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The effect of health-related information seeking and financial strain on medication nonadherence among patients with diabetes and/or hypertension in central Texas

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Abstract

Objective To assess self-reported financial strain and persistence in asking treatment- and medication-related questions in relation to medication nonadherence.

Method Data were analysed from a cross-sectional study of adults with diabetes, hypertension or both in central Texas in 2013. Measures of medication nonadherence in the past 12 months, financial strain and patients' persistence in asking treatment- and medication-related questions were identified. Medication nonadherence resulting from cost, transportation or work was compared with medication nonadherence resulting from other reasons. Binary and multinomial regression models were fitted to identify factors associated with medication nonadherence among the respondents.

Key findings In the bivariate model, medication nonadherence from any cause was significantly associated with financial strain, not asking questions about treatments or medications, and all demographic characteristics. However, in the multinomial model, medication nonadherence resulting from cost, work or transportation was only associated with not asking medication-related question about financial strain, lack of health insurance, age and gender. This was true for nonadherence resulting from other reasons except that ethnicity was significant while gender was not.

Conclusions While removing financial strain could aid medication adherence, clinicians should also encourage patients to be persistent in asking questions about their medications until they understand the purpose for taking them. Our findings have implications for empowering patients to be more proactive in enhancing their adherence to medications.

Keywords financial strain; medication adherence; patients' persistence in asking questions

Introduction

Diabetes and hypertension are two leading causes of morbidity in the United States. The number of U.S. adults with diagnosed diabetes increased from 5.5 million in 1980 to 21.9 million in 2014,[1] with hypertension being diagnosed in 75 million adults by 2014.[2] Although the increase is partly due to changes over the years in systolic and diastolic blood pressure levels considered to be hypertensive, the number of adults with hypertension still remains high.[3] Controlling diabetes and hypertension could reduce the risk for developing cardiovascular diseases.[4] However, adequate control of these diseases is a challenge. Among U.S. adults with hypertension, for instance, only 54% were adequately controlling it for the period 2013–2014,[2] which falls short of the Healthy People 2020 goal of 69.5%.[5]

Medication adherence can help in effective control of diabetes and hypertension. However, nonadherence to medications for controlling these two diseases is rampant.[6–9] Factors affecting medication nonadherence are related to the patients,[10,11] healthcare providers[12] and the healthcare system.[13,14] One's financial position could also lead to nonadherence and other health outcomes, thus prompting the Institute of Medicine to call

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for the inclusion of a measure of financial strain as one of the social and behavioural domains in electronic health records.[15,16]

Financial strain has been assessed with a single question in a number of related ways. For example, Kahn and Pearlin[17] measured it with a single question; 'How hard is it for you pay for the very basics like food, housing, medical care, and heating? Would you say it is very hard, somewhat hard or not hard at all?' Others have assessed it with the question, 'How difficult is it for you (and your family) to pay your monthly bills?' with response options being from not at all difficult to very difficult.[18] Moreover, some scholars include a time element to assessing financial strain: 'During the past 12 months, how often did it happen that you did not have enough money to buy food, clothes or other things you needed?' with response options ranging from never to very often.[19]

Although high cost of medications contributes to nonadherence, even if medications were free, rates of nonadherence could still be almost 40%.[20] Thus, there is a need to examine both cost-related factors such as financial strain and non-cost-related factors. Among the non-cost-related factors, patients' perception of the quality of communication with their healthcare providers could influence their use of health care[21–25] and health outcomes.[25–28] Patient–provider communication as a measure assesses how both patients and their providers interact or perceive communication.[28] Studies that explore the effect of patients' information-seeking style or persistence in asking questions about their treatments or medications on medication nonadherence – and not necessarily patient–provider communication – appear to be unexplored. Patients' persistence in asking relevant questions about their treatments and medications can help them understand their diseases and make them take active roles in the decision-making process. Nonadherence to medications has been found to be associated with patients' lack of understanding of their medical problems[29] and inadequate involvement in the treatment decision-making process.[30]

Some studies have independently examined the impact of patient–provider communication[21,24] and financial strain[18,31] on medication adherence, but those that examine the combined impact of financial strain and patient's persistence in seeking medication-related information on medication nonadherence are lacking.

Thus, the objective of this study was to evaluate the combined effect of financial strain (cost-related factor) and patients' information-seeking style (communication-related factor) on medication nonadherence among adults with diabetes and/or hypertension. The influence of information-seeking style on medication adherence was premised on the Information, Motivation and Behavioral (IMB) model. According to the IMB model of medication adherence, patients' likelihood of adhering to their medications is influenced by the extent to which they are informed about their regimens, are motivated and possess the behavioural skills to adhere to their medications (Figure 1).[32] The IMB model of medication adherence has been validated with cross-sectional data on diabetes,[33] but its exploration with cross-sectional data on both diabetes and hypertension is unknown.

Methods

Study data

Data were obtained from respondents who took part in the 2013 Brazos Valley Health Assessment (BVHA). The BVHA is undertaken every 3–4 years among adult residents of central Texas in the United States to aid in planning of community health actions. The assessments have been conducted for the years 2002, 2006, 2010, 2013, 2016 and 2019. The 2013 cross-sectional survey involved nine counties and included an overall response rate of 22%, representing 5230 respondents. A professional research firm identified potential respondents through random digit dialling and follow-up mailed survey. All participants provided informed consent. We used the 2013 survey data because the latter years did not include items on medication adherence and patients' information-seeking style on their treatments and medications. For the purpose of the study, 2367 patients with diabetes, hypertension or both who answered the question on medication adherence were selected from the dataset. Because the IMB model does not include financial strain as a construct, and the dataset did not include questionnaire items on medication adherence skills, we limited the IMB model to only the constructs: information and medication adherence.

Measures

Medication nonadherence

The survey asked respondents to answer the question: 'Have you skipped taking your medicine in the past 12 months?' Responses were 'no', 'yes because of work', 'yes because of transportation', 'yes because of cost' and 'yes, for another reason'.

Based on the distribution of responses, this variable was trichotomized to form three categories – 'no', 'yes because of work, transportation or cost' or 'yes, for another reason'. This variable was used as the dependent variable in bivariate analysis as presented in Table 1 and multinomial regression analysis in Table 2.

Chronic disease indicator

The survey included an item for participants to select whether they have ever been told by a doctor, nurse or other health professionals that they had one or more of the following health problems: obesity or overweight, congestive heart failure, high cholesterol, stroke, skin cancer, cancer, asthma, emphysema, chronic bronchitis or chronic obstructive pulmonary disease (COPD), arthritis or rheumatism, depression, anxiety, human immunodeficiency virus (HIV/AIDS), addiction to alcohol or other drugs, serious memory problems including Alzheimer's and dementia, diabetes and hypertension. Those who selected diabetes, hypertension or both were included in the study.

Health insurance

Respondents were asked to indicate whether they had health insurance and to select one of eight categories of insurance. The responses were (1) I do not have health insurance of

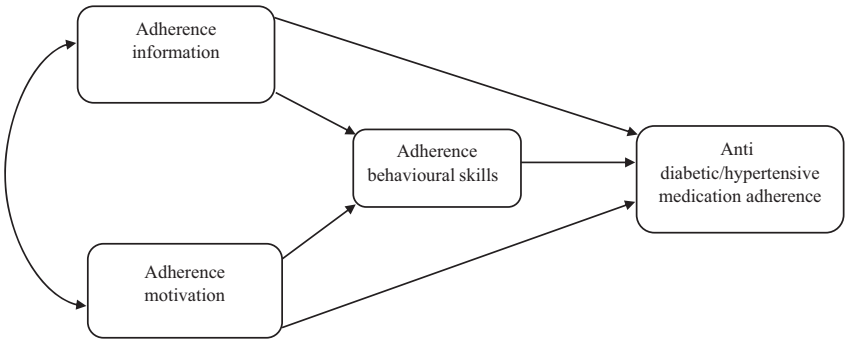

Figure 1 Information-Motivation-Behavioral skills model of diabetes/hypertension medication adherence, adapted from Fisher *et al*.[32]

any kind, (2) health insurance plan through a current or former employer or union (including spouse's or parent's insurance plan), (3) health insurance plan that I purchase directly from an insurance company, (4) Medicaid only, including Medicaid HMO, (5) Medicare only, Medicare plus other insurance (Medicaid, Medigap, other), (6) student health insurance, (7) CHAMPUS, VA, Tricare or other military insurance and (8) others. The responses from the above categories were then dichotomized into whether or not the respondents had insurance with responses, 'yes' or 'no'.

Patient's information seeking

Two items on patients' information-seeking styles were used in this analysis. Respondents were asked to indicate how often they asked their healthcare providers questions about their treatments or medications. The two items were 'Ask questions about the things you want to know and things you don't understand about your treatment' and 'Ask questions until you clearly understand the purpose for taking each of your medication'. Response choices for both items were 'never', 'almost never', 'sometimes', 'fairly often' and 'always'.

Table 1 Bivariate relationships involving demographic and other characteristics and medication nonadherence and their reasons

	No (%)	Yes, because of work, cost or transportation (%)	Yes, for another reason (%)	χ^2	df	*P*
Age (n = 2279)						
18–34 years	1.3	4.8	2.0	110.638	8	0.000
35–44 years	2.9	7.5	7.4			
45–54 years	11.6	24.6	23.0			
55–64 years	33.8	39.6	35.5			
65+ years	50.4	23.5	32.0			
Gender (n = 2328)						
Male	41.3	23.7	41.7	22.716	2	0.000
Female	58.7	76.3	58.3			
Race/Ethnicity (n = 2198)						
White	89.1	74.2	77	52.829	2	0.000
Nonwhite	10.9	25.8	23			
Education (n = 2274)						
Less than high school	6.6	13.8	7.9	40.908	6	0.000
High school	25.2	34.9	20.5			
4 years beyond high school	41.9	38.6	50.8			
More than 4 years beyond high school	26.3	12.7	20.9			
Income (n = 1639) federal poverty level (FPL) four category						
Category 1 (<100% FPL)	6.3	27.3	10.3	150.667	6	0.000
Category 2 (between 100 and 200% FPL)	13.5	35.6	19.0			
Category 3 (between 201 and 300% FPL)	11.5	17.4	12.3			
Category 4 (>300% FPL)	68.7	19.7	58.5			
Insurance (n = 2330)						
No	3.5	20.5	5.6	106.536	2	0.000
Yes	96.5	79.5	94.4			
Financial strain (n = 2308)						
Yes	5.7	71.1	14.7	694.754	2	0.000
No	94.3	28.9	85.3			

Table 2 Multinomial regression showing relationships involving demographic and other characteristics and medication nonadherence and their reasons

					95 % CI for exp (B)	
	Beta (B)	df	*P*	Odds ratio	Lower bound	Upper bound
Yes because of work, cost or transportation						
Intercept	−0.573	1	0.0430			
Age	−0.037	1	0.000	0.964	.947	.981
Educational attainment	0.058	1	0.613	1.059	0.827	1.325
Ask questions about the things you want to know and things you do not understand about your treatment	0.101	1	0.318	1.107	0.907	1.351
Ask questions until you understand about medication	−0.278	1	0.002	0.757	0.633	0.906
Health insurance: No	0.941	1	0.001	2.562	1.443	4.547
Health insurance: Yes		–	–	–	–	–
Financial strain: Yes	3.473	1	0.000	32.242	21.387	48.608
Financial strain: No		–	–	–	–	–
Nonwhite	−0.017	1	0.942	0.984	0.627	1.543
White		–	–	–	–	–
Female	−0.504	1	0.019	0.604	0.397	0.919
Male		–	–	–	–	–
Yes, for another reason						
Intercept	0.857	1	0.101			
Age	0.038	1	0.000	.965	0.952	.978
Educational attainment	0.092	1	0.276	1.097	0.929	1.295
Ask questions about the things you want to know and things you do not understand about your treatment	0.075	1	0.345	1.077	0.923	1.258
Ask questions until you understand about medication	0.200	1	0.000	0.767	0.667	0.881
Health insurance: No	0.469	1	0.036	1.760	1.038	2.984
Health insurance: Yes		–	–	–	–	–
Financial strain: Yes	0.692	1	0.000	2.308	1.488	3.580
Financial strain: No		–	–	–	–	–
Nonwhite	0.627	1	0.016	0.654	0.462	0.925
White		–	–	–	–	–
Male	0.057	1	0.653	1.067	0.805	1.413
Female		–	–	–	–	–

Financial strain

Financial strain was conceptualized by an item asking respondents: 'Thinking about the prescription medications you have been prescribed during the last 6 months, have you experienced days when you had to choose between buying food, paying rent or bills and paying for medications?'[18] Response options were 'yes' or 'no'.

Sociodemographic characteristics

Data were collected about participants' age (18–64, 65+ years), gender (male, female), race/ethnicity, education (less than high school, high school, 4 years beyond high school and more than 4 years beyond high school) and total household income earned before taxes in 2012. To facilitate analysis, the incomes were converted to four categories based on their income compared to the federal poverty level (FPL): group 1 made <100% FPL, group 2 made between 100 and 200% FPL, group 3 made between 201 and 300% FPL, and group 4 made >300% FPL. Also, race was dichotomized into nonwhite and white to facilitate analysis.

Statistical analyses

All analyses were performed using SPSS (version 23, IBM Corp., Armonk, NY, USA). Descriptive statistics were used to describe variables of interest. Bivariate analyses were used to assess associations between medication nonadherence and variables of interest. Most variables that were statistically significant were used in a multinomial logistic regression analysis to assess factors associated with medication nonadherence because of cost, transportation or work and medication nonadherence for another reason. In the multinomial analysis, medication adherence served as the referent group.

Results

Medication nonadherence, demographic factors and health insurance

Among the 2367 participants with hypertension, diabetes or both, 80.6% were over 55 years of age, 60% were female, 86.2% were white, 92.6% had at least a high school education, and 94.5% had health insurance. About 19% reported

to have skipped their medication in the past 12 months due to either work, cost, transportation or other reasons.

About 63% of the patients who skipped their medication due to cost, transportation or work were 55 years of age and above (Table 1). Higher proportion of females than males skipped their medication due to cost, transportation or work (76.3%) or other reasons (58.3%). Among 326 whites who skipped their medications, 40.5% did so because of work, cost or transportation whereas 59.5% did so for other reasons. Among 59 African Americans and 25 Hispanics who skipped their medications, 44.1% and 44.0% did so because of work, cost or transportation, with 55.9 and 56.9% doing so for other reasons respectively (not shown in the table).

Bivariate analysis showed statistically significant associations between medication nonadherence and sociodemographic factors, namely age ($\chi^2 = 110.638$, df = 8, $P < 0.001$), gender ($\chi^2 = 22.716$, df = 2, $P < 0.001$), race ($\chi^2 = 52.829$, df = 2, $P < 0.001$), income ($\chi^2 = 150.667$, df = 6, $P < 0.001$) and educational attainment ($\chi^2 = 40.908$, df = 6, $P < 0.001$; Table 1). Further bivariate analysis showed a statistically significant relationship between medication nonadherence and health insurance ($\chi^2 = 106.536$, df = 2, $P < 0.001$; Table 1).

Medication nonadherence and financial strain

About 71% of those who were not adherent to their medications due to transportation, cost or work had a situation where they had to choose between buying food, paying rent or bills and paying for medications. Among those who missed their medications for other reasons besides transportation, cost or work, 14.7% reported similar situation. Smaller proportion (5.7%) of those who were adherent to their medications reported financial strain.

Patients who experienced some form of financial strain where they had to choose between food, paying rent or bills and paying for medication were less likely to adhere to their medication ($\chi^2 = 694.754$, df = 2, $P < 0.001$) than those who did not have such financial strain.

Medication nonadherence and patients' information seeking

There were statistically significant associations between medication nonadherence and the frequency of a) asking questions about the things respondents would like to know and things they do not understand about their treatment ($\chi^2 = 21.166$, df = 10, $P < 0.02$), and b) asking questions until respondents understand the purpose of taking medications ($\chi^2 = 48.454$, df = 10, $P < 0.001$).

Multinomial logistic regression

Although bivariate analysis showed statistically significant association between medication nonadherence and sociodemographic variables such as age, gender, education level, race and income, multinomial logistic regression for medication nonadherence because of work, cost or transportation showed statistically significant associations only with age (OR 0.964, 95% CI 0.947–0.981, $P < 0.001$) and gender (OR = 0.604, 95% CI 0.397–0.919, $P < 0.05$). Patients who never asked questions to the healthcare provider until they understood the purpose of taking their medications were less likely to adhere to their medications due to work, cost or transportation (OR = 0.757, 95% CI = 0.633–0.906). Moreover, never asking questions to understand treatment was not significantly associated with both medication nonadherence resulting from work, cost or transportation, and other reasons.

There was a strong association between nonadherence due to work, cost or transportation and financial strain (OR 32.242, 95% CI 21.387–48.608, $P = 0.000$). Patients without health insurance were also more likely to be nonadherent to their medications due to work, cost or transportation (OR 2.562, 95% CI 1.443–4.547, $P = 0.001$).

For nonadherence to medications due to other reasons besides work, cost and transportation, multinomial regression analysis revealed statistically significant associations for demographic variables, such as age (OR = 0.965, 95% CI = 0.952–0.978) and ethnicity (OR = 0.654, 95% CI = 0.462–0.925) with whites less likely to adhere to their medication due to reasons other than work, cost or transportation. Similarly, financial strain (OR 2.308, 95% CI 1.488–3.580, $P = 0.000$) and never asking questions until patient understands the purpose for each medication (OR 0.767, 95% CI 0.667–0.881, $P = 0.000$) were both significantly associated with medication nonadherence due to reasons other than work, cost or transportation.

Respondents without health insurance (OR 1.760, 95% CI 1.038–2.984, $P = 0.036$) were more likely to be medication nonadherent due to reasons other than work, cost and transportation.

Sociodemographic factors (age, gender, race, educational attainment and income), patient's information-seeking style, financial strain and health insurance explained 21.5% of the variance (Cox and Snell pseudo *R*-square test) in respondents' likelihood of not adhering to their medications.

Discussion

The overall nonadherence rate of 19% appears low when compared with that of a previous study that had an overall mean nonadherence rate of cardiovascular and antidiabetic medication of 41%.[34]

We found that financial strain and never asking questions until they understood the purpose of their medications were both associated with medication nonadherence among patients with diabetes and/or hypertension in central Texas. However, never asking questions about treatment was not associated with medication nonadherence. That medication adherence is associated with patients' persistence in asking questions about their medications until they understood the purpose for taking them is the most important contribution of this study. This finding shows that the type of question patients ask about their medications is key to medication adherence. Moreover, the findings indicate that relevant

information could positively influence medication adherence as espoused in the IMB model of adherence.[32]

These important findings have implications for practice and research. First, the role of patients as active participants in their health care cannot be underestimated.[35] The outcome of this study calls for a need to require patients to ask relevant questions on their medications and enhance health literacy of patients. This could include having directions in clinicians' offices encouraging patients to ask questions about their medications until they understood the purpose for taking them. Having these directions in English and Spanish would be culturally appropriate. While healthcare providers need to ask patients relevant questions about the purpose for taking medications and their side effects, patients should also be encouraged to ask relevant questions that pertain to their medications. There is a need to shift from passive patient–provider communication – which is characterized by patients being mere listeners to healthcare provider advice – to active or participatory patient–provider communication whereby patients ask relevant questions.[36] Practitioners should consider educational interventions that target patients and their caregivers.[37]

Some studies on patient–provider communication ask patients to indicate what their healthcare providers did during their encounter, but perhaps also asking patients to indicate what they did, as shown by the current study, could be relevant. Second, given the association between ethnicity and medication nonadherence resulting from issues other than cost, work or transportation, there is a need for culturally relevant interventions, especially focusing on communication. According to the IMB model of adherence, the beliefs of patients about outcomes of adherent and nonadherent behaviour may motivate them to adhere to their medications.[32] Differences in such beliefs among different ethnicities may impact nonadherence. Thus, medication interventions need to be tested in relevant populations, especially nonwhite populations such as blacks and Latinos. Knowing patient's preferences for particular communication interventions could help them engage with their healthcare providers and caregivers in meaningful ways to promote medication adherence.

In regard to the effect of financial strain on medication nonadherence, our findings are consistent with previous studies that linked financial strain to medication nonadherence resulting from costs.[38,39] Moreover, for medication nonadherence resulting from reasons other than cost, work or transportation, it was surprising that those with financial strain were associated with it. It may be possible that financial strain could impact the patient's well-being and self-esteem, which could further lead to medication nonadherence. Such reasons need to be explored. Moreover, there is a need to address financial strain among patients with diabetes or hypertension. Providing financial incentives could help decrease medication nonadherence.[40] While access to health insurance is necessary, the potential role of transportation in enhancing medication adherence should not be ignored.

Our findings linking sociodemographic factors – age, gender and educational attainment – to medication nonadherence are similar to other studies that showed that gender[38,39] and educational attainment[41–43] have no effect, but age[44] and ethnicity[45] have an effect on medication nonadherence. Our study shows that for those who reported nonadherence to medications because of other reasons besides cost, work and transportation, ethnicity and health insurance were statistically significant. Prior studies show health insurance as statistically associated with the likelihood of medication nonadherence because of cost, work or transportation,[46] but not for other factors.[47]

Our study also shows that the odds ratio for nonadherence due to work, cost or transportation and health insurance is higher than that for nonadherence due to other factors and health insurance. This finding is not surprising given that cost was a factor in the former case. However, the significant association between ethnicity and medication nonadherence because of other factors besides cost, work or transportation was an unexpected finding. We expected ethnicity to be linked to cost, transportation or work in part because a systematic review of transportation barriers to access to health care found that five out of six studies had differences across ethnic groups.[46] That ethnicity was statistically associated with medication nonadherence resulting from other reasons may be linked to the potential impact of health literacy[47,48] and culture. For example, a study has found that African Americans were more likely than whites to use religion to cope with systemic lupus erythematous and were more concerned about long-term medication effects.[49]

In our study, nonwhites were 1.5 times more likely than whites to miss their medications because of reasons other than cost, transportation or work. Unlike, asking questions until respondents understand the purpose for taking each medication, merely asking questions about the things respondents would like to know and things they do not understand about their treatment was not significant in the multinomial model. Such a finding suggests that the nature and quality of communication that relates to medication use could be more important in addressing nonadherence to medications. Poor patient–provider communication has been found to increase nonadherence among patients with diabetes.[50,51]

To the best of our knowledge, this is an important study because it explores self-reported medication nonadherence resulting from cost, work and transportation, and other reasons and factors such as patients' information seeking and financial strain in adults with diabetes, hypertension or both.

The study's population-based data source and the regional focus are strengths. Our measure of nonadherence to medications also includes reasons for medication nonadherence. Most studies estimate nonadherence to medications generally without differentiating between cost and non-cost-related factors.[52,53] One of the studies that explored cost- and non-cost-related medication adherence found that whites reported less nonadherence than blacks and Hispanics, but there were no racial or ethnic differences in non-cost-related adherence factors such as experiences.[54]

Race also has been associated with not following physician instructions on how to take medications, with elderly African Americans more likely than whites to have this problem.[50]

Therefore, our analysis failing to identify associations between ethnicity and medication nonadherence resulting from cost, transportation or work, but finding a statistically significant relationship between ethnicity and medication nonadherence resulting from other factors suggests a need to further explore cost- and non-cost-related factors that influence medication nonadherence among adults with hypertension, diabetes or both.

Nevertheless, our study has some limitations. Methodologically, the sampling approach likely underestimated the number of younger people, blacks and Hispanics. The response rate of only 22% might have also played a role in this underestimation. Thus, the findings in terms of sociodemographic characteristics must be interpreted with caution. Our study relied on the recall of medication nonadherence in the past 12 months, which appears to be a long time frame when compared with many studies,[52,53] and could thus result in recall bias.[55] Its focus on a single questionnaire item on medication adherence could impact its accuracy in measurement. Many studies on medication nonadherence use validated instruments with multiple items for measuring medication adherence, which was not the case for our study. However, studies show that single-item measures are good at predicting medication nonadherence and that no particular medication adherence measure appears superior.[52] The use of self-reports rather than objective measures might have also affected the result. However, self-reported measures could help researchers identify reasons for medication nonadherence.[56] Moreover, health literacy and even illiteracy, which were both not assessed in this study,– can be a strong confounder in this study. Our study also did not specify the type of healthcare provider, and thus, it is unknown whether posing relevant questions to specific healthcare providers may lead to different medication adherence outcomes.

Combining the three reasons for nonadherence – work, transportation and cost – into one measure might have resulted in financial strain potentially confounding it. This may explain the finding that whereas those with financial strain were 32 times more likely to not adhere to their medications for cost, work and transportation reasons, they were only 2.3 times more likely to not adhere to medications because of other reasons. Future studies with large samples may need to consider medication nonadherence resulting from cost, work or transportation separately.

We also did not look at the individual diseases separately. Thus, it is unknown whether the results could favour one disease more than the other. Nevertheless, our study mirrors others that simultaneously assessed adherence among patients with diabetes and hypertension. The survey did not have information on the number of medications respondents were taking, which may have affected the results. For example, as the number of medications increase for a patient, nonadherence is likely to increase. Qualitative studies are needed to help explore more contexts. Future mixed studies that explore medication nonadherence from the perspectives of clinicians, caregivers and patients could elucidate more context-specific or culturally relevant factors.

Conclusion

An important contribution of our study is that requiring patients to ask questions about their medications until they clearly understand the purpose for taking them is significantly associated with medication adherence among adults with diabetes and/or hypertension, thus supporting the IMB model of medication adherence. Moreover, the impact of financial strain on medication nonadherence resulting from factors other than cost, transportation or work indicates that such factors need to be explored.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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Authors' contributions

BA was involved in research concept, study design, data analysis, interpretation of results, writing and reviewing the manuscript. JNB was involved in study design, data analysis, interpretation of results and reviewing the manuscript. SC was involved in data analysis, interpretation of results and reviewing the manuscript. AP was involved in interpretation of results, writing and reviewing the manuscript RWH was involved in study design and review of manuscript. SNF was involved in study design and review of manuscript KRM was involved in study design and review of manuscript. All authors reviewed and approved the final draft of the manuscript.

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