first to apply a theoretically grounded conceptual model using all of these predictors simultaneously and to conduct an empirical analysis of CRN in a national sample. We sought to test each of these domains concurrently among patients with multiple chronic diseases and diverse sources of medication coverage.

Methods

Study Populations

We used data from the 2004 wave of the Health and Retirement Study (HRS) as well as data from the 2005 HRS Prescription Drug Study (PDS). The HRS is a longitudinal study of a nationally representative cohort of older Americans that was designed to assess the predictors and consequences of transitions out of the workforce in later life, and it includes detailed questions about participants' health insurance including prescription drug coverage [24]. The PDS is a subsample of the HRS drawn from respondents who participated in the HRS in 2004. It was designed to help track potential changes in prescription medication utilization among beneficiaries as Medicare Part D was phased in (a second wave of PDS data was collected in 2007 and is not yet available). To be eligible for inclusion in the present study, respondents needed to be aged 65 or older in 2005 (e.g.,

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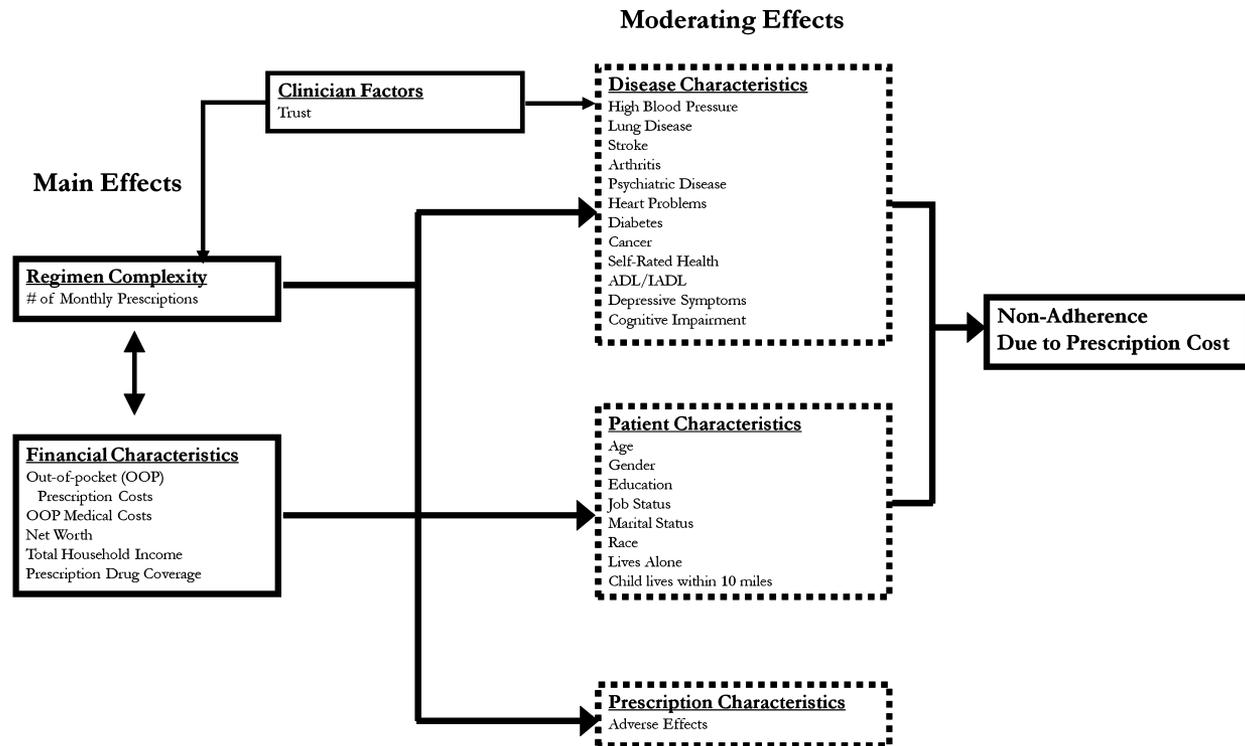


Figure 1 Conceptual framework for the factors influencing patients' risk of cost-related nonadherence (adapted from Piette et al. [18]). ADL, activities of daily living; IADL, instrumental activities of daily living.

age eligible for Medicare when the PDS data were collected), and be self-respondents (i.e., they were able to provide responses without a proxy respondent). Approximately 40% of the 2004 HRS sample was approached for possible inclusion in the PDS study, which had a response rate of 88%. Out of the 4684 people who completed the PDS, 3997 were aged 65+, 3394 had data on CRN, and 3071 responded without a proxy. Therefore, our final study sample size was 3071.

The HRS and PDS provide excellent data for testing our conceptual model because they include indicators of several of the posited domains, including indicators of financial pressures for CRN (income, insurance coverage, and number of prescriptions), as well as nonfinancial factors that could mitigate or exacerbate patients' risk of CRN: patient sociodemographic characteristics, health status indicators, and medication characteristics. Less information is included in these datasets regarding other domains described in the conceptual model such as clinician counseling and health system characteristics [6,18]. Variables from the PDS included: CRN, OOP medication costs, drug coverage, adverse medication effects, number of monthly prescriptions, and age. All other variables were taken from the HRS. These variables are included in a modification of Piette et al.'s [16] conceptual model in Figure 1.

All analyses were weighted and adjusted for HRS' complex sampling design (stratification and clustering) and used SAS 9.2 (SAS Institute, Cary, NC). The Institutional Review Board of the University of Michigan Medical School approved this research project and it received exempt status.

Dependent Variable

Participants were considered to have experienced CRN if they reported any of the following behaviors during the past year: 1)

not filling a new prescription because of cost; 2) stopping taking a medication because of cost; or 3) skipping doses of a medication to save money. This study used similar measures to other studies of CRN [25], and other studies have used a similar approach to group CRN behaviors to create a global measure of "any CRN" [11,13]. In auxiliary analyses, we also examined each CRN measure separately and found similar but not identical results. Therefore, we present results using both the "any CRN" measure and each individual CRN item as outcomes.

Independent Variables

We chose independent variables based on data from the HRS and PDS that were in accordance with the domains of our conceptual model:

Measures of financial pressures included out-of-pocket expenditures (measured in quartiles: \$0 to \$20, \$20.01 to \$50, \$50.01 to \$110, >\$110) for a month supply of "regular" drugs, other OOP medical expenses from the previous 2-year period (measured in quartiles: \$0 to \$580, \$580.01 to \$1792.50, \$1792.51 to \$4570, >\$4570), net worth (measured in quartiles: \$0 to \$38,000, \$38,000.01 to \$154,500, \$154,500.01 to \$425,000, >\$425,000), annual household income (measured in quartiles: \$0 to \$14,042.11, \$14,042.12 to \$25,660, \$25,660.01 to \$48,384, >\$48,384), and any drug coverage (yes or no and including employer, private purchase, Medicaid, VA, Medicare HMO or Medicare + Choice plan, or state pharmacy assistance program).

Demographic characteristics included age (65–74, 74–85, 85+), education (high school graduate or less, at least some college), sex, employment status (working, not working, retired), current marital status (married, separated/divorced, widowed, never married), and race/ethnicity (white, black, Hispanic, other).

Patients' burden of chronic illness was measured using indicators for each of eight chronic medical conditions: 1) high blood pressure or hypertension; 2) diabetes or high blood sugar; 3) cancer or a malignant tumor of any kind except skin cancer; 4) chronic lung disease except asthma such as chronic bronchitis or emphysema; 5) heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems; 6) stroke or transient ischemic attack; 7) emotional, nervous, or psychiatric problems; and 8) arthritis or rheumatism. Other health-related characteristics included patients' perception of their overall health (excellent vs. very good, good, fair, or poor), limitations in each of five activities of daily living (eating, getting in and out of bed, dressing, bathing, and walking across a room, measured as 0 vs. ≥ 1) and five instrumental activities of daily living (preparing meals, grocery shopping, making phone calls, taking medications, and managing money measured as 0 vs. ≥ 1) [26].

To determine depressive symptoms, each respondent was asked the following eight depressive symptoms questions taken from the Center for Epidemiologic Studies Depression (CES-D) scale [27,28] (with response options of "yes" or "no"): 1) Much of the time during the past week, I felt depressed; 2) I felt everything I did was an effort; 3) My sleep was restless; 4) I was happy; 5) I felt lonely; 6) I enjoyed life; 7) I felt sad; and 8) I could not "get going." The total number of "yes" responses to questions 1, 2, 3, 5, 7, 8, and the "no" responses to questions 4 and 6 were summed to arrive at a total depressive symptom score that ranged from 0 to 8, which has been shown to have a Cronbach's alpha of >0.8 in the HRS data [28]. In our multivariable models, we used a three-level aggregated measure of CES-D scores of 0 (no symptoms), 1–3 (depressive symptoms), and ≥ 4 (depressed). This cut point of ≥ 4 has been found to produce comparable results to the 16-symptom cutoff for the well-validated 20-item CES-D scale [28].

Prescription regimen characteristics included the number of different prescriptions a respondent reported using in the last month (0–2, 3–4, 5–6, ≥ 7). Patients also reported whether they experienced any adverse effects associated with medication use (yes or no).

An additional variable was used from the clinician factors domain from the theoretical model. This question asked respondents who they trust to make decisions about health insurance and response choices included family members (spouse, child, other), friends, financial advisors, as well as doctors, nurses or other health-care providers (measured as no one, family/friend, or professional).

Analytic Framework

We used chi-square tests for categorical or dichotomous measures, to determine the bivariate association between respondent characteristics and CRN. Next, we used logistic regression analysis to identify which factors influenced whether a respondent experienced CRN in unadjusted and adjusted analyses. Predictors that had a *P*-value of 0.2 in unadjusted analyses were considered as candidate predictors in our full model. We removed predictors from the full model that were no longer significant at the *P* < 0.05 level (e.g., the backward elimination regression analysis procedure) to arrive at our final model. To further test the robustness of our findings, we conducted several adjusted logistic regression analyses (all using backward elimination regression analysis). First, we examined "any CRN" (i.e., not filling, stopping, or skipping as defined above) as an outcome variable. Second, we examined each of the three individual CRN items as a separate outcome variable. Finally, we conducted a subgroup analysis in which we only examined "any CRN" among low income respon-

dents with high OOP payments for medications (defined as below median income and above median OOP payments for medications). All analyses were conducted using SAS 9.2 and were weighted and adjusted for the complex sampling design (stratification and clustering) of the HRS and PDS in order to achieve estimates reflective of the US population ≥ 65 years of age.

Results

There were several factors associated with CRN in bivariate analyses, as shown in Table 1. Of note, respondents experiencing CRN had higher OOP costs per month, lower net worth, had lower household income, were less likely to have prescription drug coverage, were younger, were more often female, had more chronic conditions, had lower self rated health, had more functional limitations, reported greater levels of depressive symptoms, and were more likely to report adverse effects of medication treatment, than those not experiencing CRN.

Table 2 illustrates the results from multivariable logistic regression analyses. Since respondents' job status, heart problems, diabetes, and cancer were no longer significant independent predictors in the context of other covariates, they were dropped from the final model. Of the remaining candidate predictors, several nonfinancial factors were found to be independently associated with CRN controlling for respondents' OOP prescription costs, household income, prescription medication coverage, and net worth. In particular, more depressive symptoms had a strong independent association with CRN (compared to no depression symptoms, odds ratio (OR)_{1–3 symptoms} 1.59; 95% confidence interval (CI) 1.21, 2.08; OR_{4–8 symptoms} 2.23; 95% CI 1.56, 3.18). Women were more likely than men to experience CRN (OR 1.62; 95% CI 1.23, 2.13). Respondents who were younger were more likely to experience CRN (compared to respondents aged 65–74, OR_{75–84} 0.74; 95% CI 0.57, 0.98; OR₈₅₊ 0.49; 95% CI 0.26, 0.63). Finally, hypertension was independently associated with lower rates of CRN (OR 0.74; 95% CI 0.56, 0.98), whereas lung disease was associated with higher rates of CRN (OR 1.50; 95% CI 1.12, 2.02). We found no evidence of lack of fit in our final model (assessed using the Hosmer-Lemeshow goodness-of-fit test [29], which was equal to 0.49) and we used Nagelkerke's *r*² to examine the model fit (given that our outcome variable was dichotomous), which was equal to 0.20 [30].

Table 3 replicates results from Table 2 indicating our findings from our trimmed multivariable model after backward elimination of nonsignificant terms predicting "any CRN." In addition, we present findings from analyses of each individual CRN item. While there were some individual differences among items that were associated with CRN, consistent predictors of CRN included OOP per month for prescription medications, lower net worth, younger–old age (65–74), and depressive symptoms.

Finally, in our analyses of the subgroup of the most vulnerable respondents (low income and high OOP), we found remarkably similar predictors of any CRN: highest quartile of OOP per month for prescription medications, lower net worth, age < 85, depressive symptoms, female gender, nonhypertensive, and adverse effects of medication use.

Discussion

Although our study differed from past studies by simultaneously considering many financial, socioeconomic, and health factors, our results were similar to the findings of previous studies that considered only limited subsets of these factors [6,10,11,14,23,31]. We found the main drivers of CRN to be associated with patients' ability to pay for their medications,

Table 1 Baseline predictors of CRN

		No CRN N = 2457		CRN N = 614		P-value
		N	%	N	%	
Financial characteristics						
OOP Rx cost per month	\$0.00–\$20.00	610	29.99	86	16.20	<0.0001
	\$20.01–\$50.00	533	26.20	98	18.46	
	\$50.01–\$110.00	479	23.55	142	26.74	
	≥\$110.01	412	20.26	205	38.61	
Other OOP medical costs	\$0.00–\$580.00	630	25.64	121	19.71	<0.0001
	\$580.01–\$1,792.50	646	26.29	139	22.64	
	\$1,792.51–\$4,570.00	644	26.21	153	24.92	
	≥\$4,570.01	537	21.86	201	32.74	
Net worth	≤\$38,000.00	516	21.00	201	32.74	<0.0001
	\$38,000.01–\$154,500.00	583	23.73	195	31.76	
	\$154,500.01–\$425,000.00	640	26.05	141	22.96	
	≥\$425,000.01	718	29.22	77	12.54	
Total household income	\$0–\$14,042.11	531	21.63	178	29.18	<0.0001
	\$14,042.12–\$25,660.00	580	23.63	193	31.64	
	\$25,660.01–\$48,384.00	641	26.11	149	24.43	
	≥\$48,384.01	703	28.64	90	14.75	
Prescription drug coverage	No	527	21.45	192	31.27	<0.0001
	Yes	1,930	78.55	422	68.73	
Demographic characteristics						
Age	65–74	1,303	53.03	384	62.54	<0.0001
	75–84	835	33.98	183	29.80	
	≥85	319	12.98	47	7.65	
Gender	Female	1,423	57.92	442	71.99	<0.0001
	Male	1,034	42.08	172	28.01	
Education	High school grad or less	1,537	62.58	467	76.18	<0.0001
	At least some college	919	37.42	146	23.82	
Job status	Working	256	10.42	54	8.79	0.4896
	Not working	283	11.52	72	11.73	
	Retired	1,918	78.06	488	79.48	
Marital status	Married	1,481	60.30	323	52.61	0.0005
	Separated/divorced	218	8.88	68	11.07	
	Widowed	695	28.30	201	32.74	
Race	Never married	62	2.52	22	3.58	0.0002
	White	2,075	84.45	482	78.50	
	Black	292	11.88	111	18.08	
	Hispanic	39	1.59	14	2.28	
Lives alone	Other	51	2.08	7	1.14	0.1926
	No	1,766	71.88	425	69.22	
Child lives within 10 miles	Yes	691	28.12	189	30.78	0.0072
	No	1,483	60.36	334	54.40	
Yes	Yes	974	39.64	280	45.60	
	No					
Disease characteristics						
Ever had high blood pressure	No	906	36.90	204	33.22	0.0897
	Yes	1,549	63.10	410	66.78	
Ever had lung disease	No	2,231	90.84	512	83.39	<0.0001
	Yes	225	9.16	102	16.61	
Ever had stroke	No	2,222	90.51	561	91.37	0.5126
	Yes	233	9.49	53	8.63	
Ever had arthritis	No	790	32.21	139	22.71	<0.0001
	Yes	1,663	67.79	473	77.29	
Ever had a psychiatric disorder	No	2,133	86.92	475	77.36	<0.0001
	Yes	321	13.08	139	22.64	
Ever had heart problems	No	1,702	69.38	418	68.19	0.5666
	Yes	751	30.62	195	31.81	
Ever had diabetes	No	1,951	79.57	467	76.18	0.0662
	Yes	501	20.43	146	23.82	
Ever had cancer	No	2,034	82.99	520	84.97	0.2390
	Yes	417	17.01	92	15.03	
Self-rated health	Excellent	228	9.29	28	4.56	<0.0001
	Very good	680	27.70	118	19.22	
	Good	853	34.75	199	32.41	
	Fair	524	21.34	191	31.11	
	Poor	170	6.92	78	12.70	
ADLs	0	2,069	84.21	469	76.38	<0.0001
	≥1	388	15.79	145	23.62	
IADLs	0	2,100	85.47	492	80.13	0.0011
	≥1	357	14.53	122	19.87	
CES-D score	0	1,124	45.86	159	25.90	<0.0001
	1–3	996	40.64	299	48.70	
	≥4	331	13.50	156	25.41	
Cognitive impairment	No	2,336	95.27	585	95.28	0.9936
	Yes	116	4.73	29	4.72	
Regimen complexity						
# of monthly prescriptions	0–2	649	27.79	119	20.24	0.0001
	3–4	716	30.66	172	29.25	
	5–6	468	20.04	132	22.45	
	≥7	502	21.50	165	28.06	
Medication characteristics						
Adverse events	No	2,102	85.55	451	73.45	<0.0001
	Yes	355	14.45	163	26.55	
Clinician characteristics						
Trust for insurance decisions	No one	473	19.78	85	14.31	0.0031
	Family/friend	1,596	66.75	437	73.57	
	Professional	322	13.47	72	12.12	

ADL, activities of daily living; CES-D, Center for Epidemiologic Studies Depression Scale; CRN, cost-related nonadherence; IADL, instrumental ADL; OOP, out-of-pocket.

Table 2 Unadjusted and adjusted predictors of cost-related nonadherence

		Unadjusted models*		Full model†		Final model‡	
		OR	95% CI	OR	95% CI	OR	95% CI
Financial characteristics							
OOP Rx cost per month (reference is \$0.00–\$20.00)	\$20.01–\$50.00	1.45	1.07–1.96	1.56	1.12–2.17	1.61	1.16–2.22
	\$50.01–\$110.00	2.28	1.57–3.30	2.29	1.42–3.70	2.40	1.61–3.58
	≥\$110.01	4.13	3.09–5.53	4.38	2.95–6.50	4.74	3.56–6.30
Other OOP medical costs (reference is \$0.00–\$580.00)	\$580.01–\$1,792.50	1.04	0.77–1.39	1.07	0.74–1.55		
	\$1,792.51–\$4,570.00	1.27	0.97–1.67	1.05	0.74–1.50		
	≥\$4,570.01	2.03	1.50–2.75	1.16	0.75–1.80		
Net worth (reference is ≤\$38,000.00)	\$38,000.01–\$154,500.00	0.89	0.67–1.18	0.88	0.64–1.21	0.80	0.58–1.09
	\$154,500.01–\$425,000.00	0.56	0.43–0.73	0.60	0.42–0.88	0.52	0.37–0.72
	≥\$425,000.01	0.30	0.21–0.43	0.40	0.26–0.59	0.28	0.18–0.43
Total household income (reference is \$0.00–\$14,042.11)	\$14,042.12–\$25,660.00	0.97	0.73–1.28	0.97	0.67–1.40		
	\$25,660.01–\$48,384.00	0.69	0.52–0.90	0.92	0.63–1.33		
	≥\$48,384.01	0.42	0.28–0.62	0.65	0.40–1.06		
Any drug coverage (reference is no)	Yes	0.59	0.44–0.79	0.77	0.54–1.09		
Demographic characteristics							
Age (reference is 65–74)	75–84	0.80	0.61–1.04	0.69	0.51–0.94	0.71	0.54–0.94
	≥85	0.52	0.35–0.77	0.36	0.21–0.63	0.38	0.25–0.58
Gender (reference is male)	Female	1.86	1.50–2.30	1.47	1.12–1.94	1.51	1.16–1.96
Education (reference is high school grad or less)	At least some college	0.59	0.49–0.71	0.86	0.67–1.12		
Job status (reference is working)	Not working	1.10	0.72–1.69				
	Retired	1.06	0.74–1.51				
	Never married	1.68	1.00–2.82	1.80	0.97–3.36		
Marital status (reference is married)	Separated/divorced	1.37	1.05–1.78	1.16	0.66–2.03		
	Widowed	1.37	1.07–1.76	1.07	0.73–1.58		
	Black	1.71	1.24–2.36	1.15	0.76–1.73		
Race (reference is white)	Hispanic	1.78	0.79–4.01	0.67	0.17–2.60		
	Other	0.50	0.22–1.14	0.53	0.23–1.22		
	Yes	1.19	0.96–1.47	0.83	0.56–1.23		
Lives alone (reference is no)	Yes	1.24	1.00–1.54	1.06	0.83–1.35		
Disease characteristics							
Ever had high blood pressure (reference is no)	Yes	1.18	0.93–1.50	0.73	0.55–0.98	0.75	0.57–0.98
Ever had lung disease (reference is no)	Yes	2.03	1.50–2.74	1.51	1.08–2.12	1.48	1.10–1.98
Ever had stroke (reference is no)	Yes	0.86	0.63–1.18				
Ever had arthritis (reference is no)	Yes	1.67	1.33–2.11	1.19	0.85–1.68		
Ever had a psych disorder (reference is no)	Yes	2.03	1.59–2.59	1.10	0.78–1.53		
Ever had heart problems (reference is no)	Yes	1.01	0.83–1.23				
Ever had diabetes (reference is no)	Yes	1.13	0.91–1.40				
Ever had cancer (reference is no)	Yes	0.93	0.70–1.25				
Self-rated health (reference is poor)	Excellent	0.31	0.18–0.53	1.28	0.58–2.82		
	Very good	0.37	0.26–0.54	1.08	0.63–1.84		
	Good	0.52	0.37–0.74	1.08	0.65–1.77		
	Fair	0.79	0.55–1.14	1.18	0.71–1.96		
ADLs (reference is 0)	≥1	1.58	1.29–1.93	0.96	0.65–1.42		
IADLs (reference is 0)	≥1	1.46	1.11–1.92	1.01	0.71–1.44		
CES-D score (reference is 0)	1–3	1.81	1.38–2.38	1.53	1.13–2.07	1.64	1.25–2.14
	≥4	2.96	2.28–3.84	2.09	1.38–3.17	2.25	1.59–3.20
Cognitive impairment (reference is no)	Yes	1.15	0.72–1.84				
Regimen complexity							
# of monthly prescriptions (reference is 0–2)	3–4	1.49	1.13–1.97	1.06	0.73–1.54		
	5–6	1.60	1.07–2.40	0.85	0.51–1.40		
	≥7	1.91	1.34–2.71	0.83	0.53–1.30		
Medication characteristics							
Adverse events (reference is no)	Yes	2.19	1.77–2.71	1.87	1.43–2.45	1.75	1.36–2.24
Clinician characteristics							
Trust for insurance decisions (reference is no one)	Family/friend	1.44	1.11–1.86	1.37	0.99–1.91		
	Professional	1.21	0.80–1.83	1.41	0.89–2.24		
Nagelkerke's R ²		—		0.22		0.20	
Hosmer-Lemeshow goodness-of-fit test		—		0.94		0.49	

*Goodness-of-fit test statistics and R² are not available for unadjusted models.

†Covariates were considered for the full model if they had a P-value of 0.2 or less in its unadjusted model.

‡The final model was derived using backward elimination on the full model with P-value cutoff of 0.05.

ADL, activities of daily living; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; IADL, instrumental activities of daily living; OOP, out-of-pocket; OR, odds ratio.

particularly among those with low income and high OOP drug costs. Nevertheless, we also found that in addition to sociodemographic correlates of CRN (such as younger age and female gender) some potentially modifiable predictors of CRN include comorbid illness such as depression.

This study replicates findings from other studies indicating that depression is significantly associated with CRN [19,32], independent of patients' ability to pay. In fact, the current study

indicates that depression is the strongest correlate of CRN once financial pressures have been taken into account. In other words, this association cannot be explained by lack of drug coverage, poverty, or higher OOP among more depressed respondents [6], because the relationship was maintained even when we controlled for these and other potential confounders.

Although chronic health conditions such as diabetes are usually associated with CRN [31], even when controlling for

Table 3 Adjusted predictors of “any CRN” as well as predictors of individual CRN items

		Any		Not fill		Stop taking		Skip doses	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Financial characteristics									
OOP Rx cost per month (reference is \$0.00–\$20.00)	\$20.01–\$50.00	1.61	1.16–2.22	1.34	0.87–2.05	1.30	0.80–2.12	2.70	1.75–4.16
	\$50.01–\$110.00	2.40	1.61–3.58	1.92	1.20–3.07	2.48	1.50–4.11	3.05	1.89–4.93
	≥\$110.01	4.74	3.56–6.30	3.06	2.03–4.62	3.55	2.26–5.59	8.37	5.38–13.04
Net worth (reference is ≤\$38,000.00)	\$38,000.01–\$154,500.00	0.80	0.58–1.09	0.82	0.60–1.14	0.86	0.55–1.35	0.73	0.51–1.05
	\$154,500.01–\$425,000.00	0.52	0.37–0.72	0.54	0.37–0.80	0.51	0.34–0.77	0.46	0.30–0.71
	≥\$425,000.01	0.28	0.18–0.43	0.26	0.15–0.45	0.29	0.15–0.56	0.45	0.29–0.70
Total household income (reference is \$0.00–\$14,042.11)	\$14,042.12–\$25,660.00							1.18	0.79–1.76
	\$25,660.01–\$48,384.00							0.78	0.51–1.19
	≥\$48,384.01							0.51	0.30–0.88
Any drug coverage (reference is no)	Yes			0.64	0.48–0.85	0.55	0.39–0.78		
Demographic characteristics									
Age (reference is 65–74)	75–84	0.71	0.54–0.94	0.69	0.51–0.94	0.63	0.45–0.87	0.67	0.51–0.89
	≥85	0.38	0.25–0.58	0.38	0.25–0.58	0.48	0.31–0.74	0.35	0.20–0.59
Gender (reference is male)	Female	1.51	1.16–1.96	1.44	1.08–1.93				
Disease characteristics									
Ever had high blood pressure (reference is no)	Yes	0.75	0.57–0.98						
Ever had lung disease (reference is no)	Yes	1.48	1.10–1.98	1.56	1.10–2.22				
Ever had cancer (reference is no)	Yes					0.59	0.39–0.90		
CES-D score (reference is 0)	1–3	1.64	1.25–2.14	2.31	1.78–3.00	2.19	1.48–3.26	1.59	1.14–2.21
	≥4	2.25	1.59–3.20	3.21	2.29–4.49	2.79	1.85–4.20	2.27	1.49–3.48
Medication characteristics									
Adverse events (reference is no)	Yes	1.75	1.36–2.24	2.27	1.75–2.94	2.96	2.10–4.17		
Nagelkerke’s R ²		0.20		0.21		0.20		0.15	
Hosmer-Lemeshow goodness-of-fit test		0.49		0.52		0.68		0.47	

CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; CRN, cost-related nonadherence; OOP, out-of-pocket; OR, odds ratio.

depression [19], we did not find an association between diabetes, cancer, stroke, arthritis, or heart disease and CRN. While we do not know of any prior literature documenting the relationship between lung disease and CRN directly, one study demonstrated significantly higher rates of lung disease among depressed Medicare beneficiaries than among nondepressed Medicare beneficiaries, where depressed beneficiaries experienced significantly higher rates of CRN than their nondepressed counterparts [19]. Given the importance of medications for prevention of disease progression and adverse disease outcomes for lung disease such as asthma and chronic obstructive pulmonary disease, it will be important to further investigate reasons for these observed high rates of CRN among older adults with lung disease. In contrast, our study found that hypertension was associated with lower rates of CRN. While the explanation for this relationship is unclear, the association is consistent with another study demonstrating that patients may forego other medications due to CRN before antihypertensives, perhaps motivated by the life-threatening nature of hypertension [16]. We note as well that it may be difficult to interpret the meaning of individual chronic disease predictors in the absence of additional information about patient health-related quality of life or life expectancy [18].

While sex is not usually found to be a significant predictor of CRN [6], the current study as well as a few other studies have found that women are more likely to experience CRN [12,33]. In order to better understand possible mechanisms for these gender effects, we examined potential interactions between sex and indicators of respondents’ financial status. None of these interactions was significant and more research is needed to determine the conditions under which women may be more likely than men to forego their medication due to financial pressures.

We note that several of our measures of patients’ financial burden that were significant in bivariate analyses were not significant predictors of CRN in the final model, including drug coverage, OOP for other medical costs, and household income. We suspect that OOP for medications would have already accounted for drug coverage (as OOP is the remainder that a

patient would pay after any drug coverage has kicked in), that other medical costs are not as strong of a predictor of CRN in the presence of OOP for prescription medications, and that net worth and household income are too highly correlated for both of them to be significant predictors of CRN, with net worth being a better indicator of overall ability to afford items such as medications.

Adverse events associated with medication use also appeared to be associated with higher odds of CRN. It makes sense that adverse effects might provide patients with an incentive to discontinue medication use when they are faced with relatively high or increasing medications costs. Given this, it may be important for providers to discuss potential adverse effects of medications with their patients and make modifications to patients’ medication regimens as soon as possible to mitigate the negative impact of adverse events as well as increase patient adherence and well being.

Some of the strengths of the current study include its use of a large nationally representative sample of older adults and its ability to examine multiple possible domains of predictors simultaneously. Nevertheless, despite the wealth of data available for our analyses, there are some limitations. We did not have information on a variety of patient level factors including patient preferences for or beliefs about medication treatment that could influence adherence to medication and potentially CRN [34]. We also could not measure variation in CRN across treatments in the patients’ regimen. Prior studies suggest that patients may respond differently when facing costs for essential versus nonessential treatments or treatments that vary in their importance for longevity and symptom relief [16,23]. Our analyses suggest that much of the variance in patient CRN remains unexplained.

In addition, we did not have information on factors related to the patient–physician relationship including more details about physician trust [10,32] and communication about costs [22,35], which may be important influences on adherence and CRN. Patients and providers may have different treatment objectives and goals [36], and may have different ideas about the balance

between necessity and risks associated with medication use that could also influence adherence and CRN. Perceived importance influences perceived worth and thereby adherence, especially among high cost drugs [37]. Therefore, future studies should seek to examine these facets of the patient-provider dynamic concurrently with the patient level factors examined in the present study.

There are some additional limitations associated with our depression and chronic disease measurement in this study. Patients' burden of chronic disease was measured in 2004 and CRN was measured in 2005. It is possible that disorders, particularly depression, can be transient. Nevertheless, conversely, the analyses are largely cross sectional, and future research should examine the relationship between disease (and other factors) and CRN over time. Furthermore, variation in CRN by particular chronic medication conditions may be difficult to interpret, as they may be proxies for other unmeasured patient characteristics such as self efficacy.

Our analyses are also based on self-reported survey measures, and there may be gaps in respondent knowledge, as research indicates that people may not be fully aware of their drug coverage and cost-sharing arrangements [23,25,38], which could also influence reports of CRN. These analyses were also limited to older adults (65+) yet we found that the youngest members of our study experienced the highest levels of CRN. It is possible that including data from even younger respondents (say middle-aged adults who were not yet Medicare eligible) would reveal even higher rates of CRN than in the study sample. Prior studies suggest that this would be the case [23,34].

Conclusions

Despite these limitations, this research has generated important conceptually and empirically tested findings regarding which factors most strongly influence CRN. Some of the factors identified as predictors of CRN are not modifiable (e.g., age and gender), but should be considered risk factors, thereby potentially requiring additional screening for CRN. Factors that may be modifiable, with varying degrees of difficulty, include decreasing levels of depression and lung disease, decreasing OOP expenditures for medications, and even net worth (which could be slightly modifiable depending on the availability of government programs that could influence wealth redistribution). Treating depression may involve incurring additional costs (particularly if treated with medications). Thus, while an important target for improving CRN would be to expand medication coverage, thereby decreasing OOP expenditures associated with prescription drugs, other factors clearly also affect CRN besides costs and coverage. For example, learning more about why some patients with hypertension appear to have lower rates of CRN could be instructive, and identification of other presently unmeasured factors like coping skills could allow clinicians and health educators to address these issues, decreasing rates of CRN even when costs themselves cannot be reduced. Researchers should examine the influences of changes in drug coverage on CRN over time, as it is known that there is a negative impact of caps on consumption and outcomes [9], and there is evidence to indicate that broader coverage may improve outcomes [39]. In particular, we should measure whether Medicare Part D successfully decreases CRN for older adults when it is examined in a comprehensive context such as the model tested here.

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