

Individual patients hold different beliefs to prescription medications to which they persist vs nonpersist and persist vs nonfulfill

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Objective: Our objective was to explore whether adults hold different beliefs about medications to which they persist vs nonpersist and persist vs nonfulfill.

Methods: We conducted a cross-sectional survey of adults with asthma, hypertension, diabetes, hyperlipidemia, osteoporosis, or other cardiovascular disease from the Harris Interactive Chronic Illness Panel. A quota was set to obtain a sample of respondents who were persistent to a medication for one disease and nonpersistent or nonfulfilling to a medication for a second, different disease. Respondents completed 32 items yielding five multi-item scales: perceived need for medication ($k = 12$), side-effect concerns ($k = 5$), medication-safety concerns ($k = 5$), perceived disease severity ($k = 3$), and knowledge about the prescribed medication ($k = 7$). Respondents completed the 32 items twice – once for their persistent medication and a second time for their nonpersistent or nonfulfilling medication. Paired sample *t*-tests (bivariate) and generalized estimating equations (GEE) models (multivariate) were used to test the study hypotheses.

Results: Overall, 178 respondents were sampled for being persistent to one medication and nonpersistent to another, while 48 respondents were persistent to one medication and nonfulfilling to a second. For the medication to which an individual patient was persistent vs nonpersistent, there was significantly higher perceived need, fewer side-effect concerns, higher perceived disease severity, and better knowledge about the medication. For the medication to which an individual patient was persistent vs nonfulfilling, there was significantly higher perceived need, fewer side-effect concerns, and better knowledge about the medication.

Conclusion: Individual patients hold different beliefs about medications to which they persist vs nonpersist or nonfulfill. Patients exhibit different medication-taking behaviors for different medications because they weigh the perceived risks and benefits for each medication separately. These results suggest that adherence interventions should be tailored to patients' beliefs about specific medications.

Keywords: adherence, persistence with therapy, medication beliefs, chronic disease, primary nonadherence, medication nonfulfillment

Introduction

Prescription medications are an essential pillar of primary and specialty care with 70% of ambulatory visits involving a provided, prescribed, or continued medication.¹ Nonadherence to prescription medications is a problem of international importance that knows no demographic, geographic, or political boundaries. A recent systematic review reported that, across 79 studies, approximately 16% of patients fail to fill a new prescription (otherwise known as primary nonadherence or medication nonfulfillment).² Approximately one half of patients who fill a new prescription stop taking their medication in the first year of therapy (otherwise known as medication nonpersistence).³

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Three key adherence ‘myth busters’ have emerged from five decades of adherence research. First, there are very weak associations between sociodemographic characteristics and adherence.^{4,5} In a seminal meta-analysis, DiMatteo⁵ found the average correlation between adherence and age and gender to be zero and the average correlation between adherence and education and income to be less than 0.10. Second, across⁶ and within^{6–10} chronic diseases, there is weak correspondence between medication adherence and adherence to lifestyle and self-care recommendations. Third, many researchers have dismissed the plausibility of an ‘adherent personality.’^{11–14} Hevey¹⁴ asserts that ‘there is little evidence of personality traits influencing adherence and the search for the “nonadherent” personality type has provided limited insight.’ These three findings have gone far towards redirecting research away from trait characteristics and toward patients’ mutable characteristics, ie, their beliefs about their treatment and their disease.

Conceptual work has described adherence as a reasoned decision^{15,16} and has explained how patients differentially value different medications.^{16,17} Qualitative research has shed light on how medication taking is a decision-making process and has illustrated how patients balance their concerns about medications against their perceived need for the therapy and its perceived benefits.^{13,15,18–24} Quantitative research has documented that patient beliefs about their treatment, condition, and prognosis, as well as their objective experiences with their treatment, differentiate adherers from nonadherers.^{25–38}

If adherence is not a trait characteristic, it stands to reason that individual patients should exhibit different adherence patterns to different medications because they make decisions for each medication according to their beliefs as well as to the information they possess about the medication and the condition. Thus, adherence should represent shades of grey – individual patients can be persistent to some medications, nonpersistent to others, and fail to fill others because they make separate decisions about each medication. Research has indeed demonstrated that individual patients have distinct adherence patterns to assorted medications.^{30,39–53} For example, Chapman^{41,49} reported differential persistence to concomitant antihypertensive and lipid-lowering therapy, and Piette⁴⁸ found differential persistence to antihyperglycemic, antihypertensive, and antipsychotic medications. Research has also shown that individual patients attach differential worth and value to different medications^{13,34,54} and have diverse beliefs for different medications in regard to their perceived importance, effectiveness, safety, and expected benefits.^{13,55,56} For example, Aikens and Piette⁵⁶ demonstrated that patients

prescribed both antihyperglycemic and antihypertensive medications rated the former as more necessary to them; the antihyperglycemic medications also induced more medication concerns than did the antihypertensive medications. Finally, quantitative research has shown that patients with different adherence behaviors have different beliefs about their medications and conditions.^{30,36,38,57,58} In one study, there was a striking distinction between self-reported medication persisters and nonpersisters on 14 different proximal and intermediate adherence drivers.³⁸

Despite the totality of this research, we know of no published studies that show different belief structures within individual patients who exhibit different medication-taking behaviors for different medications for different chronic diseases. Herein we report a small study of: (1) 178 patients who reported being persistent to one medication for one chronic disease and nonpersistent to a different medication for a second chronic disease; and (2) 48 patients who reported being persistent to one medication for one chronic disease and not filling a different medication for a second chronic disease.

Methods

Study design

Sampling procedure

As described in detail elsewhere,³⁸ survey participants were selected from the Harris Interactive Chronic Illness Panel (CIP), a nationally-representative, Internet-based panel of hundreds of thousands of adults with chronic disease. Respondents were eligible for the survey if they were aged 40 and older, resided in the U.S., and reported having at least one of six chronic diseases prevalent among U.S. adults: asthma, diabetes, hyperlipidemia, hypertension, osteoporosis, or other cardiovascular disease. Panel members responding to an email invitation were instructed to read the informed consent form and click on *yes* if they agreed to participate. The protocol for the survey was approved by the Essex IRB.

Three groups of respondents were identified based on their medication-taking behavior: self-reported persisters, self-reported nonpersisters, and self-reported nonfulfillers to prescription medications. Of the 1,283 respondents to the survey, 1,072 were sampled for a single medication-taking behavior while 226 were sampled for more than one medication-taking behavior (ie, persistent to a medication for one disease and nonpersistent to a medication for a different disease [$n = 178$]; persistent to a medication for one disease and nonfulfilling to a medication for a different disease [$n = 48$]). These latter sample members ($n = 226$) are used in the analyses reported herein.

Definition of medication persisters, nonpersisters, and nonfulfillers

During the screening portion of the survey, panel members' chronic disease status was reconfirmed. The screener solicited the number of medications respondents currently took for each disease as well as the length of time they reported they had been continuously taking the medication. These items were used to classify respondents as currently persistent to their medication. To identify respondents as nonpersisters, the survey asked if, in the last year, they had stopped taking a prescription medication for one of the six conditions without their providers telling them to do so. To identify respondents as nonfulfillers, the survey asked if, in the last year, they had received, but did not fill, a new prescription from their provider for one of the six target conditions.

Survey content

The 226 respondents sampled for more than one medication-taking behavior completed a core set of questions on demographics (including age, gender, education, income, and race) and self-reported health. The 226 respondents also completed two identical sets of 32 questions assessing perceived need for medication ($k = 12$), side-effect concerns ($k = 5$), medication-safety concerns ($k = 5$), perceived disease severity ($k = 3$), and knowledge about the prescribed medication ($k = 7$). Respondents completed each of the 32 items twice: once for each of the two medications for which they self-reported different medication-taking behaviors. As described in detail elsewhere,³⁸ multi-item scales were created by summing raw items into a scale score and linearly transforming each sum to a 0–100 metric, with 100 representing the most favorable belief (highest perceived need, fewest side-effect concerns, fewest medication-safety concerns, highest perceived disease severity, and best knowledge), 0 the least favorable, and scores in between representing the percentage of the total possible score.³⁸ The multi-item scales were internally consistent, with Cronbach's alpha coefficients ranging from 0.76–0.96 (median of 0.87).³⁸

Statistical analysis

It was hypothesized that respondents would express statistically-different beliefs about the different medications to which they showed (1) persistence vs nonpersistence and (2) persistence vs nonfulfillment. Paired sample *t*-tests and generalized estimating equations (GEE) models were used to determine whether patients' scores were significantly different for the different medication-taking behaviors.

Most standard multivariate techniques assume that observations used in an analysis are independent of all others. This assumption is violated if repeated observations are taken within subjects, such as in this study, because such observations tend to be correlated with each other. When faced with such data, researchers must account for the correlation within responses when estimating regression parameters.⁵⁹ Failure to incorporate correlation of responses can lead to incorrect estimation of model parameter estimates; in particular, the standard error can be too small, increasing the likelihood that a parameter is statistically significant when it truly is not.

Generalized estimating equations (GEE)^{60,61} are employed as a means of testing hypotheses regarding the influence of factors on response variables collected within subjects across time. The GEE models in this study were estimated specifying a Gaussian distribution of the dependent variable, an identity link function, and an exchangeable correlation matrix with robust standard errors. The principal independent variable in the GEE models was a dichotomous indicator of whether a person's response for a specific scale was for a medication for which they were persistent or not (either nonpersistent or nonfulfiller). Covariates included patient-level demographics (age, gender, race, education, income, and self-reported health) as well as dummy variables for the diseases groups.

Results

Persistent vs nonpersistent

Table 1 shows the demographic characteristics of the persistent versus nonpersistent sample. Two-thirds of respondents were female and had a mean age of 60 years. A majority of the respondents were white (90%), had better than a high-school education (79%), and reported their health as being fair or poor (63%).

Table 2 reports the results of paired *t*-tests. For four of the five scales, the mean scores for the nonpersistent medication were significantly lower than those for the persistent medication. Side-effect concerns showed the largest difference between persistent and nonpersistent medications (15.6% lower for nonpersistent medication), followed by perceived need for medications (14.5% lower for nonpersistent medication), perceived disease severity (9.2% lower for nonpersistent medication), and knowledge (3.6% lower for nonpersistent medication).

Table 3 shows results of the GEE models. After controlling for several covariates, respondents had significantly lower perceived need, more side-effect concerns, lower perceived disease severity, and less knowledge for the medication to which they were nonpersistent vs persistent.

Table 1 Demographic characteristics

Variable	Persistent versus nonpersistent N = 178		Persistent versus nonfulfillment N = 48	
	N	%	N	%
Age, mean (SD)	59.8	10.8	63.4	10.8
40–49	37	20.8%	4	8.3%
50–59	48	27.0%	13	27.1%
60–69	62	34.8%	20	41.7%
70–79	24	13.5%	8	16.7%
80+	7	3.9%	3	6.3%
Gender				
Male	61	34.8%	18	37.5%
Female	117	65.7%	30	62.5%
Education				
High school or less	38	21.4%	8	16.7%
Some college	74	41.6%	26	54.2%
College degree	23	12.9%	5	10.4%
Greater than college degree	43	24.2%	9	18.8%
Income				
<25K	39	24.7%	8	19.1%
≥25K <50K	46	29.1%	14	33.3%
≥50K <75K	30	19.0%	7	16.7%
≥75K <100K	21	13.3%	8	19.1%
≥100K	22	13.9%	5	11.9%
Race				
White	158	89.8%	46	95.8%
Black	5	2.8%	1	2.1%
Hispanic	4	2.3%	0	0%
Other	9	5.1%	1	2.1%
Health				
Fair/poor	111	62.7%	23	47.9%
Good	50	28.1%	21	43.8%
Very good/excellent	17	9.6%	4	8.3%
Medication^a				
Hypertension medication	29	16.3%	14	29.2%
Asthma medication	85	47.8%	17	35.4%
Diabetes medication	83	46.6%	13	27.1%
Lipid medication	56	31.5%	18	37.5%
Osteoporosis medication	57	32.0%	14	29.2%
Other CVD medication	46	25.8%	20	41.7%

Notes: ^aThe N's sum up to twice the number of subjects and the percents sum up to 200% because each subject was sampled for their medication-taking behavior on two separate medications in two different therapeutic areas.

Persistent vs nonfulfillment

Table 1 shows the demographic characteristics of the persistent versus nonfulfillment sample. Two-thirds of the sampled respondents were female with a mean age of 63 years and a majority were white (96%). Almost equal numbers of respondents reported their health as being fair/poor (48%) and good (44%).

Table 2 reports the results of paired sample *t*-tests. Across three of the five scales (perceived need for medications,

side-effect concerns, and knowledge), the mean score for the nonfulfilled medication was significantly lower than that for the persistent medication. Side-effect concerns scale showed the largest difference between scores for persistent and nonfulfilled medications (20.2% lower for nonfulfilled medication), followed by perceived need for medications (17.9% lower for nonfulfilled medication), and knowledge (6.3% lower for nonfulfilled medication).

Table 3 shows results of the GEE models. After controlling for several covariates, respondents had significantly less perceived need for medications, more side-effect concerns, and less knowledge for the medication which was not filled compared to the persistent medication.

Discussion

Interpretation of study findings

Of the five studied multi-item scales, perceived need for medications and medication concerns best differentiated between individuals who persisted to one medication and stopped taking another, as well as persons who persisted to one medication and failed to fill another. These findings are consistent with past research which has demonstrated that perceived need for medications and medication concerns, variously operationalized, predict medication adherence.^{25–38} Patients' beliefs should be modifiable: negative beliefs – such as medication concerns – could be assuaged, and positive beliefs – such as perceived need for medications – could be reinforced through appropriate information and counseling. Recent research has demonstrated that patients' medication beliefs can be altered through intervention.^{62–64}

Perceived disease severity is a key component of the health belief model⁶⁵ – an organizing framework that has been frequently applied in adherence research. Perceived disease severity significantly differentiated persons persistent and nonpersistent to different medications for different diseases but not so for persistent vs nonfulfillment. Some primary research studies^{45,66,67} and one meta-analysis⁶⁸ found perceived disease severity to be related to medication nonpersistence, while other primary research studies have not.^{69–73} We are aware of only one study that related perceived disease severity to medication nonfulfillment, and no significant relationship was found.⁷⁴ We hypothesize that perceived disease severity was a weaker differentiator of different medication-taking behaviors within individuals because it may influence medication decision-making through its direct effect on perceived need for medications and medications concerns,³⁸ which is consistent with tenets of the health belief model.⁷⁵

Table 2 Results of paired sample *t*-tests

Persistent versus nonpersistent medications (N = 178)					
Multi-item scale	Persistent medication	Nonpersistent medication	(Persistent) – (Nonpersistent)		
	Mean	Mean	Difference (% lower)	<i>t</i>-score	<i>P</i>-value
Perceived need for medications	77.4	66.2	11.2 (14.5%)	6.7	<0.001
Side-effect concerns	68.5	57.8	10.7 (15.6%)	6.1	<0.001
Medication-safety concerns	52.2	51.6	0.6 (1.2%)	0.5	0.64
Perceived disease severity	65.3	59.3	6.0 (9.2%)	3.1	<0.01
Knowledge about the prescribed medication	83.1	80.1	3.0 (3.6%)	3.0	<0.01
Persistent versus nonfulfilled medications (N = 48)					
Multi-item scale	Persistent medication	Nonfulfilled medication	(Persistent) – (Nonfulfilled)		
	Mean	Mean	Difference (% lower)	<i>t</i>-score	<i>P</i>-value
Perceived need for medications	79.8	65.5	14.3 (17.9%)	3.9	<0.001
Side-effect concerns	71.3	56.9	14.4 (20.2%)	3.9	<0.001
Medication-safety concerns	53.6	53.8	–0.2 (–0.4%)	–0.1	0.95
Perceived disease severity	63.7	59.4	4.3 (6.8%)	1.3	0.21
Knowledge about the prescribed medication	87.9	82.4	5.5 (6.3%)	2.9	<0.01

Medication-related information is a necessary, but not sufficient, condition for effective medication-taking behavior.⁷⁶ Knowledge about the prescribed medication significantly differentiated both nonfulfillers and nonpersisters from persisters. This finding is consistent with past research which has demonstrated that patients desire information about their conditions,⁷⁷ are unaware of the possible clinical sequelae of untreated/uncontrolled chronic disease,⁷⁸ and report significant unmet needs for information about the risks and benefits of their medications.^{22,23,77,79–81} While statistically significant, knowledge was not as strong a differentiator of different medication-taking behaviors as perceived need, side-effect concerns, or disease severity. Knowledge has been hypothesized to indirectly affect medication-taking behaviors through behavioral skills (eg, objective and perceived medication-taking skills as well as adherence self-efficacy),⁸²

personal motivation,⁷⁶ and health beliefs (general as well as medication- and disease-specific).^{38,83} Thus, the smaller effects observed for knowledge in this study may be due to its mediating, rather than direct effect, on medication decision-making. Consistent with this interpretation, a recent meta-analysis showed rather small effect sizes for information and educational adherence intervention,⁸⁴ a finding similar to other meta-analyses.^{85,86}

The multi-item scale assessing long-term medication safety-concerns was not statistically significant in the bivariate or multivariate analyses. The five items included in the scale measured long-term concerns (eg, worry about building up a tolerance, worry my body will become dependent on the medication). Given the long-term and future focus of the items, it is intuitive that they would have less impact on contemporaneous medication decision-making.

Table 3 GEE models predicting subjects' score on the five multi-item scales

Multi-item scale	Persistent versus nonpersistent medications^a (N = 338)^b		Persistent versus nonfulfilled medications^a (N = 90)^b	
	Coefficient on the GEE model^c	<i>P</i>-value	Coefficient on the GEE model^c	<i>P</i>-value
Perceived need for medications	–10.9	<0.001	–13.0	0.01
Side-effect concerns	–10.7	<0.001	–14.3	<0.001
Medication-safety concerns	0.3	0.85	2.0	0.59
Perceived disease severity	–6.1	<0.01	–2.3	0.68
Knowledge about the prescribed medication	–2.5	0.02	–5.9	0.01

Notes: ^aReference category: Persistent medication; ^bEach subject is included twice in the GEE models, once for the persistent medication and once for their nonpersistent/nonfulfilled medication; ^cCovariates in the GEE models included: age, gender, education, income, race, self-reported health, and index medication therapeutic area.

Limitations of the study

Our study is not without limitations. Information on medication-taking behaviors was collected by self report and was not corroborated using external indicators, such as pharmacy claims, refill records, pill counts, or electronic monitoring. However, every direct and indirect method of assessing adherence has its limitations, and none are measured without error. Past research has demonstrated that patients reliably report nonadherence.^{87–89} Thus, we have greater confidence in the classification of nonpersisters and nonfulfillers than the self-reported persisters. Any misclassification of the self-reported persisters would have served to provide lower-bound estimates of the observed findings. We did not sample persons who were persistent to prescription medications for two or more different diseases or who were persistent to two or more medications for the same chronic disease. A natural extension of the results reported herein would be to test whether persons persistent to multiple medications have equivalent beliefs about those medications.

The study involved adults with self-identified chronic disease, and none of the six study conditions were substantiated with medical records. However, a well-defined, chronic disease panel was accessed and the six conditions were verified using a separate, independent screener than that used to enroll the CIP. Only six conditions were studied, although they are highly prevalent in the U.S. adult population. No psychiatric conditions were studied. It is possible that our results may vary for certain subgroups of patients, such as those based on race/ethnicity. We did not have sufficient sample size within the different ethnic groups to conduct a subgroup analysis.

The use of an internet-based sample excludes persons without regular access to computers or the internet. However, the 'digital divide' has narrowed considerably in the past decade. According to a 2010 PewInternet report, 74% of Americans aged 18 years and older use the Internet.⁹⁰ Gender differentials in internet use have disappeared.⁹⁰ However, age, racial, education, and income differentials remain, with older persons, those with less income and education, and nonwhite Hispanics being less likely to use the internet. In the larger study from which the present sample was derived, we noted that, compared to the U.S. adult population, the internet-based sample had a slight under-representation of adults with income less than \$25,000 annually, an over-representation of adults with a college education, and over-representation of Caucasians.³⁸ Given that the analysis focused on different medication-taking behaviors within individuals, we have no

reason to suspect that these possible sample biases would have confounded the observed results.

We controlled for the moderating effect of income on the relationship between patients' beliefs and their medication-taking behavior. However, we did not have information on patients' out-of-pocket cost associated with the prescribed medications or patients' total cost burden for their medications. Future studies should examine perceived medication affordability with respect to different medication-taking behaviors within individual patients. Finally, given the relatively small sample size ($n = 90$) for the GEE modeling of persistent versus nonfulfilling behavior, we cannot negate the possibility that our estimates may be biased. However, there is no agreement in literature as to what represents a sufficient sample size for GEE models.⁹¹ Also, the number of clusters (ie, subjects with multiple responses) in our models far exceeds 30, a common rule of thumb for minimum number of clusters required.⁹²

Conclusion

To the best of the authors' knowledge, the results reported herein are the first to empirically demonstrate that patients have different beliefs about medications for chronic disease to which they persist vs nonpersist and persist vs nonfulfill. Patients exhibit different medication-taking behaviors for different medications because they weigh the perceived risks and benefits for each medication separately.

If adherence is to be improved, then nonfulfillment and non-persistence needs to be, firstly, recognized and, secondly, intervened upon. Suboptimal prescription-medication beliefs that make patients vulnerable to nonfulfillment and nonpersistence should be addressed relatively early in therapy. At the point of initiating new prescriptions and during routine follow up visits, health care providers can influence patients' nascent medication beliefs by eliciting the patient's perspective of the perceived benefits and risks of therapy. Addressing the risks and benefits of therapy could reinforce positive medication beliefs (such as perceived need for medication) and assuage negative ones (such as medication concerns). Results from two recent meta-analyses support this approach: better physician-patient collaboration⁹³ and communication⁹⁴ was significantly associated with better adherence.

The results of our study suggest that health care providers cannot assume equivalent medication-taking behaviors within individual patients. Fulfillment of and persistence with prescribed therapy should be monitored on an individual-medication basis. Our results also suggest that claims-based predictive modeling using historical refill patterns for medications other

than an index medication of interest are likely to explain a negligible amount of variance in persistence.

The results reported herein support the premise that the next generation of adherence interventions must address patient beliefs about their medications and conditions and not merely focus on reminders, which may only be useful for unintentional nonadherence. This study further demonstrates that, within individual patients, salient beliefs vary across different medication-taking behaviors. This suggests that interventions aimed at improving adherence for patients on multiple chronic medications must be tailored to patients' beliefs about specific medications rather than developed generically.

Disclosure

Drs McHorney and Gadkari are full-time employees of and own stock in Merck and Co., Inc. This research was funded by Merck and Co., Inc.

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