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Complete List of Authors:	Shiyanbola, Olayinka; University of Wisconsin Madison School of Pharmacy, Social and Administrative Sciences Unni, Elizabeth; Roseman University of Health Sciences, Huang, Yen-ming; University of Wisconsin Madison School of Pharmacy, Social and Administrative Sciences Lanier, Cameron; University of Wisconsin Madison School of Pharmacy, Social and Administrative Sciences
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Utilizing the Extended Self-Regulatory Model to Characterize Diabetes Medication Adherence: A Cross-Sectional Study

Olayinka O Shiyanbola, [1] Elizabeth Unni, [2] Yen-Ming Huang, [1] Cameron Lanier[1]

[1] Division of Social and Administrative Sciences, School of Pharmacy, University of Wisconsin-Madison, Wisconsin, USA

[2] Department of Pharmaceutical Sciences, College of Pharmacy, Roseman University of Health Sciences, Utah, USA

Corresponding Author: Olayinka O. Shiyanbola; Division of Social and Administrative Sciences, School of Pharmacy, University of Wisconsin-Madison, 777 Highland Avenue Madison, WI 53705, USA (e-mail: Olayinka.Shiyanbola@wisc.edu)

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Keywords: Medication Adherence, Beliefs in Medicines, Illness Perceptions, Type 2 diabetes, Clustering

Objectives: To cluster the adherence behaviors of patients with type 2 diabetes based on their beliefs in medicines and illness perceptions and examine the psychosocial, clinical and socio-demographic characteristics of patient clusters.

Design: Cross-sectional study

Setting: A face-to-face survey was administered to patients in two family medicine clinics in the Midwest, USA.

Participants: One hundred and seventy four English-speaking ≥ 20 years old adult patients with type 2 diabetes who were prescribed at least one oral diabetes medicine daily were recruited using convenience sampling.

Primary and secondary outcome measures: Beliefs in medicines and illness perceptions were assessed using the Beliefs about Medicines Questionnaire and the Brief Illness Perceptions Questionnaire respectively. Self-reported medication adherence was assessed using the Morisky Medication Adherence Scale. Psychosocial correlates of adherence, health literacy and self-efficacy, were measured using the Newest Vital Sign and the Self-efficacy for Appropriate Medication Use respectively. Two-step cluster analysis was used to classify patients.

Results: Participants' mean age was 58.74 (SD = 12.84). The majority were female (57.5%). Four clusters were formed (ambivalent, skeptical (non-adherent clusters), indifferent, and accepting (adherent clusters)). The ambivalent cluster (n = 30, 17.2%) included low adherent patients with high necessity beliefs, high concern beliefs, and high illness perceptions. The skeptical cluster (n = 53, 30.5%) included low adherent patients with low necessity beliefs, but high concern beliefs and high illness perceptions. Both the accepting (n = 40, 23.0%) and indifferent (n = 51, 29.3%) clusters were comprised of patients with high adherence. Significant differences between the ambivalent, skeptical, accepting and indifferent adherent clusters were

based on self-efficacy, illness perception domains (treatment control, coherence), and hemoglobin A1c ($p < 0.01$).

Conclusions: Patients with diabetes in specific non-adherent and adherent clusters still have distinct beliefs as well as psychosocial characteristics that may help providers target tailored medication adherence interventions.

Strengths and limitations of this study

- This is the first study to use a clustering technique to allow for algorithm-based grouping based on both beliefs in medicines and illness perceptions founded on the Extended Self-Regulatory Model among patients with diabetes.
- This study highlighted the importance of content and theory-driven components to enable replication of successful adherence interventions.
- This study focused on the impact of patient psychosocial factors such as their individual perceptions of medication and illness, self-efficacy, and health literacy in the management of diabetes.
- Convenience sample from two clinics in one state, hereby limiting the generalizability of the study.
- The use of a self-reported measure to evaluate medication adherence, rather than objective measures.

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Author Contributors: OOS and EU designed the study. OOS, YH, and CL were involved in data collection and data analysis. OOS wrote the manuscript and EU and YM critically revised the content. All authors approved the final version of the manuscript.

Patient Consent: Obtained

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Ethical approval: The Health Sciences Institutional Review Board of the University of Wisconsin-Madison.

Data sharing statement: No additional data are available.

Introduction

Medication adherence, defined as the extent to which taking medications corresponds with recommendations by a healthcare provider is essential for treatment success. [1] Poor adherence results in increased risk of mortality, increased emergency room visits, and reduced quality of life. [2-5] In general, rates of medication adherence are below 50%. [6] However, for patients with type 2 diabetes, these rates are as low as 36%. [7] It is estimated that a 10% improvement in diabetes medication adherence would lead to at least a 6.6% reduction in hospitalizations. [7]

Among patients with diabetes, medication adherence has been found to be influenced by psychosocial factors, such as beliefs about illness and treatment, self-efficacy and perceived control, self-regulation, and emotional states. [8] However, the sparse studies on patients with diabetes has generated inconsistent results and does not indicate which factors mainly affect medication adherence. [8-10] Of the various factors that influence medication adherence, Horne and Weinman (2002) showed that socio-demographic and clinical factors explain only a small amount of variance in medication adherence, whereas illness perceptions and patient beliefs in medicines are substantial independent predictors. [11] Since patient clinical and sociodemographics are difficult to change, it makes sense to focus on patient factors that are modifiable, practical for intervention, and can be addressed by health providers.

Studies based on the Extended Self-Regulatory Model show that when patients are diagnosed with an illness, they develop a pattern of beliefs about their condition and treatment, which then influences their medication adherence. [12-17] The Self-Regulatory Model (also called the Common Sense Model) was developed to explain illness-related coping behaviors including adherence to treatment, based on patient perceptions of their illness. [18] When research identified beliefs about treatment as proximal determinants of coping strategies such as medication

adherence compared with illness perceptions, Horne et al. extended the Self-Regulatory Model by integrating beliefs about treatment into the original model. [11,12] In prior research, Phillips and colleagues suggested that patient adherence was greater when illness and treatment perceptions were addressed or discussed during patients' medical encounter and that healthcare providers were better able to judge patient agreement regarding the illness and treatment when patients reported these discussions occurred. [19,20]

To design feasible and useful medication adherence interventions, Horne et al originally classified patients with chronic illnesses into four attitudinal groups (accepting, ambivalent, skeptical, and indifferent) based on their beliefs about their treatment. [21] While "accepting" patients, with high necessity beliefs and low concerns had the highest medication adherence, "skeptical" patients, with low perceived need of medications and high concerns, had the lowest adherence levels. Other patient groups, the "ambivalent" (high necessity beliefs and high concerns), and the "indifferent" (low necessity beliefs and low concerns) were also likely to be non-adherent. Though medication non-adherence is a common problem among patients with chronic illnesses, they hardly discuss this behavior with their health providers during routine visits. [22] Various available tools used to identify medication adherence are not usable in clinical consultations because of the short time available to providers. [23] Hence, clustering patients' adherence behavior based on their beliefs may provide a mechanism for providers to focus on the specific belief needs of the patients in the context of their psychosocial characteristics. A previous study based on the Extended Self-Regulatory Model used both illness perceptions and beliefs in medicines to cluster patients with asthma and was able to develop the same clusters as developed by Horne et al. [24] Additionally, each cluster had psychosocial characteristics that was

unique to them. However, further studies were needed to determine whether the four attitudinal group structure that includes illness perceptions also holds with other chronic disease conditions.

The objectives of this study were to:

1) Cluster the adherence behaviors of patients with type 2 diabetes based on their beliefs in medicines and illness perceptions.

2) Examine the psychosocial, clinical and sociodemographic characteristics of patient clusters.

This study hypothesized that patient clusters with high concern beliefs and low necessity beliefs will also have high threatening illness perceptions, and groups with low concern beliefs and high necessity beliefs will have low threatening illness perceptions.

Methods

Using a cross-sectional study design, a face-to-face survey was administered to English-speaking ≥ 20 years old patients with type 2 diabetes who were prescribed at least one oral diabetes medicine daily. Patients were recruited using convenience sampling. Information on eligible patients were retrieved from the electronic health record database of two family medicine clinics in a Midwestern state in the United States.

Data collection

Front desk receptionist at the two clinics provided study information sheets to eligible patients who were waiting for their appointment. After patients reviewed the information, they met with a research assistant to indicate their interest in participating. The research assistant verified the patient's eligibility from the clinic's patient log, administered the informed consent form, and completed the 20-30 minutes survey with the consented participant in a private area in the clinic. Participants were allowed to complete the survey before or after their scheduled clinic appointments, depending on clinic flow and their preferences. Informed consent was obtained

from all individual participants included in the study. All data collection occurred from March 2016 to August 2016. Patients were compensated with $25 cash, upon completion of the survey. The University Health Sciences Institutional Review Board approved the study.

Measures

Self-reported medication adherence was assessed using the 8-item Morisky Medication Adherence Scale (MMAS-8), a widely used scale in patients with diabetes. [25-29] The total score of the MMAS-8 ranged from 0 to 8 and MMAS-8 scores of < 6, 6 to < 8, and 8 reflected low, medium, and high medication adherence, respectively. [26] The 10-item Beliefs in Medicines Questionnaire (BMQ) was used to measure patient beliefs in medications. [30] The BMQ includes the necessity beliefs and concern beliefs sub-scales measured on five-point Likert-type scales with 'strongly disagree' to 'strongly agree' response options. [30] The range of scores for each sub-scale is 5-25, with a higher score meaning stronger concern beliefs or stronger necessity beliefs about the medicine. The 8-item Brief-Illness Perceptions Questionnaire (B-IPQ) was used to measure patients' perceptions about diabetes. [31] This validated instrument includes survey items assessing patient illness perceptions about diabetes along the cognitive domains of the self-regulatory model as well as their emotional responses to having diabetes. [31] Each survey item of the B-IPQ was assessed on a scale of 0-10 with higher scores indicating stronger threatening perceptions along the illness perception dimensions.

Finally, we assessed other patient psychosocial correlates of medication adherence, i.e. health literacy and self-efficacy. Health literacy assessed using the 6-item Newest Vital Sign (NVS) [32,33] has been extensively used across studies including patients with type 2 diabetes and can be completed in a short time (3-5minutes). [34,35] Each question was scored as "0" for an incorrect response and "1" for a correct response for a total score of 0 to 6. Patients with scores

less than 2 represented a high likelihood of inadequate health literacy, 2 to 3 indicated the possibility of marginal health literacy, and more than 3 suggested adequate health literacy.

Self-efficacy measured using the 13-item Self-efficacy for Appropriate Medication Use Scale (SEAMS) was used in examining medication self-efficacy in chronic disease management, and is appropriate regardless of patient literacy skills. [36,37] Patients indicated under a range of situations, their level of confidence regarding taking medications correctly using a 3-point Likert scale (1 = not confident, 2 = somewhat confident, and 3 = very confident). The total score of the SEAMS ranged from 13 to 39 with higher scores indicating more confidence in adhering to medication use. [36]

Other variables included sociodemographic factors such as age, gender, highest education level, race, health insurance, and the annual household income level; patient clinical factors such as the number of chronic illnesses, self-reported health status, number of medications used, frequency of daily diabetes medication use, duration of diagnosis of type 2 diabetes, and whether the patient used insulin or not. Besides the main predictor variables, patients' hemoglobin A1c (HbA1c) values in the prior six months were retrieved from electronic medical records, with lower HbA1c values $\leq 7.0\%$ representing better glycemic control. The average duration between the day of the latest HbA1c testing and the day of patient completing the survey was 43.3 ± 84.6 days (median: 7 days).

Data analysis

A two-step cluster analysis was used to classify patients' medication adherence behavior based on their beliefs in medicines and illness perceptions. The number of clusters to be formed was kept a priori at four, a number determined by the researchers based on Horne's earlier studies and our prior work. [21,24,38-40] The cluster analysis technique organizes observed data (e.g. patients)

into meaningful groups or clusters based on combinations of the independent variables. This process maximizes the similarity of cases within each cluster but also maximizes the dissimilarity between the groups based on the log-likelihood distance between the data points. Using this method allows the clusters to be created without a preconceived notion of what the clusters may look like. In the first step, each data record was either considered as a new cluster or was added to a previously formed cluster. In the second step, the clusters formed from the first step were compared and merged based on the distance between them. Then, we assessed the goodness of fit of the clustering solution. The silhouette measure of cohesion and separation was used to evaluate the overall goodness-of-fit of the clusters. [41] A silhouette measure varies between -1 and 1 based on the average distances between the objects. The value of a silhouette measure less than 0.20 indicates a poor solution quality, a value between 0.20 and 0.50 suggests a fair solution, whereas a value of more than 0.50 represents a good solution. [42] Once categorized, the clusters were then characterized based on various sociodemographic and clinical characteristics. For the continuous variables, one-way ANOVA was used to determine the psychosocial (health literacy and self-efficacy), clinical (e.g. number of medicines) and socio-demographic (e.g. age) factors that varied between the clusters. For the categorical variables such as gender and race, chi-square tests were used to examine the differences between the clusters. SPSS version 23 was used for all the analyses.

Patient and Public involvement

No patients were involved in the study design, development of the research questions and outcome measures, recruitment, or implementation. The results of the study will be disseminated to study participants through access to the published article once published in the journal.

Results

One hundred and ninety-nine patients were approached and 174 patients participated (87.4% response rate). The participant's mean age was 58.74 (SD = 12.84). The majority were female (57.5%), non-Hispanic white (67.8%) and African American (24.7%). Approximately 62.1% had completed at least a college or technical degree, and 57.5% had an annual household income of equal or more than $20,000. Of the 174 patients, 40.8% had low medication adherence, 35.1% had medium medication adherence, and 24.1% had high medication adherence.

The two-step cluster analysis produced four distinctive clusters categorized as ambivalent, skeptical, indifferent, and accepting. The characteristics of the clusters based on medication adherence, beliefs in medicines, illness perceptions, health literacy, self-efficacy, and all demographics are reported in Table 1. The distribution of participants across the clusters ranged from 17.2% to 30.5%. The silhouette measure was 0.4 which indicated a satisfactory cluster quality and the ratio of the largest to smallest cluster was acceptable at 1.77. As hypothesized, high concern beliefs was related to high threatening illness perceptions and low adherence and vice versa. Table 2 describes the distinctive psychosocial and clinical characteristics of each cluster. The ambivalent cluster (n = 30, 17.2%) included low adherent patients with high necessity beliefs, high concern beliefs, and high illness perceptions. The skeptical cluster (n = 53, 30.5%) included low adherent patients with low necessity beliefs, but high concern beliefs and high illness perceptions. Both the accepting (n = 40, 23.0%) and indifferent (n = 51, 29.3%) clusters were comprised of patients with high adherence. Significant differences were found between the ambivalent, skeptical, accepting and indifferent adherent clusters based on self-efficacy ($p = 0.002$), beliefs in medicines ($p < 0.001$), illness perception domains (consequence ($p < 0.001$), personal control ($p < 0.001$), treatment control ($p < 0.001$), identity ($p < 0.001$),

concern ($p < 0.001$), coherence ($p = 0.027$), and emotional representations ($p < 0.001$)), and hemoglobin A1c ($p < 0.05$) (Table 1). While non-adherent clusters had low self-efficacy and high HbA1c levels, it was vice versa for the adherent clusters. Patients in the ambivalent non-adherent cluster were younger in age compared to those in the adherent clusters, less likely to have attended some college or technical school, and likely to be non-white.

Discussion

This study used the Extended Self-Regulatory Model to cluster the adherence behavior of patients with type 2 diabetes based on beliefs in medicines and illness perceptions, as well as examine the characteristics of the clusters and the significant differences between them. Four clusters with distinct beliefs and psychosocial characteristics associated with each group were formed. The adherence clusters developed in this study by using both beliefs in medicines and illness perceptions are similar to the clusters formed by Horne et al in his previous studies where only beliefs in medicines were used. By including illness perceptions and other psychosocial correlates of adherence, this study identified other pertinent information related to each cluster that may help in developing guided and targeted interventions for providers working with diabetes patients who may be non-adherent.

Patients in the ambivalent cluster were the least adherent to their medicines followed by the skeptical cluster. These clusters together comprised 48% of the whole sample. These results are similar to previous studies where these specific clusters represent the non-adherent proportion of a sample. [21,24] Contrary to a prior study [39], ambivalent patients had the lowest adherence to diabetes medicines, the strongest concerns about their medicines and the strongest threatening illness perceptions. In spite of their strong concerns about medicines, ambivalent patients also perceived that their medications were necessary to maintain their health. Further

analysis revealed that their strong threatening perceptions about diabetes were from their individual illness perception domains including high emotional representations, lack of treatment control, high concern about illness, less coherence, and experiencing many severe symptoms due to diabetes. Despite the belief that medications are necessary, patients in the ambivalent cluster may be cognitively and emotionally overwhelmed with the demands of managing diabetes. Diabetes is psychologically demanding and requires adaptive self-care tasks related to being chronically ill, including taking medications as prescribed. [43-45] Because of this, when patients fail to self-manage their disease, it may give rise to feelings of guilt, frustration, anger, and hopelessness. These negative feelings may foster a pessimistic attitude towards diabetes, leading to negative beliefs about the illness and medication, and poor medication adherence. [46]

Ambivalent patients in this study also had the least self-confidence that they could take and manage their medications correctly and had the lowest health literacy scores. These patients also took the highest number of medicines, had the highest number of chronic illness, and had poor glycemic control (highest hemoglobin A1c values). In addition, ambivalent patients were the youngest among the four clusters and had the least education which might account for their inadequate health literacy and concerns about illnesses and medicines. Tailored adherence interventions aimed at these patients may need to build their self-efficacy and address their low health literacy. Prior research shows that by providing information in simple plain language, using teach-back techniques, and showing patients how they can be expert self-managers and engage in self-monitoring; patients are more likely to feel more in control of their illness, less concerned about the illness, and manage their illness more effectively. [47]

In the skeptical cluster, patients had strong concerns about medicines and threatening illness perceptions, although not at a pronounced degree as the ambivalent group. They also did

not think their medications were necessary. Contrary to previous studies in asthma, epilepsy, inflammatory bowel disease, depression and cardiac disease, where the skeptical groups were most non-adherent to their medications [24,39,40], the skeptical group of patients with diabetes in this study did not have the lowest medication adherence. Though this cluster of patients had perceptions of strong consequences from the illness, lack of treatment control, high concerns, high emotional representations, less understanding of their illness, were experiencing many symptoms due to diabetes, and were not confident they could manage their medications; they also had high health literacy. For these patients, it is possible that because they have an increased ability to search, understand, and process health information; they are engaged in seeking information to manage their diabetes themselves, perform other diabetes self-management practices, and therefore do not believe they need medicines. A prior study has shown that patients with no educational qualifications (possibly tied to health literacy) are likely to have doubts about their personal need for medicines compared with patients with any formal educational qualifications. [40] Additionally, their self-perceived better health status may also be contributing to their perception that medications are not necessary for maintaining their health, hence, making them skeptical. In spite of their high health literacy, skeptical patients' low self-efficacy may lead to their poor glycemic control especially as prior studies report the strong influence of self-efficacy on diabetes control. [48,49] Adherence interventions that target concerns about medicines and illness, but also aim to motivate patients towards medication use might need to be developed for these group of patients.

Patients in the indifferent and accepting clusters were adherent to their medicines, though different in their beliefs in medicines. Similar to prior studies [21,24,39,40], patients in the accepting group were more likely to be adherent to their medicines. These patients are generally not

concerned about their illness, believe that their medications are necessary and are least concerned about them, feel the most confident that they can take their medications correctly, and have the ability to process and understand health information. This group of patients however still believe that their diabetes affects their life, and still have some concern about it. The accepting patients were the oldest in age, the most educated, and have had their diabetes longer compared to patients in other clusters. Since these patients' HbA1c values still show that their diabetes is uncontrolled and using medications as part of diabetes management may not be concerning; interventions may seek to address concerns about their diabetes, especially as it relates to other complex diabetes self-management issues such as checking blood sugars, exercising, and diet etc. Since these older and well educated patients have had diabetes for a long time and use a lot of medications, providers may continue to encourage self-monitoring of symptoms, adverse drug events, and check for other indicators of poor diabetes outcomes such as high blood pressure and high cholesterol. [50]

Contrary to previous studies [21,24] where patients who were in the indifferent cluster were reported to be non-adherent to their medicines, the current study showed that the patients in this cluster were adherent to their medicines and their diabetes seemed to be in better control than patients in the three other clusters. Though the patients in the indifferent cluster were the least likely to believe that their medications were necessary, they were also least concerned about their medicines, were not threatened by their illness, and were not emotionally affected by it (low emotional representation). Also, they experienced few symptoms due to their illness, and had the least concern about their illness. It is also possible that because these patients were taking the lowest number of medicines and had the lowest number of chronic illness, they were healthier compared to other patients, and therefore more likely to easily manage their medicines. Providers

may continue to address the needs for taking medicines and provide interventions that emphasize the need for taking medicines.

This study has several strengths. Horne et al (2009) classified patients' adherence behaviors based on beliefs in medicines using the mid-point score of the Beliefs in Medicines questionnaire. However, this current study used the clustering technique to allow for algorithm-based grouping based on both beliefs in medicines and illness perceptions founded on the Extended Self-Regulatory Model. Prior research has highlighted the importance of content and theory-driven components to enable replication of successful adherence interventions. [47] While it is important to address diabetes nonadherence via clinical interventions, we cannot underestimate the impact of patient psychosocial factors such as their individual perceptions of medication and illness, self-efficacy, and health literacy in the management of diabetes. Brief, valid, and reliable questionnaires that can easily quantify these psychosocial factors are available and may be included in adherence support programs. [40]

The study limitations are the use of a convenience sample from two clinics in one state, hereby limiting the generalizability of the study. The use of a self-reported measure to evaluate medication adherence, rather than objective measures such as the use of pill counts might lead to overestimation. However, prior studies show the reliability and validity of self-report adherence measures. Data were collected either before or after patients' medical encounter depending on the flow of the clinic. The timing of the medical encounter may influence patient responses to questions about illness and treatment beliefs. This variable was not accounted for in the data analysis. The concurrent assessment of illness perceptions, beliefs in medicines, and adherence in a cross-sectional manner is a limitation. A longitudinal study that evaluates changes in beliefs overtime and examines how these changes relate to changes in behavior and outcomes will be

considered in the future. HbA1c was measured retrospectively. Though we used the most recent values from patients' medical record which is acceptable by clinical practitioners for standard diabetes care, this retrospective measurement ofbA1c could have limited our results. Though the B-IPQ total score categorizes respondents into two categories without taking into consideration the individual domains of the illness perceptions, this was needed for clustering their adherence. Once the clusters were formed, the illness perception domain characteristics of each cluster were analyzed and compared.

Conclusions

This study used a cluster analysis to characterize patients' adherence behavior based on their beliefs in both medicines and illnesses and psychosocial factors. Using evidence-based theoretical approaches, four clusters were formed with characteristics that suggest different types of interventions for each cluster. Medication nonadherence is a complex behavior to understand and targeted interventions are often recommended. Data that can help discriminate between large groups of non-adherent individuals is needed in developing more personalized interventions. Though a large number of patients in two separate clusters (ambivalent and skeptical) were non-adherent to their medicines; patients within each non-adherent clusters still had distinct beliefs in medicines, illness perceptions, and other psychosocial characteristics that may help providers target tailored behavioral, psychological-based adherence interventions (for ambivalent clusters), as well as education and motivation-based adherence interventions (for skeptical clusters). Also, patients who are adherent may still need interventions that support and/or enhance their use of medicines (for indifferent clusters), and support individualized self-management strategies used for control of illness (for accepting clusters).

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Table 1 Mean score and percentage comparison of adherence, psychosocial factors, and demographics between clusters (n=174)

Variables	Total	Cluster 1 (Ambivalent)	Cluster 2 (Skeptical)	Cluster 3 (Indifferent)	Cluster 4 (Accepting)
Number of subjects	174	30 (17.2%)	53 (30.5%)	51 (29.3%)	40 (23.0%)
Medication adherence[a, ***]	5.87 ± 1.87	4.87 ± 1.78[g, h]	5.43 ± 1.89[j]	6.39 ± 1.67[g]	6.53 ± 1.72[h, j]
Necessity beliefs (Mean ± SD)[***]	18.88 ± 4.27	21.93 ± 2.77[f, g]	18.23 ± 1.76[f, i, j]	14.59 ± 3.71[g, i]	22.93 ± 2.18[j]
Concern beliefs (Mean ± SD)[***]	13.24 ± 4.35	18.83 ± 3.66[f, g, h]	14.85 ± 2.07[f, i, j]	11.12 ± 2.71[g, i]	9.60 ± 3.41[h, j]
Illness perceptions (IP) (Mean ± SD)[b, ***]	37.13 ± 11.06	48.33 ± 8.39[f, g, h]	41.72 ± 6.23[f, i, j]	27.63 ± 9.87[g, i, k]	34.78 ± 8.07[h, j, k]
Consequence IP [b, ***]	4.88 ± 2.91	7.30 ± 2.55[f, g, h]	5.13 ± 2.43[f, i]	2.94 ± 2.60[g, i, k]	5.20 ± 2.55[h, k]
Timeline IP [b]	8.20 ± 2.44	8.07 ± 2.49	8.51 ± 1.85	7.53 ± 2.98	8.73 ± 2.18
Personal control IP [b]	3.53 ± 2.51	3.73 ± 3.06	4.13 ± 2.31	3.20 ± 240	3.00 ± 2.33
Treatment control IP [b, ***]	1.93 ± 2.03	2.57 ± 2.54[h]	2.57 ± 1.82[j]	1.75 ± 2.01	0.83 ± 1.34[h, j]
Identity IP [b, ***]	4.51 ± 2.91	7.17 ± 2.30[f, g, h]	5.17 ± 2.41[f, i, j]	2.35 ± 2.50[g, i]	4.40 ± 2.43[h, j]
Concern IP [b, ***]	6.85 ± 2.82	8.63 ± 2.09[g]	7.38 ± 2.11[i]	4.98 ± 3.22[g, i, k]	7.20 ± 2.31[k]
Coherence IP [b, *]	2.79 ± 2.52	3.53 ± 3.56	3.15 ± 1.91[j]	2.69 ± 2.65	1.88 ± 1.84[j]
Emotional representation IP [b, ***]	4.45 ± 3.32	7.33 ± 2.71[g, h]	5.68 ± 2.56[i, j]	2.20 ± 2.99[g, i]	3.55 ± 2.72[h, j]

Self–efficacy (Mean ± SD)[c, **]	33.24 ± 5.96	31.30 ± 6.65[h, J]	32.02 ± 6.18[J]	33.47 ± 6.11	36.00 ± 3.64[h, J]
Health literacy (Mean ± SD)[d]	3.72 ± 2.02	3.13 ± 1.94	3.96 ± 1.91	3.80 ± 2.11	3.75 ± 2.08
Inadequate		7 (23.3%)	7 (13.2%)	7 (17.5%)	10 (19.6%)
Marginal		11 (36.7%)	10 (18.9%)	9 (22.5%)	9 (17.6%)
Adequate		12 (40.0%)	36 (67.9%)	24 (60%)	32 (62.7%)
Age	58.74 ± 12.84	55.17 ± 14.00	57.85 ± 11.48	59.04 ± 13.92	62.20 ± 11.73
White[**]	118 (67.8%)	12 (40.0%)	38 (71.7%)	29 (72.5%)	39 (76.5%)
Female	100 (57.5%)	18 (60.0%)	30 (56.6%)	20 (50.0%)	32 (62.7%)
Education higher than high school	108 (62.1%)	15 (50.0%)	32 (60.4%)	35 (68.6%)	26 (65.0%)
Education					
Completed 8th grade or less	4 (2.3%)	1 (3.3%)	0 (0.0%)	1 (2.0%)	2 (5.0%)
Some high school	15 (8.6%)	5 (16.7%)	3 (5.7%)	5 (9.8%)	2 (5.0%)
High school graduate or GED	47 (27.0%)	9 (30.0%)	18 (34.0%)	10 (19.6%)	10 (25.0%)
Some college or technical school	67 (38.5%)	10 (33.3%)	14 (26.4%)	26 (51.0%)	17 (42.5%)
College graduate	24 (13.8%)	3 (10.0%)	12 (22.6%)	6 (11.8%)	3 (7.5%)
Graduate degree	17 (9.8%)	2 (6.7%)	6 (11.3%)	3 (5.9%)	6 (15.0%)

Number of medications (Mean ± SD)[***]	7.77 ± 3.89	9.07 ± 4.21[g]	8.19 ± 4.03[l]	5.80 ± 2.86[g, l, k]	8.75 ± 3.75[k]
Number of illness (Mean ± SD)[**]	3.86 ± 1.82	4.50 ± 2.03[g]	3.89 ± 1.96	3.22 ± 1.47[g, k]	4.28 ± 1.66[k]
Duration of diabetes diagnosed (Mean ± SD)[*]	9.58 ± 7.08	8.75 ± 5.79	9.25 ± 6.30	8.03 ± 7.14[k]	12.61 ± 8.13[k]
HbA1c level[*]	7.66 ± 1.64	8.31 ± 2.14[g]	7.86 ± 1.58	7.17 ± 1.32[g]	7.52 ± 1.51
Health status[e, **]	2.64 ± 0.80	2.13 ± 0.90[f, g]	2.72 ± 0.77[f]	2.86 ± 0.75[g]	2.65 ± 0.70

[a] Self-reported medication adherence was measured with the 8-item Morisky Medication Adherence Scale.

[b] Higher scores indicate higher specific illness perceptions. Personal control, treatment control, and coherence are reverse scored.

[c] The score of the self-efficacy on medication use ranges from 13 to 39. 13 items on a 3 point scale. Higher scores indicate higher levels of self-efficacy.

[d] Heath literacy was measured with the Newest Vital Sign (NVS).

[e] One item on a 5 point scale. Higher scores indicate better self-reported health status.

[f-k] Significant differences based on the post-hoc analysis.

[*]$p < 0.05$, [**]$p < 0.01$, [***]$p < 0.001$

Table 2 Beliefs, psychosocial and clinical characteristics of the clusters

	Clusters with non-adherence behavior		**Clusters with adherence behavior**	
	Cluster 1 (Ambivalent)	**Cluster 2 (Skeptical)**	**Cluster 3 (Indifferent)**	**Cluster 4 (Accepting)**
Medication Adherence	Low adherence	Low adherence	High adherence	High adherence
Beliefs in medicines	High NB	Low NB	Low NB	High NB
	High CB	High CB	Low CB	Low CB
Illness perceptions	High IP	High IP	Low IP	Low IP
Self-efficacy	Low SE	Low SE	High SE	High SE
Health literacy	Low HL	High HL	High HL	High HL
Glycemic control	High HbA1c	High HbA1c	Low HbA1c	Low HbA1c
Illness perception domains	High Consequence	High Consequence	Low consequence	High consequence
	High treatment control	High treatment control	Low treatment control	Low treatment control
	High identity	High identity	Low identity	Low identity
	High concern	High concern	Low concern	High concern
	High coherence	High coherence	Low coherence	Low coherence

	High emotional representation	High emotional representation	Low emotional representation	Low emotional representation

The high and low values for each variable is compared based on the mean values from all participants.

CB: concern beliefs; HbA1c: hemoglobin A1c levels; HL: health literacy; IP: illness perceptions; NB: necessity beliefs; SE: self-efficacy.

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Hartley Murray, C.P.M.
Assistant Director, Purchasing Services
UW Madison 21 N Park St. Suite 6101 Madison, WI. 53715

Appendix 1

Required citations, acknowledgement and footnotes for the MMAS-8 are as follows.

Morisky DE, Ang A, Krousel-Wood M, Ward H. Predictive Validity of a Medication Adherence Measure for Hypertension Control. Journal of Clinical Hypertension 2008; 10(5):348-354

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Utilizing the Extended Self-Regulatory Model to Characterize Diabetes Medication Adherence: A Cross-Sectional Study

Olayinka O. Shiyanbola,[1] Elizabeth Unni,[2] Yen-Ming Huang,[1] Cameron Lanier[1]

[1] Division of Social and Administrative Sciences, School of Pharmacy, University of Wisconsin-Madison, Wisconsin, USA

[2] Department of Pharmaceutical Sciences, College of Pharmacy, Roseman University of Health Sciences, Utah, USA

Corresponding Author: Olayinka O. Shiyanbola; Division of Social and Administrative Sciences, School of Pharmacy, University of Wisconsin-Madison, 777 Highland Avenue Madison, WI 53705, USA (e-mail: Olayinka.Shiyanbola@wisc.edu)

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Objectives: To cluster the adherence behaviors of patients with type 2 diabetes based on their beliefs in medicines and illness perceptions and examine the psychosocial, clinical, and sociodemographic characteristics of patient clusters.

Design: Cross-sectional study

Setting: A face-to-face survey was administered to patients at two family medicine clinics in the Midwest, USA.

Participants: One hundred and seventy four English-speaking ≥ 20 years old adult patients with type 2 diabetes who were prescribed at least one oral diabetes medicine daily were recruited using convenience sampling.

Primary and secondary outcome measures: Beliefs in medicines and illness perceptions were assessed using the Beliefs about Medicines Questionnaire and the Brief Illness Perception Questionnaire respectively. Self-reported medication adherence was assessed using the Morisky Medication Adherence Scale. Psychosocial correlates of adherence, health literacy and self-efficacy, were measured using the Newest Vital Sign and the Self-efficacy for Appropriate Medication Use respectively. Two-step cluster analysis was used to classify patients.

Results: Participants' mean age was 58.74 (SD = 12.84). The majority were female (57.5%). Four clusters were formed (non-adherent clusters: ambivalent and skeptical; adherent clusters; indifferent and accepting). The ambivalent cluster (n = 30, 17.2%) included low adherent patients with high necessity beliefs, high concern beliefs, and high illness perceptions. The skeptical cluster (n = 53, 30.5%) included low adherent patients with low necessity beliefs, but high concern beliefs and high illness perceptions. Both the accepting (n = 40, 23.0%) and indifferent (n = 51, 29.3%) clusters were comprised of patients with high adherence. Significant differences between the ambivalent, skeptical, accepting, and indifferent adherent clusters were

based on self-efficacy, illness perception domains (treatment control, coherence), and hemoglobin A1c ($p < 0.01$).

Conclusions: Patients with diabetes in specific non-adherent and adherent clusters still have distinct beliefs as well as psychosocial characteristics that may help providers target tailored medication adherence interventions.

Strengths and limitations of this study

- This is the first study to use a clustering technique to allow for algorithm-based grouping based on both beliefs in medicines and illness perceptions founded on the Extended Self-Regulatory Model among patients with diabetes.
- This study highlighted the importance of content and theory-driven components to enable a possible mechanism for the development of tailored adherence interventions.
- This study focused on the impact of patient psychosocial factors such as their individual perceptions of medication and illness, self-efficacy, and health literacy in the management of diabetes.
- A convenience sample from two clinics in one state, hereby limiting the generalizability of the study.
- The use of a self-reported measure to evaluate medication adherence, rather than objective measures.

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Author Contributors: OOS and EU designed the study. OOS, YH, and CL were involved in data collection and data analysis. OOS wrote the manuscript, and EU and YH critically revised the content. All authors approved the final version of the manuscript.

Patient Consent: Obtained

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Ethical approval: The Health Sciences Institutional Review Board of the University of Wisconsin-Madison.

Data sharing statement: No additional data are available.

Introduction

Medication adherence, defined as the extent to which taking medications corresponds with recommendations by a healthcare provider is essential for treatment success.[1] Poor adherence results in increased risk of mortality, increased emergency room visits, and reduced quality of life.[2-5] In general, rates of medication adherence are below 50%.[6] However, for patients with type 2 diabetes, these rates are as low as 36%.[7] It is estimated that a 10% improvement in diabetes medication adherence would lead to at least a 6.6% reduction in hospitalizations.[7]

Among patients with diabetes, medication adherence has been found to be influenced by psychosocial factors, such as beliefs about illness and treatment, self-efficacy and perceived control, self-regulation, and emotional states.[8] Of the various factors that influence medication adherence, Horne and Weinman (2002) showed that sociodemographic and clinical factors explain only a small amount of variance in medication adherence, whereas illness perceptions and patient beliefs in medicines are substantial independent predictors.[9] Since patient clinical and sociodemographics are difficult to change, it makes sense to focus on patient factors that are modifiable, practical for interventions, and can be addressed by health providers.

Studies based on the Extended Self-Regulatory Model show that when patients are diagnosed with an illness, they develop a pattern of beliefs about their condition and treatment, which then influences their medication adherence.[10-15] The Self-Regulatory Model (also called the Common Sense Model) was developed to explain illness-related coping behaviors including adherence to treatment, based on patient perceptions of their illness.[16] Horne et al. extended the Self-Regulatory Model by integrating beliefs about treatment when research identified beliefs about treatment as proximal determinants of coping strategies such as medication adherence compared with illness perceptions.[9,10] In prior research, Phillips and colleagues suggested that

patient adherence was greater when illness and treatment perceptions were addressed or discussed during patients' medical encounter, and that healthcare providers were better able to judge patient agreement regarding the illness and treatment when patients reported these discussions occurred.[17,18]

To design feasible and useful medication adherence interventions, Horne et al. originally classified patients with chronic illnesses into four attitudinal groups (accepting, ambivalent, skeptical, and indifferent) based on their beliefs about their treatment.[19] While "accepting" patients, with high necessity beliefs and low concerns, had the highest medication adherence, "skeptical" patients, with low perceived need of medications and high concerns, had the lowest adherence levels. The other patient groups, including the "ambivalent" (high necessity beliefs and high concerns), and the "indifferent" (low necessity beliefs and low concerns) were also likely to be non-adherent.[19] Though medication non-adherence is a common problem among patients with chronic illnesses, they hardly discuss this behavior with their health providers during routine visits.[20] Various available tools used to identify medication adherence are not usable in clinical consultations because of the short time available to providers.[21] Hence, clustering patients' adherence behavior based on their beliefs may provide a mechanism for providers to focus on the specific belief needs of the patients in the context of their psychosocial characteristics. A previous study based on the Extended Self-Regulatory Model used both illness perceptions and beliefs in medicines to cluster patients with asthma and was able to develop the same clusters as developed by Horne et al.[22] Additionally, each cluster had psychosocial characteristics that were unique to them. However, further studies were needed to determine whether the four attitudinal group structure that includes illness perceptions also holds with other chronic disease conditions.

Clustering will provide a mechanism for providers to have a more tailored approach to addressing adherence than the general 'one size fits all' approach. For example, the counseling needed for a skeptical patient can be very different from an ambivalent patient. Though both these sets of patients have issues with their beliefs in medicines, they are quite different in their beliefs and psychosocial characteristics. Clustering can be done during the visit with the provider. A short validated questionnaire or online profiling tool that patients complete in advance of a consultation could be developed, which automatically calculates which cluster a patient belongs to. The patient's cluster with its unique characteristics can be included in a patient's record, and available to providers during the patient visit, similar to reviewing a patient's medical history. This will allow for an effective tailored counseling approach during the short visit time.

Diabetes is a chronic disease condition with reportedly high non-adherence rates.[23,24] Thus, developing a mechanism that will assist physicians in providing tailored communications to patients who are non-adherent with their diabetes medications can be effective and beneficial.

The objectives of this study were to:

1) Cluster the adherence behaviors of patients with type 2 diabetes based on their beliefs in medicines and illness perceptions.

2) Examine the psychosocial, clinical and sociodemographic characteristics of patient clusters.

This study hypothesized that patient clusters with high concern beliefs and low necessity beliefs will also have high threatening illness perceptions, and groups with low concern beliefs and high necessity beliefs will have low threatening illness perceptions. It is also hypothesized that identified patient clusters will have unique psychosocial, clinical, and sociodemographic characteristics.

Methods

Using a cross-sectional study design, a face-to-face survey was administered to English-speaking, ≥ 20 years old patients, with type 2 diabetes who were prescribed at least one oral diabetes medicine daily. Patients were recruited using convenience sampling. Information on eligible patients was retrieved from the electronic health record database of two family medicine clinics in a Midwestern state in the United States.

Data collection

Front desk receptionist at two clinics provided study information sheets to eligible patients who were waiting for their appointment. After patients reviewed the information, they met with a research assistant to indicate their interests in participating. The research assistant verified the patient's eligibility from the clinic's patient log, administered the informed consent form, and completed the 10-to-20-minute survey with the consented participant in a private area at the clinic. Participants were allowed to complete the survey before or after their scheduled clinic appointments, depending on clinic flow and their preferences. Informed consent was obtained from all individual participants included in the study. All data collection occurred from March 2016 to August 2016. Participants were compensated with US$25 cash, upon completion of the survey. The University Health Sciences Institutional Review Board approved the study.

Measures

Self-reported medication adherence was assessed using the 8-item Morisky Medication Adherence Scale (MMAS-8), a widely used scale in patients with diabetes.[25-29] The total score of the MMAS-8 ranged from 0 to 8, and MMAS-8 scores of < 6, 6 to < 8, and 8 reflected low, medium, and high medication adherence, respectively.[25] The 10-item Beliefs in Medicines Questionnaire (BMQ) was used to measure patient beliefs in medications.[30] The BMQ includes the necessity beliefs and concern beliefs sub-scales measured on five-point Likert-type scales

with 'strongly disagree' to 'strongly agree' response options. The range of scores for each sub-scale was 5-25, with a higher score meaning stronger concern beliefs or stronger necessity beliefs about the medicine.[30] The 8-item Brief-Illness Perception Questionnaire (B-IPQ) was used to measure patients' perceptions about diabetes.[31] This validated instrument includes survey items assessing patient illness perceptions about diabetes along the cognitive domains of the self-regulatory model as well as their emotional responses to having diabetes. Each survey item of the B-IPQ was assessed on a scale of 0-10 with higher scores indicating stronger threatening perceptions along the illness perception dimensions.[31]

Finally, we assessed other patient psychosocial correlates of medication adherence, i.e. health literacy and self-efficacy. Health literacy assessed using the 6-item Newest Vital Sign (NVS) has been extensively used across studies including patients with type 2 diabetes and can be completed in a short time (3-5 minutes).[32-35] Each question was scored as "0" for an incorrect response and "1" for a correct response for a total score of 0 to 6. Patients with scores less than 2 represented a high likelihood of inadequate health literacy, 2 to 3 indicated the possibility of marginal health literacy, and more than 3 suggested adequate health literacy.[32,36]

Self-efficacy measured using the 13-item Self-efficacy for Appropriate Medication Use Scale (SEAMS) was used in examining medication self-efficacy in chronic disease management, and is appropriate regardless of patient literacy skills.[37,38] Patients indicated under a range of situations, their level of confidence regarding taking medications correctly using a 3-point Likert scale (1 = not confident, 2 = somewhat confident, and 3 = very confident). The total score of the SEAMS ranged from 13 to 39 with higher scores indicating more confidence in adhering to medication use.[37]

Other variables included sociodemographic factors, such as age, gender, highest education level, race, health insurance, and the annual household income level; patient clinical factors, such as the number of chronic illnesses, self-reported health status, number of medications used, frequency of daily diabetes medication use, duration of diagnosis of type 2 diabetes, and whether the patient used insulin or not. Besides the main predictor variables, patients' hemoglobin A1c (HbA1c) values in the prior six months were retrieved from electronic medical records, with lower HbA1c values ≤ 7.0% representing better glycemic control.[39] The average duration between the day of the latest HbA1c testing and the day of the patient completing the survey was 43.3 ± 84.6 days (median: 7 days).

Data analysis

A two-step cluster analysis was used to classify patients' medication adherence behavior based on their beliefs in medicines and illness perceptions.[40] The number of clusters to be formed was kept a priori at four, a number determined by the researchers based on Horne's earlier studies and our prior work.[19,21,22,41,42] The cluster analysis technique organizes observed data (e.g. patients) into meaningful groups or clusters based on combinations of the independent variables (e.g. beliefs in medicines and illness perceptions). This process maximizes the similarity of cases within each cluster, but also maximizes the dissimilarity between the groups based on the log-likelihood distance between the data points.[40] Using this method allows the clusters to be created without a preconceived notion of what the clusters may look like. Though there are no rules-of-thumb about the sample size necessary for cluster analysis, prior researchers suggested that the adequate sample size for cluster analysis should be at least 2^m cases, preferably 5×2^m cases, where m is the number of clustering variables.[40,43] Since we used 3 variables (i.e. concern beliefs, necessity beliefs, and illness perceptions) for the clustering analysis, a minimal sample size to

include no less than 8 cases, preferably more than 40 cases, is sufficient to perform a cluster analysis. Additionally, based on an analysis of cluster studies, Dolnicar reports that the median sample size is 293.[44] In the first step, each data record was either considered as a new cluster or was added to a previously formed cluster. In the second step, the clusters formed from the first step were compared and merged based on the distance between them. Then, we assessed the goodness of fit of the clustering solution. The silhouette measure of cohesion and separation was used to evaluate the overall goodness-of-fit of the clusters.[45] A silhouette measure varies between -1 and 1 based on the average distances between the objects. The value of a silhouette measure less than 0.20 indicates a poor solution quality, a value between 0.20 and 0.50 suggests a fair solution, whereas a value of more than 0.50 represents a good solution.[46] Once categorized, the clusters were then characterized based on various sociodemographic and clinical characteristics. For the continuous variables, one-way ANOVA was used to determine the psychosocial (e.g. health literacy and self-efficacy), clinical (e.g. number of medicines) and sociodemographic (e.g. age) factors that varied between the clusters. For the categorical variables such as gender and race, chi-square tests were used to examine the differences between the clusters. SPSS (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) was used for all the analyses.

Patient and Public involvement

No patients were involved in the development of the study design, the research questions, and outcome measures. The results of the study will be disseminated to study participants through access to the published article once published in the journal.

Results

One hundred and ninety-nine patients were approached and 174 patients participated (87.4% response rate). The participant's mean age was 58.74 (SD = 12.84). The majority were female (57.5%), non-Hispanic white (67.8%) and African American (24.7%). Approximately 62.1% had completed at least a college or technical degree, and 57.5% had an annual household income of equal or more than $20,000. Of the 174 patients, 40.8% had low medication adherence, 35.1% had medium medication adherence, and 24.1% had high medication adherence.

The two-step cluster analysis produced four distinctive clusters categorized as ambivalent, skeptical, indifferent, and accepting. The characteristics of the clusters based on medication adherence, beliefs in medicines, illness perceptions, health literacy, self-efficacy, and all demographics are reported in Table 1. The distribution of participants across the clusters ranged from 17.2% to 30.5%. The silhouette measure was 0.4, which indicated a satisfactory cluster quality and the ratio of the largest to smallest cluster was acceptable at 1.77 (Figure 1). As hypothesized, high concern beliefs were related to high threatening illness perceptions and low adherence and vice versa. Table 2 describes the distinctive psychosocial and clinical characteristics of each cluster. The ambivalent cluster (n = 30, 17.2%) included low adherent patients with high necessity beliefs, high concern beliefs, and high illness perceptions. The skeptical cluster (n = 53, 30.5%) included low adherent patients with low necessity beliefs, but high concern beliefs and high illness perceptions. Both the accepting (n = 40, 23.0%) and indifferent (n = 51, 29.3%) clusters were comprised of patients with high adherence. Significant differences were found between the ambivalent, skeptical, accepting, and indifferent adherent clusters based on self-efficacy ($p = 0.002$), beliefs in medicines ($p < 0.001$), illness perception domains [consequence ($p < 0.001$), personal control ($p < 0.001$), treatment control ($p < 0.001$), identity ($p < 0.001$), concern ($p < 0.001$), coherence ($p = 0.027$), and emotional representations

($p < 0.001$)], and HbA1c ($p < 0.05$) (Table 1). While non-adherent clusters had low self-efficacy and high HbA1c levels, it was vice versa for the adherent clusters. Patients in the ambivalent non-adherent cluster were younger in age compared to those in the adherent clusters, less likely to have attended some college or technical school, and likely to be non-white.

Discussion

This study used the Extended Self-Regulatory Model to cluster the adherence behavior of patients with type 2 diabetes based on beliefs in medicines and illness perceptions, as well as examine the characteristics of the clusters, and the significant differences between them. Four clusters with distinct beliefs and psychosocial characteristics associated with each group were formed. The adherence clusters developed in this study by using both beliefs in medicines and illness perceptions are similar to the clusters formed by Horne et al. in his previous studies where only beliefs in medicines were used.[19,47] By including illness perceptions and other psychosocial correlates of adherence, this study identified other pertinent information related to each cluster that may help in developing guided and targeted interventions for providers working with patients with diabetes who may be non-adherent.

Patients in the ambivalent cluster were the least adherent to their medicines followed by the skeptical cluster. These clusters together comprised 48% of the whole sample. These results are similar to previous studies where these specific clusters represent the non-adherent proportion of a sample.[19,22] Contrary to a prior study, ambivalent patients had the lowest adherence to diabetes medicines, the strongest concerns about their medicines and the strongest threatening illness perceptions.[41] In spite of their strong concerns about medicines, ambivalent patients also perceived that their medications were necessary to maintain their health. Further analysis revealed that their strong threatening perceptions about diabetes were from their

individual illness perception domains including high emotional representations, lack of treatment control, high concern about illness, and less coherence. Despite the belief that medications are necessary, patients in the ambivalent cluster may be cognitively and emotionally overwhelmed by the demands of managing diabetes. Diabetes is psychologically demanding and requires adaptive self-care tasks related to being chronically ill, including taking medications as prescribed.[48-50] Because of this, when patients fail to self-manage their disease, it may give rise to feelings of guilt, frustration, anger, and hopelessness. These negative feelings may foster a pessimistic attitude towards diabetes, leading to negative beliefs about the illness and medication, and poor medication adherence.[51]

Ambivalent patients in this study also had the least self-confidence that they could take and manage their medications correctly, and had the lowest health literacy scores. These patients also took the highest number of medicines, had the highest number of chronic illness, and had poor glycemic control (highest HbA1c values). In addition, ambivalent patients were the youngest among the four clusters and had the least education, which might account for their inadequate health literacy and concerns about illnesses and medicines. Tailored adherence interventions aimed at these patients may need to build their self-efficacy and address their low health literacy. Prior research shows that by providing information in simple plain language, using teach-back techniques, and showing patients how they can be expert self-managers and engage in self-monitoring; patients are more likely to feel more in control of their illness, less concerned about the illness, and manage their illness more effectively.[52]

In the skeptical cluster, patients had strong concerns about medicines and threatening illness perceptions, although not at a pronounced degree as the ambivalent group. They also did not think their medications were necessary. Contrary to previous studies in asthma, epilepsy,

inflammatory bowel disease, depression, and cardiac disease, where the skeptical groups were most non-adherent to their medications, the skeptical group of patients with diabetes in this study did not have the lowest medication adherence.[21,22,41] Though this cluster of patients had perceptions of strong consequences from the illness, lack of treatment control, high concerns and emotional representations, were experiencing many symptoms due to diabetes, and were not confident they could manage their medications; they also had high health literacy and good understanding of their diabetes. For these patients, it is possible that because they have an increased ability to search, understand, and process health information; they are engaged in seeking information to manage their diabetes themselves, perform other diabetes self-management practices, and therefore do not believe they need medicines. A prior study has shown that patients with no educational qualifications (possibly tied to health literacy) are likely to have doubts about their personal need for medicines compared with patients with any formal educational qualifications.[21] Additionally, their self-perceived better health status may also be contributing to their perception that medications are not necessary for maintaining their health, hence, making them skeptical. In spite of their high health literacy, skeptical patients' low self-efficacy may lead to their poor glycemic control especially as prior studies report the strong influence of self-efficacy on diabetes control.[53,54] Adherence interventions that target concerns about medicines and illness, but also aim to motivate patients towards medication use might need to be developed for these group of patients.

Patients in the indifferent and accepting clusters were adherent to their medicines, though different in their beliefs in medicines. Similar to prior studies, patients in the accepting group were more likely to be adherent to their medicines.[19,21,22,41] These patients are generally not concerned about their illness, believe that their medications are necessary and are least concerned

about them, feel the most confident that they can take their medications correctly, and have the ability to process and understand health information. This group of patients, however, still believe that their diabetes affects their life, and still have some concern about it. The accepting patients were the oldest in age, the most educated, and have had their diabetes longer compared to patients in other clusters. Since these patients' HbA1c values still show that their diabetes is uncontrolled and using medications as part of diabetes management may not be concerning; interventions may seek to address concerns about their diabetes, especially as it relates to other complex diabetes self-management issues, such as checking blood sugars, exercising, and diet, etc. Since these older and well-educated patients have had diabetes for a long time and used many medications, providers may continue to encourage self-monitoring of symptoms, adverse drug events, and check for other indicators of poor diabetes outcomes, such as high blood pressure and high cholesterol.[55]

Contrary to previous studies where patients who were in the indifferent cluster were reported to be non-adherent to their medicines, the current study showed that the patients in this cluster were adherent to their medicines and their diabetes seemed to be in better control than patients in the three other clusters.[19,22] Though the patients in the indifferent cluster were the least likely to believe that their medications were necessary, they were also least concerned about their medicines, were not threatened by their illness, and were not emotionally affected by it (low emotional representation). Also, they experienced few symptoms and had the least concern about their illness. It is also possible that because these patients were taking the lowest number of medicines and had the lowest number of chronic illness, they were healthier compared to other patients, and therefore more likely to easily manage their medicines. Providers may continue to

address the needs for taking medicines and provide interventions that emphasize the need for taking medicines.

This study has several strengths. Horne et al. (2009) classified patients' adherence behaviors based on beliefs in medicines using the mid-point score of the Beliefs in Medicines questionnaire.[19] However, this current study used the clustering technique to allow for algorithm-based grouping based on both beliefs in medicines and illness perceptions founded on the Extended Self-Regulatory Model. Prior research has highlighted the importance of content and theory-driven components to enable replication of successful adherence interventions.[52] While it is important to address diabetes nonadherence via clinical interventions, we cannot underestimate the impact of patient psychosocial factors such as their individual perceptions of medication and illness, self-efficacy, and health literacy in the management of diabetes. Brief, valid, and reliable questionnaires that can easily quantify these psychosocial factors are available and may be included in adherence support programs.[21]

The study limitations are the use of a convenience sample from two clinics in one state, hereby limiting the generalizability of the study. The use of a self-reported measure to evaluate medication adherence, rather than objective measures such as the use of pill counts might lead to overestimation. However, prior studies show the reliability and validity of self-report adherence measures.[25,27] Data were collected either before or after patients' medical encounter depending on the flow of the clinic. The timing of the medical encounter may influence patient responses to questions about illness and treatment beliefs. This variable was not accounted for in the data analysis. The concurrent assessment of illness perceptions, beliefs in medicines, and adherence in a cross-sectional manner is a limitation. A longitudinal study that evaluates changes in beliefs over time and examines how these changes relate to changes in behavior and outcomes will be

considered in the future. Hemoglobin A1c was measured retrospectively. Though we used the most recent values from patients' medical record which is acceptable by clinical practitioners for standard diabetes care, this retrospective measurement of HbA1c could have limited our results. Though the B-IPQ total score categorizes respondents into two categories without taking into consideration the individual domains of the illness perceptions, this was needed for clustering their adherence. Once the clusters were formed, the illness perception domain characteristics of each cluster were analyzed and compared.

Conclusions

This study used a cluster analysis to characterize patients' adherence behavior based on their beliefs in both medicines and illnesses and psychosocial factors. Using evidence-based theoretical approaches, four clusters were formed with characteristics that suggest different types of interventions for each cluster. Medication nonadherence is a complex behavior to understand, and targeted interventions are often recommended. Data that can help discriminate between large groups of non-adherent individuals is needed in developing more personalized interventions. Though a large number of patients in two separate clusters (ambivalent and skeptical) were non-adherent to their medicines; patients within each non-adherent clusters still had distinct beliefs in medicines, illness perceptions, and other psychosocial characteristics that may help providers target tailored behavioral, psychological-based adherence interventions (for ambivalent clusters), as well as education and motivation-based adherence interventions (for skeptical clusters). Also, patients who are adherent may still need interventions that support and/or enhance their use of medicines (for indifferent clusters), and support individualized self-management strategies used for control of illness (for accepting clusters).

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Table 1 Mean score and percentage comparison of adherence, psychosocial factors, and demographics between clusters (n=174)

Variables	Total	Cluster 1 (Ambivalent)	Cluster 2 (Skeptical)	Cluster 3 (Indifferent)	Cluster 4 (Accepting)
Number of subjects	174	30 (17.2%)	53 (30.5%)	51 (29.3%)	40 (23.0%)
Medication adherence[a, ***]	5.87 ± 1.87	4.87 ± 1.78[g, h]	5.43 ± 1.89[j]	6.39 ± 1.67[g]	6.53 ± 1.72[h, j]
Necessity beliefs (Mean ± SD)[***]	18.88 ± 4.27	21.93 ± 2.77[f, g]	18.23 ± 1.76[f, i, j]	14.59 ± 3.71[g, i]	22.93 ± 2.18[j]
Concern beliefs (Mean ± SD)[***]	13.24 ± 4.35	18.83 ± 3.66[f, g, h]	14.85 ± 2.07[f, i, j]	11.12 ± 2.71[g, i]	9.60 ± 3.41[h, j]
Illness perceptions (IP) (Mean ± SD)[b, ***]	37.13 ± 11.06	48.33 ± 8.39[f, g, h]	41.72 ± 6.23[f, i, j]	27.63 ± 9.87[g, i, k]	34.78 ± 8.07[h, j, k]
Consequence IP [b, ***]	4.88 ± 2.91	7.30 ± 2.55[f, g, h]	5.13 ± 2.43[f, i]	2.94 ± 2.60[g, i, k]	5.20 ± 2.55[h, k]
Timeline IP [b]	8.20 ± 2.44	8.07 ± 2.49	8.51 ± 1.85	7.53 ± 2.98	8.73 ± 2.18
Personal control IP [b]	3.53 ± 2.51	3.73 ± 3.06	4.13 ± 2.31	3.20 ± 240	3.00 ± 2.33
Treatment control IP [b, ***]	1.93 ± 2.03	2.57 ± 2.54[h]	2.57 ± 1.82[j]	1.75 ± 2.01	0.83 ± 1.34[h, j]
Identity IP [b, ***]	4.51 ± 2.91	7.17 ± 2.30[f, g, h]	5.17 ± 2.41[f, i, j]	2.35 ± 2.50[g, i]	4.40 ± 2.43[h, j]
Concern IP [b, ***]	6.85 ± 2.82	8.63 ± 2.09[g]	7.38 ± 2.11[i]	4.98 ± 3.22[g, i, k]	7.20 ± 2.31[k]
Coherence IP [b, *]	2.79 ± 2.52	3.53 ± 3.56	3.15 ± 1.91[j]	2.69 ± 2.65	1.88 ± 1.84[j]
Emotional representation IP [b, ***]	4.45 ± 3.32	7.33 ± 2.71[g, h]	5.68 ± 2.56[i, j]	2.20 ± 2.99[g, i]	3.55 ± 2.72[h, j]

Self–efficacy (Mean ± SD)[c, **]	33.24 ± 5.96	31.30 ± 6.65[h, J]	32.02 ± 6.18[J]	33.47 ± 6.11	36.00 ± 3.64[h, J]
Health literacy (Mean ± SD)[d]	3.72 ± 2.02	3.13 ± 1.94	3.96 ± 1.91	3.80 ± 2.11	3.75 ± 2.08
Inadequate		7 (23.3%)	7 (13.2%)	7 (17.5%)	10 (19.6%)
Marginal		11 (36.7%)	10 (18.9%)	9 (22.5%)	9 (17.6%)
Adequate		12 (40.0%)	36 (67.9%)	24 (60%)	32 (62.7%)
Age	58.74 ± 12.84	55.17 ± 14.00	57.85 ± 11.48	59.04 ± 13.92	62.20 ± 11.73
White[**]	118 (67.8%)	12 (40.0%)	38 (71.7%)	29 (72.5%)	39 (76.5%)
Female	100 (57.5%)	18 (60.0%)	30 (56.6%)	20 (50.0%)	32 (62.7%)
Education higher than high school	108 (62.1%)	15 (50.0%)	32 (60.4%)	35 (68.6%)	26 (65.0%)
Education					
Completed 8th grade or less	4 (2.3%)	1 (3.3%)	0 (0.0%)	1 (2.0%)	2 (5.0%)
Some high school	15 (8.6%)	5 (16.7%)	3 (5.7%)	5 (9.8%)	2 (5.0%)
High school graduate or GED	47 (27.0%)	9 (30.0%)	18 (34.0%)	10 (19.6%)	10 (25.0%)
Some college or technical school	67 (38.5%)	10 (33.3%)	14 (26.4%)	26 (51.0%)	17 (42.5%)
College graduate	24 (13.8%)	3 (10.0%)	12 (22.6%)	6 (11.8%)	3 (7.5%)
Graduate degree	17 (9.8%)	2 (6.7%)	6 (11.3%)	3 (5.9%)	6 (15.0%)

Number of medications (Mean ± SD)[***]	7.77 ± 3.89	9.07 ± 4.21[g]	8.19 ± 4.03[i]	5.80 ± 2.86[g, i, k]	8.75 ± 3.75[k]
Number of illness (Mean ± SD)[**]	3.86 ± 1.82	4.50 ± 2.03[g]	3.89 ± 1.96	3.22 ± 1.47[g, k]	4.28 ± 1.66[k]
Duration of diabetes diagnosed (Mean ± SD)[*]	9.58 ± 7.08	8.75 ± 5.79	9.25 ± 6.30	8.03 ± 7.14[k]	12.61 ± 8.13[k]
HbA1c level[*]	7.66 ± 1.64	8.31 ± 2.14[g]	7.86 ± 1.58	7.17 ± 1.32[g]	7.52 ± 1.51
Health status[e, **]	2.64 ± 0.80	2.13 ± 0.90[f, g]	2.72 ± 0.77[f]	2.86 ± 0.75[g]	2.65 ± 0.70

[a] Self-reported medication adherence was measured with the 8-item Morisky Medication Adherence Scale. Use of the ©MMAS is protected by US Copyright laws. Permission for use is required. A license agreement is available from: Donald E. Morisky, MMAS Research LLC 14725 NE 20th St. Bellevue WA 98007 or from dmorisky@gmail.com.

[b] Higher scores indicate higher specific illness perceptions. Personal control, treatment control, and coherence are reverse scored.

[c] Higher scores indicate higher levels of self-efficacy.

[d] Heath literacy was measured with the Newest Vital Sign (NVS).

[e] One item on a 5 point scale. Higher scores indicate better self-reported health status.

[f-k] Significant differences based on the post-hoc analysis.

[*]$p < 0.05$, [**]$p < 0.01$, [***]$p < 0.001$

Table 2 Beliefs, psychosocial and clinical characteristics of the clusters

	Clusters with non-adherence behavior		**Clusters with adherence behavior**	
	Cluster 1 (Ambivalent)	**Cluster 2 (Skeptical)**	**Cluster 3 (Indifferent)**	**Cluster 4 (Accepting)**
Medication Adherence	Low adherence	Low adherence	High adherence	High adherence
Beliefs in medicines	High NB	Low NB	Low NB	High NB
	High CB	High CB	Low CB	Low CB
Illness perceptions	High IP	High IP	Low IP	Low IP
Self-efficacy	Low SE	Low SE	High SE	High SE
Health literacy	Low HL	High HL	High HL	High HL
Glycemic control	High HbA1c	High HbA1c	Low HbA1c	Low HbA1c
Illness perception domains	High Consequence	High Consequence	Low consequence	High consequence
	High treatment control	High treatment control	Low treatment control	Low treatment control
	High identity	High identity	Low identity	Low identity
	High concern	High concern	Low concern	High concern
	High coherence	High coherence	Low coherence	Low coherence

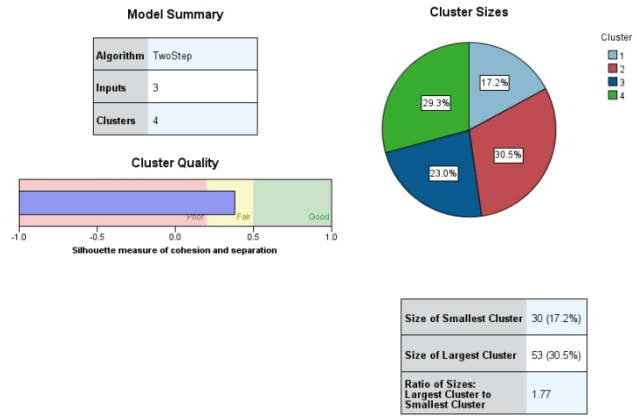
	High emotional representation	High emotional representation	Low emotional representation	Low emotional representation

The high and low values for each variable is compared based on the mean values from all participants.

CB: concern beliefs; HbA1c: hemoglobin A1c levels; HL: health literacy; IP: illness perceptions; NB: necessity beliefs; SE: self-efficacy.

Figure 1 Test statistics of clustering analysis

Figure Test statistics of cluster analysis



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