ROLE OF PATIENTS' PERCEPTION OF BARRIERS TO TAKING MEDICATION ON MEDICATION ADHERENCE AMONG PATIENTS WITH DIABETES: DEVELOPMENT AND PSYCHOMETRIC EVALUATION OF THE MURAGE-MARRERO-MONAHAN MEDICATION BARRIERS SCALE (4M SCALE), PATIENT CHARACTERISTICS ASSOCIATED WITH MEDICATION BARRIERS, AND ASSOCIATION OF MEDICATION BARRIERS AND CARDIOVASCULAR DISEASE (CVD) RISK

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DEDICATION

To My Parents,

Who taught me to gracefully surmount mountains with resilience and razor sharp focus,

“Go, See, and Conquer”.

To My Family,

Their sacrifice and patience made every task in this endeavor even more meaningful.

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Mwangi James Murage

Role of Patients' Perception of Barriers to Taking Medication on Medication Adherence Among Patients With Diabetes: Development and Psychometric Evaluation of the Murage-Marrero-Monahan Medication Barriers Scale (4M Scale), Patient Characteristics Associated With Medication Barriers, and Association of Medication Barriers and Cardiovascular Disease (CVD) Risk

Introduction

Medication adherence remains a problem among Type-2 diabetes (T2D) patients despite availability of effective treatments. Three analyses of extant data sets were conducted to examine barriers to using medication as prescribed as an alternate method to assess medication adherence: 1) development and psychometric evaluation of the Murage-Marrero-Monahan-Medication barriers (4M) scale to assess patients' perceived barriers; 2) patient demographic factors associated with barriers to using medication as prescribed, and 3) the association between patients' perceived barriers to medication use and cardiovascular disease (CVD) risk factor control.

Methods

Twelve focus groups and a cross-sectional study of 362 T2D patients contributed to develop and evaluate psychometric properties of the 4M scale. A cross-sectional survey of 964 T2D patients was used for the other two studies. Analysis of covariance identified demographic factors associated with reported barriers. Multivariable logistic

regression was used to identify barriers associated with CVD risk factors (glucose, blood pressure and lipids) categorized as either poor or good control.

Results

Exploratory factor analysis with Varimax rotation resulted in a 19-item 4M scale with acceptable psychometric properties. As a five-domain (or single-domain) structure, coefficient alpha ranged from 0.70 to 0.83 (0.92). Both structures demonstrated discriminant validity and known-group validity. Age was inversely associated with all identified barriers while income was inversely associated with poor communication with providers and side effects. A unit increase in the overall barrier mean score on the 4M scale was associated with 92% increase in the odds of having poor control of two or more CVD risk factors compared to good control of all three risk factors (adjusted OR=1.92, 95% CI: 1.16–3.17; $p<0.05$).

Conclusion

The 4M scale demonstrated acceptable psychometric properties in assessing barriers to using medication among T2D patients. Poor medication adherence has been previously associated with CVD risk. In this study, greater barriers were associated with poorer control of CVD risk factors making barriers a potential alternative to medication adherence, whose current assessment methods are limited. The 4M scale has the advantage to identify specific barriers inhibiting medication use that can facilitate patient-provider discussions and the development of targeted interventions.

G. Marie Swanson, Ph.D., M.P.H., Chair

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LIST OF ABBREVIATIONS

4M scale	Murage-Marrero-Monahan Medication Barriers Scale
ANCOVA	Analysis of covariance
BMI	Body mass index
CVD	Cardiovascular disease
CI	Confidence interval
EFA	Exploratory factor analysis
GED	General educational development
GLM	Generalized linear model
HbA1c	Glycosylated Hemoglobin A1c
IRB	Institutional review board
LDL-c	Low density lipoprotein cholesterol
mm Hg	Millimeter of mercury
M.P.H.	Master of public health
n	Sample size
NC	North Carolina
OHA	Oral antihyperglycemic agent
OR	Odds ratio
Pacss	Poor personal access barrier
Ph.D.	Doctor of philosophy
Prcom	Poor communication with providers barrier
Pundt	Poor understanding of and/or difficulty taking medicine barrier
QoL	Quality of life

r	Correlation
SAS	Statistical analysis software
SBP	Systolic blood pressure
SD	Standard deviation
Sdeft	Side effects barrier
SES	Socio-economic status
SF-36	36-item short form health survey
Sybrs	System access barrier
T2D	Type-2 diabetes
TRIAD	Translating Research Into Action for Diabetes
TRC	TRIAD research center
UCLA	University of California, Los Angeles
U.S.	United States
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

As the burden of diabetes continues on an upward trend, it is estimated that more than a third of the United States (U.S.) population will have diabetes by 2050 (1). In 2012 more than 29 million people in the U.S. had diagnosed diabetes, with an additional 89 million having pre-diabetes, which greatly increases their chances of developing diabetes (2). Diabetes has significant social and fiscal burden (3). It costs the U.S. more than 245 billion dollars annually with direct medical expenditures exceeding 176 billion: twice that of people without diabetes (4, 5).

Whereas most efforts to reduce this burden have focused on early diagnosis and aggressive diabetes management among diagnosed patients (5), most of them are not achieving optimal outcomes, in spite of a wide array of available treatment options with proven efficacy (6-14). In addition to suspected socio-economic factors, medication adherence has emerged as a potential explanation of the discrepancy, especially among patients who have access to medical care and treatment (10, 12).

Established evidence that diabetes is a risk factor for cardiovascular disease (CVD) – a leading cause of death in the U.S. – explains why most patients with diabetes proceed to develop CVD, macrovascular and microvascular complications, and eventually premature death (4, 13, 15-20). Again, the less than optimal targets on the cardinal CVD risk factors – glycosylated hemoglobin A1c (HbA1c), systolic blood pressure (SBP) and low density lipoprotein cholesterol (LDL-c) – despite availability of medication has been attributed to poor medication adherence (13, 18-22).

The need to assess medication adherence in the clinical care of diabetes patients is underscored by the findings that higher medication adherence is associated with better glycemic control, improved health outcomes, lower healthcare utilization and lower healthcare costs (10, 23-28). The need to evaluate medication adherence is further illuminated by evidence that medication adherence is a modifiable behavior that can be improved with appropriate interventions once identified (29).

Current methods of assessing medication adherence among patients are limited. Direct observations are impractical, direct inquiry is likely to be inaccurate due to social pressures influencing responses, metabolic markers are expensive, and pill counts and drug possession estimates are mostly not feasible and often inaccurate (30-33). A variety of self-reported measures have been used because they are simple to use, less expensive and can be accurate – to the extent that they have good validity and reliability and patients will correctly respond to them (34).

Social desirability bias, validity and reliability are major impediments on the accuracy of available self-reported measures of medication adherence. This study postulates that patients' perception and reporting of barriers to using medications as prescribed by their healthcare providers can indicate possible issues in medication adherence. Moreover, by focusing on general responses to medications per se, without reference to specific medications, patients may be empowered to describe issues that they face without fear of reprimand from their provider. This may help to circumvent the pitfalls of patients providing a "socially desirable" but inaccurate response when they are directly confronted about their current specific medication use.

Additionally, understanding patient demographic characteristics associated with perceived barriers to medication use would enhance use of the 4M scale with diverse populations, avoiding the tendency of trying to assess a heterogeneous population with a one size fits all mentality. Finally, understanding the link between patient perceived barriers to medication use and CVD risk would support the concept of assessing patients' perceived barriers to using medication as a means to identify issues of poor medication adherence in such a manner that possible tailored interventions may be prescribed.

1.1 Conceptual Framework

Directly confronting patients on their adherence to prescribed medication is likely to result in socially desirable responses because of the social pressure inherent in doctor-patient relationship. Doctors continue to hold a high social status that intimidates many persons. As a result, many people do not want to tell their doctor that they are not complying with his or her treatment recommendations (35). For this reason this dissertation explores an indirect method of assessing medication adherence without directly inquiring from patients about their adherence to specific medications at the point in time when the assessment is being made. By taking this approach, it is postulated that patients will be more empowered to admit to barriers that they may have experienced at some time in their life and by this perspective not having to admit that this is an active element in their current treatment. In essence, they can tell the provider that a specific barrier has been a problem for them at some time, and by indicating how often the barrier occurs, indirectly indicate that the barrier is in fact persistent. When this information is combined with laboratory data, the provider is in a better position to discuss possible ways to reduce or eliminate the barrier in the present time.

In this dissertation, barriers are defined as patients' perceived barriers or obstacles to using medications as prescribed by their healthcare provider, and are henceforth referred to as barriers. Barriers, like medication adherence, constitute a latent construct that influences several behaviors manifested externally by patients (Figure 1.1). The study postulates that barriers are inversely related to medication adherence. Therefore, it is assumed that an increase in the barriers would result in poor (lower) medication adherence whereas a decrease in the barriers would result in good (higher) medication adherence. Although studies could be designed to test the relationship between barriers and adherence (not available in the present data set), the separate association of adherence and barriers with demographic factors and CVD outcome is postulated to be evidence for the inverse relationship between adherence and barriers. Demographic factors of patients influence both the barriers and medication adherence, and possibly modify each other in their association with the two hidden constructs. Advised by this conceptual framework, this dissertation proposes to assess patients' perceived barriers to medication use as proxy to medication adherence.

Accordingly, this dissertation pursued three related objectives: i) to develop and psychometrically evaluate a self-administered scale designed to assess patients' perception of barriers to using medication as prescribed, the Murage-Marrero-Monahan Medications barrier scale (4M scale). ii) to determine whether patients' age, gender, race/ethnicity, education and household income are associated with specific barriers to using medication as prescribed. iii) to assess the association between patients' perceived barriers to medication use and cardiovascular disease risk.

The first step was to develop a valid and reliable instrument that can assess the latent construct of patients' perceived barriers to using medication as prescribed by their healthcare provider from the patients' explicit external experiences and their perceived frequency of barriers. Then to determine what specific demographic factors are associated with identified barriers. This information would facilitate interpretation and practical application of the tool in routine clinical care. Finally, the identified barriers were examined for association with CVD risk control, an intermediate stage leading to CVD, an outcome experienced by most diabetes patients.

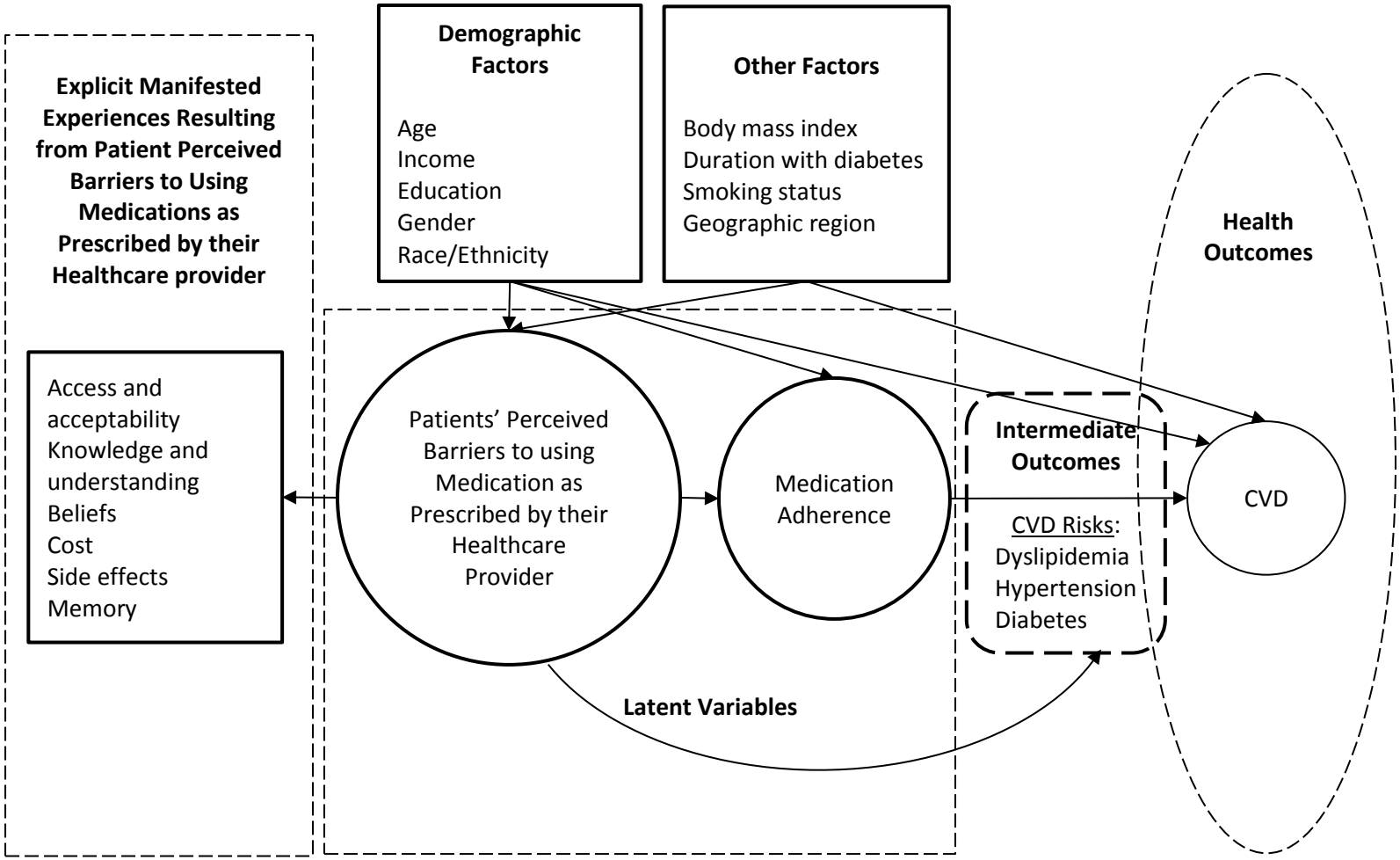


Figure 1.1 Conceptual Framework of Patient Perceived Barriers to Using Medications as Prescribed by their Healthcare Provider.

1.2 Development and psychometric evaluation of the Murage-Marrero-Monahan Medication Barriers scale (4M Scale)

While medication adherence has been attributed to less than optimal treatment outcomes among diabetes patients in spite of availability to treatments with known efficacy, current methods of assessing medication adherence are limited by cost, accuracy and feasibility. Even self-reported measures, despite having good validity and reliability, are often influenced by social desirability bias, limiting their accuracy. Therefore, this study seeks to develop a self-reported tool that indirectly assesses barriers and their frequencies as proxies to identifying issues with medication adherence. The study further evaluates psychometric properties of the instrument.

1.3 Patient demographic characteristics associated with barriers to using medications as prescribed

To help identify patients who may need additional adherence support, previous studies have focused on identifying patient characteristics associated with medication adherence. These studies have provided important insight on patient medication adherence traits but have failed to identify specific problems that can be targeted by adherence interventions, hence diminishing the likelihood of any interventions succeeding. Therefore, this study aimed to determine whether specific demographic characteristics are associated with barriers to using medications as prescribed. The purpose was to enhance interpretation of the developed scale and to allow care providers to structure personalized interventions to address the identified barriers, increasing the likelihood of interventions succeeding.

1.4 Patient perceived barriers to medication use and cardiovascular disease risk

Most people with diabetes continue to progress to full blown CVD, despite availability of treatments to control CVD risk factors. Again, this observation is attributed to medication adherence. This study sought to determine whether barriers are associated with CVD risk control, an intermediate step to CVD. An association, if found, would establish the importance of considering barriers in routine care of patients with diabetes and point toward specific interventions. By extension, these findings will provide evidence on whether barriers can indicate issues with medication adherence that would lead to similar consequences.

This dissertation is organized as follows: chapter 2 presents development and psychometric evaluation of the self-administered Murage-Marrero-Monahan Medication Barrier scale. Chapter 3 presents a study examining whether patient demographic factors are associated with barriers to using medications as prescribed. Chapter 4 presents the study determining whether patient perceived barriers to medication use are associated with poor control of cardiovascular risk factors. Finally, Chapter 5 provides an overall discussion and concluding remarks.

CHAPTER 2

DEVELOPMENT AND PSYCHOMETRIC EVALUATION OF THE MURAGE-MARRERO-MONAHAN MEDICATION BARRIERS SCALE (4M SCALE)

2.1 Abstract

Purpose

To develop and evaluate psychometric properties of the Murage-Marrero-Monahan Medication Barriers scale (4M scale), a tool for assessing patients' perceived barriers to taking medications as prescribed, as an alternate to assessing medication adherence.

Methods

Scale items were generated from literature review and 12 focus groups of diabetes patients. A cross-sectional study of diabetes patients yielded 362 surveys from 1,000 mailed surveys of the 4M scale.

Results

Analysis focused on 343 respondents with Type 2 diabetes. Mean age was 59, mean age at diagnosis 48, and mean diabetes duration 11 years. Most were female (72%) and African American (52%). Therapies included oral antihyperglycemic agents (OHA) (51%), insulin (18%), and combined OHA and insulin (28%). The initial 20 items were reduced to 19 items with valid psychometric properties as either a five-domain or a single-domain structure. The five domains were poor communication with providers, poor understanding of and/or difficulty using medicine, poor personal access, side effects

and system barriers. For the five-domain structure, factor loadings ranged from 0.37 to 0.69 (median 0.58) (single domain, 0.42 to 0.81; median 0.61), coefficient alpha ranged from 0.70 to 0.83 (single domain, 0.92). As evidence of validity, both structures had low and inverse correlations with quality of life measures, and revealed lower barrier experiences among patients on OHA than those on insulin or OHA plus insulin.

Conclusion

The 4M scale demonstrated acceptable validity and reliability both as a five-domain and single-domain instrument among patients with Type 2 diabetes from a low income population.

Keywords for indexing

Diabetes, Medication barriers, Psychometric, Validity, Reliability

2.2 Introduction

The burden of diabetes is reaching epidemic levels with estimates suggesting that the incidence will increase to 35% of the U.S. population by 2050 (1). In 2012, more than 29 million people in the US had diabetes and an additional 89 million had pre-diabetes that significantly increases their risk for developing the disease. The burden of this disease has significant social and fiscal impacts (2, 3). In 2012, a total fiscal burden of $245 billion was attributed to diabetes, a 41% increase from 2007 (4, 5). The social and psychological costs are incalculable (4).

Efforts to reduce this burden have focused on preventive measures, early diagnosis and more aggressive diabetes management (5). In spite of a wide array of effective treatment options, however, many persons with diabetes are still not achieving optimal therapeutic outcomes (6-14). Medication adherence is increasingly implicated as a potential explanation for this discrepancy (10, 12). The World Health Organization (WHO) defines adherence as "the extent to which a person's behavior – taking medication, following a diet and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" (36).

Research illuminates the importance of medication adherence, particularly among persons with diabetes. Several studies have shown that poor adherence is associated with poor glycemic control, and increased risk of cardiovascular complications, whereas higher medication adherence is linked to better glycemic control, improved health outcomes, lower healthcare utilization and lower healthcare costs (10, 23-28). For example, good medication adherence has been associated with improved glycemic control and greater weight loss (37, 38). Additional evidence has demonstrated that

medication adherence is a modifiable behavior that can be improved with appropriate intervention once poor adherence is identified (29). Unfortunately, many patients with diabetes do not report taking their medications as prescribed by their health care providers (22, 39).

There is currently no "gold standard" for assessing medication adherence and each method has limitations. Biological measures are costly and often refused by study participants (32, 33). Pill counts and drug possession measures are often inaccurate (31). Self-reported measures have many benefits, especially simplicity, low cost and accuracy that can be improved by developing scales with adequate validity and reliability (34). Existing self-report measures, however, are subject to reporting errors arising from social desirability bias; the tendency to report adherence when directly confronted by providers about a specific medication.

Therefore, our goal was to develop and evaluate psychometric properties of a self-administered scale designed to indicate adherence issues while avoiding direct confrontation by assessing respondents' perceptions of barriers experienced in using any medications as prescribed, and not tied to their immediate utilization. We postulate that this approach would lessen patient reactance to being directly confronted about their medication use and allow them to suggest areas that may be addressed during clinical encounters (40). Also, when coupled with biomarkers that suggest response to therapy, the reporting of "generalized" barriers may indicate current adherence issues. In this regard, this approach will serve as an indicator of medication adherence. In addition, defining barriers could facilitate discussion between the patient and provider when a

barrier is identified and coupled with other data suggesting poor adherence. We titled this instrument the Murage-Marrero-Monahan Medication Barriers (4M) scale.

2.3 Methods

2.3.1 Conceptual framework and item generation

The concept barriers was defined as patients' perceived obstacles to using medication as prescribed by a healthcare provider.

Item generation was a process that involved literature review and focus groups. Key concepts surrounding diabetes medication were identified from literature. The concepts were then used to guide focus group exercises. A series of twelve (12) focus groups led by trained facilitators were used to identify central themes. The 6 all-female and 6 all-male focus groups consisted of a diverse population of 121 adult patients with Type 1 or Type 2 diabetes: 73(60%) were female, 92(76%) were at least 50 years old, 71(59%) were Caucasians, and 50(41%) were African Americans. Participants in each focus group first discussed perceived barriers freely, and then further discussions were probed using concepts from the literature that had not been addressed. Themes were derived from printed transcripts reviewed by three independent raters.

A pool of 20 items was generated from six themes that emerged from the focus groups: six access and acceptability items (1, 2, 3, 15, 17 and 18), two knowledge and understanding items (4 and 5), four beliefs items (6, 9, 19 and 20), one cost item (14), four side effects items (7, 8, 10 and 11) and three memory items (12, 13 and 16). To improve understandability and readability, the items incorporated language from focus group participants.

2.3.2 Content validity

Content validity was assessed through clinical experts and a pilot test. In-person discussions with 6 clinical experts provided additional consensus on comprehensiveness of the items and affirmed their relation to the overall concept. Additionally, the pilot test conducted on a convenience sample of 28 patients with diabetes revealed acceptable interpretability and understandability of the items. Hence, all 20 items were retained as assessing barriers to medication use.

2.3.3 Survey population

A cross sectional study design was used to assess psychometric properties of the instrument. An indigent inner-city population in Indianapolis was deliberately targeted because it was expected to have a disproportionate burden of diabetes by prevalence (41), high use of polypharmacy (42), social and fiscal costs (43), diabetes related poor health outcomes (44), and lower medication adherence (45). Approval was obtained from the Indiana University-Purdue University Indianapolis, Institutional Review Board. The study survey administration and study participants are described in detail elsewhere (46).

2.3.4 Survey

In addition to responses on the 20 items of the 4M scale, the survey also obtained information on age, education, gender, race, marital status, whether living with a spouse, number of household occupants, household income, type of diabetes, age at diagnosis and current diabetes medications. Responses on type of diabetes were corrected for patients

who were unsure of their diabetes type (62 patients), or did not provide a response on the type of diabetes (9 patients), or provided a response inconsistent with age at diagnosis or insulin use. The correction was based on synthesis of the type of diabetes provided (if any) and survey responses on insulin use, age at diagnosis and current age.

All 20 items of the 4M scale assessed patients' perceived barriers to medication use as prescribed. The stem for all items read, "Sometimes people do not take their medications as prescribed by their doctor. There are many reasons why this can happen. Have you ever experienced any of the reasons listed below, and if so, how often?" Each item score ranged from 1 to 5 on a five-category frequency response scale: "Never", "Rarely", "Sometimes", "Often" and "Very Often", respectively.

Subscale scores were obtained by adding responses of all items under their respective 4M subscale, whereas the overall score was obtained by summation of responses from all 20 items. Because missing responses per item was minimal (highest 8%), subscale scores were not imputed. Lower subscale and overall scores indicated less experience with a specific barrier to medication use.

2.3.5 Statistical analysis

Scale formation and item reduction

Exploratory factor analysis (EFA) and conceptual relevance of rotated factors were used to determine number of factor and items to retain (47). To retain an item, it had to achieve a rotated factor loading of 0.40 or greater (0.30 or more was acceptable if an item demonstrated compelling conceptual relevance), be conceptually relevant, and have

a corrected item-total correlation of 0.30 or greater (48). All analyses were performed using SAS software (Version 9.4, SAS Institute, Cary, NC).

Data quality and descriptive statistics

Data quality was examined through item variability and data completeness. Item variability was assessed by item response frequency distributions, means, standard deviations, floor effects and ceiling effects. Completeness of data was evaluated by calculating the percentage of missing data for each item.

Descriptive characteristics of perceived barriers measured by the 4M instrument were estimated by calculating scale score means, medians, standard deviations, range, ceiling effects, and floor effects. Data completeness was evaluated by the proportion of participants whose scale scores were not calculable. A cut-off of more than 15% in the best or worst possible score was evidence of ceiling or floor effects for scale scores (26, 49, 50).

Factor analysis and item-convergent-discriminant validity

Exploratory factor analysis (EFA) and a scree plot were used to determine the number of factors to extract (47). The principal component method was used for estimating parameters, and squared multiple correlations was used for the initial communalities. After specifying the number of factors to retain, Varimax rotated factor loadings and conceptual relevance were used to attribute items to respective factors. Corrected item-total correlations for each item – corrected to exclude the item from the total score – were calculated to assess item-convergent validity (51). A corrected item-total correlation greater than or equal to 0.3 was considered acceptable item contribution

to its respective scale score (48). Item-discriminant validity was examined by correlating each item with subscales to which it was not assigned.

Reliability

Cronbach's coefficient alpha was used to evaluate internal consistency reliability (50, 51). A coefficient alpha of 0.7 or above was considered acceptable internal consistency reliability for group comparisons (48, 50).

Discriminant validity

Discriminant validity was examined by correlating the extracted factors (subscales and total score) with four generic quality of life (QoL) measures: SF-36 single item general health, SF-36 mental health, SF-36 vitality and Rand health distress measures (52, 53). It was hypothesized the scale factors will correlate significantly, lowly and inversely with all four QoL measures. Small significant negative correlations were expected because medication non-adherence (presumably in part from increased perceived barriers) is expected to lead to poor general and mental health, inactivity and stress. The magnitude of correlation was expected to be small because many personal and environmental variables can impact quality of life.

Known-group validity

Known-group validity was evaluated by comparing 4M scale median scores (subscale and overall total) to three medication regimens: oral antihyperglycemic agents (OHA) therapy only, insulin therapy only, and insulin plus OHA combined therapy. Previous studies have shown adherence rates are lower for insulin therapy than OHA therapy and lower for polypharmacy regimens than monotherapy regimen (6). Therefore, for each 4M scale score, we hypothesized patients on combined therapy (OHA plus

insulin) will have the highest median scores on perceived barrier scale scores, then those on insulin monotherapy the next highest and finally those on OHA with the lowest barrier scale scores. The Kruskal-Wallis test was used to test differences between the calculated medians for each subscale. The Wilcoxon rank sum test was used for further pairwise comparisons of the three possible pairs of medication regimens. Similar tests were repeated for the overall 4M scale total score.

2.4 Results

2.4.1 Sample characteristics

A response rate of 36% (362) was realized from 1,000 questionnaires sent to the target population. As reported by Monahan et al. non-responders did not differ by age or race to responders, but were more likely to be male (46).

Patients with Type 1 diabetes were excluded in subsequent analyses because most of the participants had Type 2 diabetes, 95% (343) of survey respondents. Subsequently, further development of the 4M scale focused on patients with Type 2 diabetes.

Demographic and therapy traits of the responding 343 Type 2 diabetes patients are provided in Table 2.1. Mostly they were females with low income levels, non-Hispanic African Americans, and over half were on OHA only. Nine respondents reported not taking any medication but were included in the study and considered currently non-adherent because their responses indicated experience with medication.

Scale formation and item reduction

Table 2.1 Study population characteristics

Characteristics (n = 343)	Mean (SD)	Median (Range)
Current age [years]	59.4 (11.3)	59.0 (24-95)
Age when diagnosed with diabetes	47.7 (12.8)	48.5 (6-95)
Highest year of education completed	11.0 (2.4)	12.0 (2-17)
Duration with diabetes since diagnosis [years]	11.4 (11.0)	8.0 (0-68)

Characteristics	Number (%)
Gender	
Female	247 (72)
Male	93 (27)
Unidentified	3 (1)
Race	
Non-Hispanic African American	178 (52)
Non-Hispanic Caucasian	141 (41)
Hispanic / Latino	3 (1)
Other races	11 (3)
Unidentified	10 (3)
Marital status	
Never married	72 (21)
Married	92 (27)
Divorced	77 (22)
Separated	16 (5)
Widowed	83 (24)
Unidentified	3 (1)
Living with a spouse or significant other	
Yes	139 (41)
No	200 (58)
Unidentified	4 (1)
Number of people living in Household (including participant)	
One	117 (34)
Two	120 (35)
Three	44 (13)
Four	28 (8)
Five or more	30 (9)
Unidentified	4 (1)
Total Household Income (before taxes)	
Less than or equal to $15,000	250 (73)
$15,001 to $30,000	55 (16)
$30,001 to $45,000	12 (4)
$45,001 to $100,000	8 (2)
Unidentified	18 (5)

Table 2.1 continued.

Characteristics	Number (%)
Type of diabetes medication therapy	
No Medication	9 (3)
One oral antihyperglycemic agent (OHA)	93 (27)
Two or more OHA	83 (24)
Insulin only	62 (18)
Combined Insulin and OHA	95 (28)
Unidentified	1 (0)
Insulin administration method	
Syringe	141 (90)
Insulin pen	10 (6)
Insulin pump	1 (1)
Syringe and insulin pen	2 (1)
Unidentified	3 (2)
Insulin injections per day	
One time	21 (13)
Two times	124 (79)
Three or more times	11 (7)
Unidentified	1 (1)
Number of OHAs taken	
One kind	24 (40)
Two kinds	18 (30)
Three or more kinds	7 (12)
Unidentified	11 (18)
Number of times OHA taken per day	
One time a day	10 (17)
Two times a day	32 (53)
Three or more times a day	5 (8)
Unidentified	13 (22)

n = total number of participants. SD=Standard deviation. OHA = Oral Antihyperglycemic Agents. Means and medians are rounded to the nearest one decimal place; all percentages are rounded to the nearest whole number.

Exploratory factor analysis (EFA) and conceptual relevance was used to reduce the initial 20 items to 19 items and five identified factors. The same criteria were used to evaluate a one-factor solution. EFA on all 20 items revealed poor loadings (less than 0.36) for item 19 ("I just don't like taking medicine in general") on all five potential factors. The item was dropped and subsequent scale development focused on the 19 items retained (Table 2.2).

2.4.2 Data quality and descriptive statistics

Item response rates and item distributions were satisfactory (Table 2.2). Although item response scores were skewed, in which most participants responded with favorable "never" regarding experience with the barriers, respondents used all response categories for all items. Item means ranged from 1.2 to 2.3 (median 1.7) and standard deviation from 0.7 to 1.4 (median 1.0). With the exception of item 4 ("I don't know what doses to take"), which had the highest ceiling effect (86% of participants responding "Never"), the percentage of "never" responses for all other items ranged from 44% to 74% (median 60%). Floor effects were below 13%. Rates of missing responses per item ranged from 5% to 8% (median 6%). Item 6 ("I don't feel my medicines are helping me") had the highest missing response rate (8%).

Table 2.2 Distributions and missing rates for all 20-items

Item	Item Mean	Item SD	Response scale counts					% Missing
			1	2	3	4	5	
[a]1 The pharmacy could not refill my prescription.	1.6	1.0	222	49	36	7	10	6
[a]2 My doctor or nurse forgot to write a new prescription for my medicine.	1.5	0.9	227	53	31	6	5	6
[a]3 I had to cancel or put off a visit to my doctor or nurse and ran out to medicine.	1.7	1.0	183	67	58	3	9	7
[b]4 I don't know what dose to take.	1.2	0.7	273	24	13	5	3	7
[b]5 I am not sure exactly what each medicine is for.	1.5	1.1	237	34	26	6	18	6
[c]6 I don't feel my medicines are helping me.	1.8	1.2	191	35	64	13	14	8
[e]7 They are unpleasant to take (e.g. hard to swallow, bad tasting, painful).	1.6	1.0	220	41	38	12	9	7
[e]8 My medicines make me feel bad or have side effects that I don't like.	1.7	1.1	192	54	47	15	11	7
[c]9 I have heard about side effects that I am afraid I might get.	1.7	1.1	192	52	54	12	9	7
[e]10 It's too had to keep track of what I am supposed to take when.	1.5	0.9	221	46	38	10	4	7
[e]11 There are too many doses to take each day.	1.6	0.9	206	55	45	11	4	6
[f]12 I just forget to take them.	1.9	1.0	162	73	63	14	8	6
[f]13 I forget to refill my prescription in time.	1.7	0.9	181	76	53	10	4	6

Table 2.2 continued.

Item	Item Mean	Item SD	Response scale counts 1	2	3	4	5	% Missing
[d]14 I can't afford them.	2.2	1.4	141	49	80	14	36	7
[f]16 I sometimes forget to ask my doctor or nurse about problems that I am having with my medicines.	1.9	1.1	171	49	84	13	8	5
[a]17 I sometimes find it hard to ask my doctor or nurse questions about my medicines.	1.6	1.0	215	41	50	8	10	6
[a]18 Getting to the pharmacy to pick up my medications is difficult.	2.3	1.4	146	37	87	22	32	6
[c]19 I just don't like taking medicine in general.	2.2	1.4	145	48	75	15	39	6
[c]20 Taking medicines means my health will get worse.	1.5	0.9	225	48	37	7	5	6

All items had a five-response scale: 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, and 5 = Very often. % Missing = percentage of participants with a missing response on the respective item. Item SD = Item standard deviation. The number before each item statement is arbitrary and simply identifies each barrier item number for the study. The stem for all items read, "Sometimes people do not take their medications as prescribed by their doctor. There are many reasons why this can happen. Have you ever experienced any of the reasons listed below, and if so, how often?"

[a] Generated from access and acceptability theme. [b] Generated from knowledge and understanding theme.
[c] Generated from beliefs theme. [d] Generated from cost theme. [e] Generated from side effects theme.
[f] Generated from memory theme.

2.4.3 Factor analysis and item-convergent-discriminant validity

Five factors were retained after examining the scree plot (Figure 2.1) and rotated factor loadings (Table 2.3). The five factors explained 100% of the shared variance and 53% of the total variance from 19 items. The one-factor solution was also considered because although it explained only 39% (7.46) of the total variance, it explained 79% of the shared variance, it has conceptual relevance as a single total barrier score, all its loadings exceeded 0.40, and importantly, the scree plot indicated one dominant dimension.

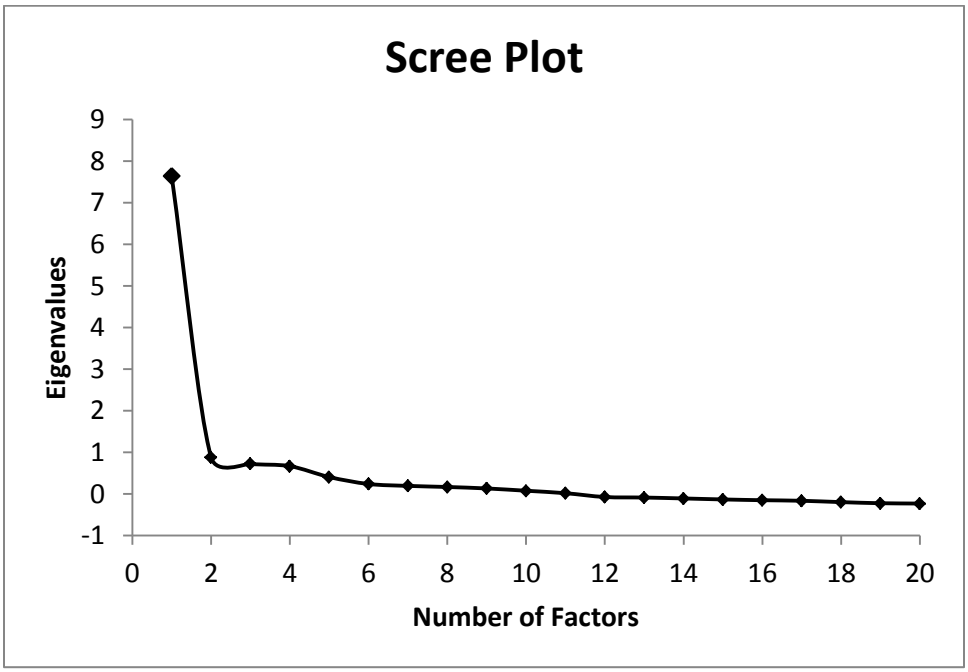


Figure 2.1 Scree plot displaying number of factors against eigenvalues from the exploratory factor analysis using squared multiple correlations as initial communalities.

Factor loadings and item total correlations on the five retained factors were estimated (Table 2.3). Except for item 6 (“I don’t feel my medicines are helping me”), all other items loaded highly (≥0.41) to one of the factors. The highest loading for item 6

was slightly below 0.40 (0.37) on factor 1 and factor 4, but was retained under factor 4 because of its conceptual relevance. Except for the case of item 6, all items loaded lower with other factors than their assigned factor.

Corrected item-total correlations between each item and its own assigned total subscale score revealed strong ($r \geq 0.46$) item-convergent validity (Table 2.3). All nineteen items correlated lower with the other four subscales (range 0.20 to 0.63; median 0.44) exhibiting acceptable item-discriminant validity.

Table 2.3 Rotated Factor Loadings – Five-factor solution

Item	Rotated Factor Loadings					*r*	Sub-scale Naming
	F1	F2	F3	F4	F5		
15 I don't have enough time to talk with my doctor or nurse about problems that I'm having with my medicines.	**.62**	.28	.26	.25	.23	.68	F1 Poor communication with providers
16 I sometimes forget to ask my doctor or nurse about problems that I am having with my medicines.	**.66**	.41	.31	.22	.14	.77	
17 I sometimes find it hard to ask my doctor or nurse questions about my medicines.	**.66**	.26	.29	.12	.25	.69	
20 Taking medicines means my health will get work.	**.52**	-.8	.11	.28	.11	.48	
4 I don't know what dose to take.	.8	**.52**	.6	.13	.37	.49	F2 Poor understanding and/or difficulty using medicine
5 I am not sure exactly what each medicine is for.	.17	**.54**	.9	.12	.24	.52	
10 It's too had to keep track of what I am supposed to take when.	.15	**.64**	.36	.26	.13	.61	
11 There are too many doses to take each day.	.13	**.57**	.35	.26	.11	.61	
12 I just forget to take them.	.15	.31	**.65**	.12	.5	.53	F3 Poor personal access
13 I forget to refill my prescription in time.	.24	.16	**.69**	.15	.19	.62	
14 I can't afford them.	.23	.7	**.48**	.26	.20	.51	
18 Getting to the pharmacy to pick up my medications is difficult.	.37	.23	**.41**	.13	.20	.52	

Table 2.3 continued

Item	Rotated Factor Loadings					*r*	Sub-scale Naming
	F1	F2	F3	F4	F5		
12 I just forget to take them.	.15	.31	**.65**	.12	.5	.53	F3 Poor personal access
13 I forget to refill my prescription in time.	.24	.16	**.69**	.15	.19	.62	
14 I can't afford them.	.23	.7	**.48**	.26	.20	.51	
18 Getting to the pharmacy to pick up my medications is difficult.	.37	.23	**.41**	.13	.20	.52	
6 I don't feel my medicines are helping me.	.37	.31	.26	**.37**	.17	.57	F4 Side effects
7 They are unpleasant to take (e.g. hard to swallow, bad tasking, painful).	.19	.35	.15	**.47**	.24	.58	
8 My medicines make me feel bad or have side effects that I don't like.	.27	.26	.31	**.61**	.13	.73	
9 I have heard about side effects that I am afraid I might get.	.36	.26	.16	**.59**	.9	.63	
1 The pharmacy could not refill my prescription.	.10	.26	.15	.14	**.60**	.54	F5 System barriers to access
2 My doctor or nurse forgot to write a new prescription for my medicine.	.24	.24	.12	.6	**.58**	.57	
3 I had to cancel or put off a visit to my doctor or nurse and ran out to medicine.	.21	.3	.42	.16	**.47**	.46	

Rotated factor loadings with items rearranged by the factors on which they load highest or to which they are assigned. *r* = corrected item-total correlation between an item and its subscale total, excluding the item from the total score. This factor analysis was based on a sample size of 286 participants (57 participants had missing data on one or several of the 19 retained items). Factor loadings of the items and their assigned factors are in bold. Sub-scales naming provides interpretations of the factors (F1to F5) based on the bolded item loadings under the factor. The five factors explain all of the shared variance and

53% of the total variance from 19 items. Item 19 “I just don’t like taking medicine in general” was dropped after initial exploratory factor analysis due to poor loadings on all five potential factors.

Similar analyses were repeated with the one-factor solution (Table 2.4). Item loadings ranged from 0.42 to 0.81 (median 0.61) and corrected item- total correlations ranged from 0.40 to 0.77 (median 0.59) for a single domain scale score.

Based on the items assigned to a factor on the five-factor solution, the factors and their corresponding subscale scores were interpreted and named as follows: factor 1 (F1) Poor communication with providers, factor 2 (F2) Poor understanding of and/or difficulty using medicine, factor 3 (F3) Poor personal access, factor 3 (F4) Side effects and factor 5 (F5) System barriers to access. The single factor from the one-factor solution was named the overall single-factor 4M scale.

Table 2.4 Factor Loadings – One factor solution (Overall single-factor 4M scale)

Item	One Factor Loadings	*r*
1 The pharmacy could not refill my prescription.	.52	.49
2 My doctor or nurse forgot to write a new prescription for my medicine.	.53	.50
3 I had to cancel or put off a visit to my doctor or nurse and ran out to medicine.	.55	.53
4 I don't know what does to take.	.51	.48
5 I am not sure exactly what each medicine is for.	.52	.49
6 I don't feel my medicines are helping me.	.67	.64
7 They are unpleasant to take (e.g. hard to swallow, bad tasking, painful).	.61	.58
8 My medicines make me feel bad or have side effects that I don't like.	.70	.67
9 I have heard about side effects that I am afraid I might get.	.65	.62
10 It's too had to keep track of what I am supposed to take when.	.71	.66
11 There are too many doses to take each day.	.66	.63
12 I just forget to take them.	.60	.56
13 I forget to refill my prescription in time.	.66	.63
14 I can't afford them.	.55	.54
15 I don't have enough time to talk with my doctor or nurse about problems that I'm having with my medicines.	.75	.72
16 I sometimes forget to ask my doctor or nurse about problems that I am having with my medicines.	.81	.77
17 I sometimes find it hard to ask my doctor or nurse questions about my medicines.	.73	.70
18 Getting to the pharmacy to pick up my medications is difficult.	.61	.59
20 Taking medicines means my health will get work.	.42	.40

r = corrected item-total correlation between an item and its subscale, excluding the item from the total score. This factor analysis was based on a sample size of 286 participants (57 participants had missing data on one or several of the 19 retained items). The single-factor explains 79% (7.46) of the shared variance (9.41) and 39% of the total variance

from 19 items. Item 19 "I just don't like taking medicine in general" was dropped after initial exploratory factor analysis due to poor loadings on all five potential factors.

2.4.4 Reliability

Cronbach's alpha is reported in Table 2.5. Cronbach's coefficient alpha for the five-factors and single-factor solutions were acceptable ($\alpha \geq 0.70$) (54).

Table 2.5 Reliability

Five-factor 4M subscales and Overall single-factor 4M Scale	**Cronbach's coefficient alpha**
F1 Poor communication with providers	.83
F2 Poor understanding and/or difficulty using medicine	.75
F3 Poor personal access	.74
F4 Side effects	.81
F5 System barriers to access	.70
Overall single-factor 4M scale	.92

F1, F2, F3, F4 and F5 are arbitrary identifiers of the factor number for the 5-factor subscales. 4M scale = Murage-Marrero-Monahan Medication Barriers scale.

2.4.5 Features of scale score distributions

The subscale means (standard deviations) ranged from 4.7 to 8.0 (2.2 to 3.5) indicating lower experiences with the barriers and acceptable variability (Table 2.6). Whereas floor effects were unnoticeably small (<1%), ceiling effects ranged from 24% to 55%. The proportion of subscale scores not computable ranged from 7% to 11%.

Observed scores for the overall single-factor 4M scale ranged from 19 to 87. The scores were adequately variable with a mean score of 32 (standard deviation 12.4) and median of 30. A ceiling effect of 18% and a negligible floor effect were observed. Seventeen percent of total scores could not be computed.

Table 2.6 Descriptive features of the five-factor 4M subscales and overall single-factor 4M scale

4M Subscales and Overall single-factor 4M Scale	Number of items	Possible Range	Observed Range	Mean	Median	SD	% Ceiling	% Floor	% missing
F1 Poor communication with providers	4	4-20	4-20	6.7	5.0	3.3	40.8	0.3	7
F2 Poor understanding and/or difficulty using medicine	4	4-20	4-20	5.9	4.0	2.8	52.8	0.3	10
F3 Poor personal access	4	4-20	4-20	8.0	8.0	3.5	23.9	0.6	8
F4 Side effects	4	4-20	4-20	6.9	6.0	3.4	40.8	0.7	11
F5 System barriers to access	3	3-15	3-15	4.7	4.0	2.2	45.7	0.6	9
Overall single-factor 4M scale	19	19-95	19-87	32.0	30.0	12.4	18.2	0	17

SD = standard deviation. 4M scale = Murage-Marrero-Monahan Medication Barriers scale. % Ceiling is the proportion of respondents per factor (or subscale) responding favorably i.e. minimum score. % floor is the proportion of respondents per factor (or subscale) responding unfavorably i.e. maximum score. % missing is the proportion of scores not calculable per factor (or subscale).

2.4.6 Scale to scale correlations

Inter-scale correlations between the five subscale scores were moderate in magnitude, ranging from 0.46 to 0.68 (median 0.56; $p<0.0001$ all correlations) (Table 2.7). The moderate correlations indicated that the subscales measured related but distinctly different domains of perceived barriers to medication use.

Table 2.7 Subscales correlations

4M Subscales	**4M Subscales**			
	F1	**F2**	**F3**	**F4**
F1 Poor communication with providers				
F2 Poor understanding and/or difficulty using medicine	0.57			
F3 Poor personal access	0.61	0.55		
F4 Side effects	0.68	0.62	0.59	
F5 System barriers to access	0.51	0.47	0.52	0.46

Pearson correlation was used to compute the correlations. 4M scale = Murage-Marrero-Monahan Medication Barriers scale. F1-F5 = factors.

2.4.7 Discriminant validity

Correlations of the five subscale scores and overall 4M total score with the four QoL measures displayed evidence of discriminant validity (Table 2.8). Pearson correlations between the QoL measures – SF-36 single item general health, SF-36 mental health, SF-36 vitality and Rand health distress scales – and the five subscales ranged from -0.45 to -0.11 (median -0.27). Except for the correlation between Vitality QoL and F5 "system barriers to access" ($p=0.055$) which was marginally significant, all other correlations were significant ($p<0.05$). Correlations of the overall single-factor 4M scale

score with the same QoL measures presented similar results: (range -0.25 to -0.43; median -0.37; all p<0.0001). The strongest correlations with QoL measures were observed for poor personal access and the total 4M barriers scale.

Table 2.8 Pearson correlation of the five-factor 4M subscales and overall single-factor 4M scale to QoL measures

Five-factor 4M Subscales and Overall single-factor 4M Scale	**SF36 single item general health**	**SF-36 Mental health**	**SF-36 Vitality**	**Rand Health Distress**
F1 Poor communication with providers	-.23	-.29	-.16	-.35
F2 Poor understanding and/or difficulty using medicine	-.20	-.26	-.13	-.28
F3 Poor personal access	-.30	-.45	-.27	-.41
F4 Side effects	-.20	-.35	-.21	-.35
F5 System barriers to access	-.13	-.19	-.11	-.22
Overall single-factor 4M scale	-.31	-.43	-.25	-.43

QoL = Quality of life. 4M scale = Murage-Marrero-Monahan Medication Barriers scale. All correlations were significant at p<0.05, except between Vitality QoL measure and F5 System barriers to access subscale (P=0.0545) which was marginally significant. All correlations are Pearson correlation coefficients.

2.4.8 Known-group validity

Median scores of the five subscales across the three medication regimens ranged from 3 to 8 (Table 2.9). Kruskal-Wallis tests comparing the three medication regimens (OHA alone, Insulin alone and OHA plus Insulin combined) revealed significant differences in median scores across three subscales: F2 “poor understanding of and/or difficulty using medicine”, F4 “side effects”, and F5 “system barriers to access”. Subsequent pairwise comparisons of their medication regimen median scores revealed

that OHA therapy alone was significantly different than insulin therapy alone, and also significantly different than OHA plus insulin combined therapy. OHA therapy alone had significantly lower median scores than the other two therapies. A similar pattern was observed on the median score of the overall single-factor 4M scale. Specifically, OHA therapy alone had significantly lower median score (26.0) than the other two therapies (31.5 and 32.0).

Table 2.9 Known-groups medication discriminant validity

Five-Factor 4M Subscales and Overall Single-Factor 4M Scale	Diabetes medication therapy			Overall comparison (χ^2)[a]	Pairwise comparisons[b]		
	OHA alone (n=176)	Insulin alone (n=62)	OHA + Insulin (n=95)		OHA alone vs. OHA + Insulin	Insulin alone vs. OHA + Insulin	OHA alone vs. Insulin alone
F1 Poor communication with providers	5.0	5.0	6.0	2.27	12,521	5,876	9,321
F2 Poor understanding of and/or difficulty using medicine	4.0	6.0	6.0	11.60**	12, 646**	5,891	9,659**
F3 Poor personal access	7.0	8.0	8.0	4.04	12,280	5,811	9,468
F4 Side effects	5.0	6.0	7.0	9.83**	12,134**	5,339	9,142*
F5 System barriers to access	3.0	4.0	4.0	6.27*	12,309*	5,681	9,373*
Overall single-factor 4M scale	26.0	31.5	32.0	9.03*	10,968**	4,539	7,768*

4M scale = Murage-Marrero-Monahan Medication Barriers scale. OHA = One or more oral antihyperglycemic agents. χ^2 denotes Kruskal-Wallis chi-square. Values in columns 2, 3, and 4 are median scores. Values in column 5 are Kruskal-Wallis chi-squares. Values in columns 6, 7, and 8 are Wilcoxon rank sum T-Statistics. N=333 respondents. The 10 respondents missing: one had a missing medication regimen and nine indicated that they were not using any diabetes medication. [b]Pairwise comparisons by Wilcoxon rank sum test. * denotes $p < 0.05$, ** denotes $p < 0.01$.

2.5 Discussion

The developed 19-item 4M scale is an adequate assessment tool for enabling patients to report barriers they experience to using medications as prescribed. It has acceptable psychometric properties – including content validity, reliability, discriminant validity and known-group validity – both as a five-domain instrument and as a single-domain instrument.

As a five-domain tool it can identify specific barriers for focused interventions, while as a single-domain it provides an overall assessment of barriers that can identify potential non-adherers. The 4M scale adequacy in assessing barriers is corroborated by its ability to capture all (as a five-domain) or over three-quarters (as a single-domain) of its items common variance, presumed as variance originating from the latent barriers to taking medication as prescribed. Additionally, the corrected item-total correlations criterion of all five domains and the single domain demonstrated acceptable item contribution to their respective scale (48, 55).

The 4M scale exhibited acceptable internal consistency reliability. Cronbach's coefficient alpha for the five domains ($\alpha \geq 0.70$) corroborated that each domain was measured with adequate internal consistency (26, 48, 50). Furthermore, removal of each item resulted in lower Cronbach's alphas, except for item 20 ("Taking medicine means my health will get worse"). Nonetheless, the item was retained because of its conceptual relevance to self-reported barriers and to its domain. Cronbach's coefficient alpha for the single-domain was even higher ($\alpha = 0.92$), evidence that the instrument as a whole was internally consistent with its measurement of the common concept, patients' perceived barriers to using medication as prescribed by their healthcare provider (50, 56).

The 4M scale revealed good discriminant validity and known-group validity both as a five-domain and as a single-domain instrument. In both instrument perspectives the instrument was correlated inversely, significantly and lowly with QoL measures confirming a priori hypothesis for discriminant validity. Likewise, median scores in both instrument perspectives revealed that patients on OHA monotherapy had lower median scores than those on Insulin and combined insulin and OHA therapies. This finding agreed with Cramer's conclusion that medication adherence is lower for patients on insulin (62%) than for those on OHA (81-85%) (57) among Type 2 diabetes patients, and that patients on monotherapy regimens (49%) have higher medication adherence than those on polypharmacy regimens (36%) (6). The results provided evidence of known-group validity. The observed median differences were significant for three of the five domains and for the single domain. Absence of significance on median differences for the two domains, "poor personal communication with providers" and "poor personal access", could be attributed to a lack of direct influence of medication regimen on the two domains.

2.5.1 Limitations

There are limitations to the development and generalizability of the 4M scale. Recall bias is possible because responses to the instrument demand recalling previous experiences. Second, a moderate ceiling effect was observed; however, there was no evidence that it affected validity or reliability perhaps because we had adequate variability on the response scale scores. Third, test-retest reliability data were not available for the barrier items. Finally, generalizability is limited by the low response rate

and the fact that non-responders were more likely to be male. Although the low-income population was ideal for this study, the population was highly transient which affected the response rate. Hence, findings are limited to the study population that was predominantly female, from low income populations, with type 2 diabetes and from Indianapolis.

Future studies should focus on testing psychometric properties of the instrument in other patient populations and regions. Likewise, assessing test-retest reliability and criterion validity of the instrument would strengthen its purpose. Studies to explore potential reduction of items while maintaining reliability and validity would be beneficial for enhancing clinical feasibility of the instrument. Also, examining its ability to detect change (responsiveness to intervention) would add great value in its role as an outcome in medication adherence randomized controlled trials.

2.6 Conclusions

The Murage-Marrero-Monahan Medication Barriers (4M) scale provides an inexpensive, practical, valid and reliable alternative to assessing medication adherence that reduces tendencies to provide socially desirable or defensive responses to questions about medication use. It can be conveniently incorporated into clinical practice and contribute to developing medication adherence interventions.

In addition to using the 4M subscales and overall score as outcomes in adherence trials, we see a potentially valuable application of the 4M scale as a tool to facilitate discussion between patients and their providers during clinical encounters. The 4M scale is easy to administer and can be easily scored to identify issues that need to be addressed. By identifying specific barriers, possible solutions are more likely to be generated.

CHAPTER 3

PATIENT DEMOGRAPHIC CHARACTERISTICS ASSOCIATED WITH PERCEIVED BARRIERS TO USING MEDICATIONS AS PRESCRIBED

3.1 Abstract

Purpose

To determine whether patient age, gender, race/ethnicity, education level and household income were associated with perceived barriers to using medications as prescribed.

Methods

A cross-sectional survey and chart audit of 964 adult, English or Spanish speaking patients with Type-2 diabetes (T2D) from the Translating Research into Action for Diabetes cohort was conducted between 2005 and 2006. Demographic factors were obtained and medication barriers assessed by the Murage-Marrero-Monahan Medication barriers scale (4M scale). Analysis of covariance (ANCOVA) was used to assess associations between patient demographic characteristics and identified medication barriers. Potential interactions of the primary demographic factors were examined with interaction tests.

Results

Age was inversely associated with all identified barriers. Household income also was inversely associated with two barriers: poor communication with providers and side effects. Gender, education level and race/ethnicity were not independently associated

with any barrier, but separately interacted with age and/or household income in influencing different barriers.

Conclusions

Age and household income clearly impact barriers to using medication as prescribed and should be considered when evaluating barriers among Type-2 diabetes patients. Moreover, consideration on how both variables separately interact with gender, education level and race/ethnicity in influencing the barriers is necessary when planning interventions.

Keywords

Diabetes, Type-2 diabetes, Medication adherence, Medication barriers, Barriers, Demographic factors

3.2 Introduction

Despite efficacy of available medication to treat diabetes and cardiovascular disease, expected treatment benefits often are not realized. This has been attributed, in part, to suboptimal medication adherence (6-14). Research also has shown that many patients with diabetes do not reliably take medications as prescribed (22). Additionally, several studies have linked the poor medication adherence to negative health outcomes, higher healthcare utilization and higher healthcare costs (10, 23-28, 38, 58, 59). Hence, the need to identify patients with poor medication adherence cannot be over emphasized, especially after it has been demonstrated that medication adherence is a modifiable behavior that can be improved with appropriate interventions targeted to patients with poor adherence (29).

To help identify patients who may need additional adherence support, previous studies have focused on identifying personal characteristics associated with medication adherence. The studies have provided important insight on patient medication adherence traits but have failed to identify specific intervention target areas that can improve adherence (60, 61). Hence, the likelihood of success with interventions is greatly diminished.

We suggest barriers, defined as patients' perceived barriers to using medication as prescribed by their healthcare providers, can identify possible issues in medication adherence. In this context, understanding of patient demographic characteristics associated with the perceived barriers can provide insight on how demographic characteristics relate to specific barriers. This will facilitate care providers to structure personalized interventions of the barriers to improve medication adherence. Therefore,

this study seeks to determine whether patient age, gender, race/ethnicity, education level and household income, are associated with barriers to using medication as prescribed among Type-2 diabetes (T2D) patients. As a secondary objective, this study explores interaction between the demographic characteristics in influencing the identified barriers among T2D patients.

3.3 Methods

3.3.1 Study population

We conducted a cross-sectional survey and chart review of patients with Type-2 diabetes (T2D) from the Translating Research into Action for Diabetes (TRIAD) Cohort (62, 63). The survey, administered between 2005 and 2006, targeted subjects who had either good or poor control of three CVD risk factors, glucose, blood pressure, and lipids, as defined by published standards of care (64, 65). The written survey assessed a wide range of issues including patient perceptions of barriers to using medications as prescribed, which is the focus of this study. The chart review abstracted medical history information and specific diabetes-related health information for the previous 18 months from the point of the survey.

In addition to the survey, data regarding medical history and related health information were obtained from chart reviews to identify and classify participants as having good or poor CVD risk factor control. Classification of quality of control used criteria set forth by the American Diabetes Association for three CVD risk factor measures: glycosylated hemoglobin A1c (HbA1c) for diabetes, systolic blood pressure (SBP) for hypertension, and low density lipoprotein cholesterol (LDL-c) for dyslipidemia

(64, 66). Poor CVD risk factor control was defined as failure in controlling any two of the three CVD risk factors, whereas good control was having all three risk factors within required targets. Poor diabetes control was defined as having an HbA1c ≥ 8 and the opposite was good control; poor hypertension control was defined as either a chart diagnosis of hypertension and an SBP ≥ 140 mm Hg, or two recent SBPs ≥ 160 mm Hg, while good hypertension control was defined as a chart diagnosis of hypertension and a most recent SBP < 140 mm Hg; poor dyslipidemia control was defined as a most recent LDL-c ≥ 130 plus either a chart diagnosis of dyslipidemia or a Statin prescription, or simply a most recent LDL-c ≥ 160, while good dyslipidemia control was defined as a chart diagnosis of dyslipidemia and a recent LDL-c < 130.

Participants were adult (18 years or older) patients with Type-2 diabetes that were enrolled in a managed care health plan for more than 12 months and spoke either English or Spanish. Also, they had to have been diagnosed with diabetes, hypertension and dyslipidemia. In addition, they were required to have had at least one laboratory test for diabetes, blood pressure and lipids within the previous 12 months from the point of the survey. Participants were recruited from four TRIAD study centers (TRC): Indiana University, Kaiser Northern California, University of Michigan and University of California Los Angeles (UCLA). Approval for secondary analysis of the data was obtained from the Indiana University Purdue University Indianapolis institutional review board (IRB). For the original TRIAD study approval was obtained from IRBs at each participating site and informed consent obtained from each participant. Details of the TRIAD prospective study are described elsewhere (63).

3.3.2 Barriers

Patients' perceived barriers to using medication as prescribed by their healthcare provider, (termed "barriers") were measured using the Murage-Marrero-Monahan medication barriers scale (4M scale). The 19-item 4M scale has demonstrated acceptable validity and reliability in assessing patients' perceived barriers to medication use (67). The 4M scale is unique in that it focuses on general responses to all medications versus specific drugs. By using this approach, it addresses social desirability bias that is common when patients are queried about their use of specific medications by healthcare providers (68, 69). This tendency to affirm medication use is a common drawback of direct assessment methods of medication adherence (68).

Five barrier constructs were assessed from each of the five domains of the 4M scale: poor personal access, poor communication with providers, poor understanding of and/or difficulty in taking medicine, side effects and system barriers to access. Each of the five domains was calculated as a mean of its barrier items. The overall mean calculated from the five domain means provided the overall barriers experience. To improve item completeness, missing items were imputed to the domain mean, if at least 50% of items in a domain had responses. All items on the instrument were scored 1 through 5 on a five-category response scale: "never", "rarely", "sometimes", "usually", and "always", respectively. Higher mean scores indicated higher frequency of experiencing the barriers suggesting poor medication adherence.

3.3.3 Primary demographic measures

Information on age, gender, race/ethnicity, education level, and household income were collected. Age was grouped in equal 10-year intervals, except to avoid sparse categories in response, the lowest and highest age groups had a wider range than 10 years, and for the same reason, income responses were grouped in the survey and further compressed into three groups for analysis.

3.3.4 Other potentially confounding covariate measures

Other variables and potential confounders obtained or computed from the survey responses were smoking status, body mass index (BMI) group, duration with diabetes and participant's TRIAD research center (TRC). Duration with diabetes was log-transformed to correct for its right-skewed distribution. All other covariates were categorical.

3.3.5 Statistical analysis

Descriptive characteristics of the sample population were calculated using frequencies and proportions for categorical variables, and means and standard deviations for continuous variables. For convenience, throughout the remainder of this paper we will use the term factors to refer to the independent variables in the models (i.e. the primary demographic variables and the potentially confounding covariates) for which the dependent variables are the different barrier scale scores. Correlations between the primary demographic factors and between all factors together were calculated to examine redundancy from related factors.

Analysis of covariance (ANCOVA) was conducted to estimate the main influence from age, gender, race/ethnicity, education level and household income level on each of the five specific barriers and the overall barriers experience, while adjusting for potentially confounding variables. All models included all the five primary demographic factors and were adjusted for duration with diabetes, BMI group, smoking status and participant's TRIAD research center (TRC). Significant categorical factors were examined for significant pairwise mean barrier differences using the simulation post-hoc test in the SAS GLM procedure.

Based on an exploratory approach, potential interactions between the primary demographic factors were evaluated by including an interaction term in the ANCOVA models, using a separate model for each interaction test. A p-value of 0.05 was considered significant for all tests. All analyses were performed using SAS software (Version 9.4, SAS Institute, Cary, NC).

3.4 Results

From 1,137 surveys mailed out, 964 (85%) eligible participants responded to the survey and met the chart review inclusion criteria. Except for CVD risk all other variables were obtained from the survey. Participants tended to be older, mostly females, and had low annual household income (Table 3.1). Participants were similar in age and race/ethnicity to that observed in the U.S. diabetes prevalence population (2). Missing data was minimal for all variables, the highest being on household annual income. Participants had low barrier mean scores suggesting they had experienced only a few specific barriers (Table 3.1).

Table 3.1. Distribution of study population characteristics and identified barriers

Patient characteristics	**All N=964 n (%)**
Duration with diabetes [mean (SD)]	13 (10)
CVD risk group	
Poor control of at least 2 CVD risk factors	405 (42%)
Good control of all 3 CVD risk factors	559 (53%)
Age groups	
18 to 39 years	19 (2)
40 to 49 years	82 (8)
50 to 59 years	267 (28)
60 to 69 years	318 (33)
70 to 79 years	217 (22)
80 years and older	56 (6)
Unknown	5 (1)
Gender	
Females	552 (57)
Males	412 (43)
Education level	
Up to high school graduate or GED	453 (47)
Some college or higher	499 (52)
Unknown	12 (1)
Household annual income level	
Low income (less than $40,000)	458 (47)
Middle income ($40,000 to < $75,000)	190 (20)
High income ($75,000 or more)	182 (19)
Unknown	134 (14)
Body mass index (BMI) group	
Normal	95 (10)
Overweight	245 (25)
Obese	419 (44)
Morbidly Obese	139 (14)
Unknown	66 (7)
Race/Ethnicity	
non-Hispanic Caucasian	485 (50)
non-Hispanic African American	196 (20)
Other races	97 (10)
Hispanic / Latino	139 (15)
Unknown	47 (5)
Smoking status	
Current Smoker	152 (16)
Former Smoker	331 (34)
Non-Smoker	428 (44)
Unknown	53 (6)

Table 3.1. Continued

Patient characteristics	**All N=964 n (%)**
TRIAD research centers	
Kaiser Northern California	415 (43)
Indiana University	235 (24)
University of Michigan	151 (16)
UCLA	163 (17)
Barriers	**Mean (SD)**
Poor personal access	1.48 (0.61)
Poor communication with providers	1.17 (0.43)
Poor understanding of and/or difficulty taking medicine	1.17 (0.42)
Side effects	1.24 (0.53)
System barriers	1.23 (0.49)
Overall Barrier Score	1.26 (0.39)

N denotes the total number of participating patients. n denotes the total number of participants under each characteristic subgroup. % denotes percentage of the total population by the number in each characteristic subgroup. SD denotes standard deviation. GED denotes general educational development. BMI denotes body mass index. TRIAD is Translating Research Into Action for Diabetes. UCLA denotes University of California at Los Angeles.

Primary demographic factors had low correlations with each other, except for education level and annual household income which had the highest though relatively moderate correlation ($r = 0.43$, $p<0.0001$) (Table 3.2). Additionally, the absolute magnitude of the correlations of all factors, including the adjustment covariates not shown on table 3.2, ranged from $r = 0.01$ for age and gender to $r = 0.43$ for education and annual household income (absolute magnitude, median $r = 0.08$); again indicating moderately low correlations. Given that there was only minor redundancy among the factors, the four primary demographic factors and adjustment covariates were included in all ANCOVA models.

Table 3.2. Correlation between age, race/ethnicity, education and household income demographic factors

Demographic factors	Race / ethnicity	Education	Household income	Gender
Age group	0.04	- 0.16***	-0.24***	0.01
Race/ethnicity		0.21***	0.17***	-0.11**
Education			0.43***	-0.19***
Household income				-0.25***

** denotes P<0.001. *** denotes P<0.0001

Adjusted ANCOVA models revealed that all five specific barrier scores and the overall barrier score differed by age group (Table 3.3). Pairwise comparisons revealed that, in general barrier mean scores decreased with increasing age, suggesting that older patients experienced barriers to using medications less frequently than younger patients (Figure 3.1).

Table 3.3. Adjusted associations of demographic factors and specific barriers as well as the overall barrier experience assessed by the 4M scale [a]

	Poor personal access	**Poor communication with providers**	**Poor understanding of and/or difficulty taking medicine**	**Side effects**	**System barriers**	**Overall Barrier Score**
	(model 1)	**(model 2)**	**(model 3)**	**(model 4)**	**(model 5)**	**(model 6)**
Overall F value	3.90****	2.77****	2.65****	2.27**	2.67****	3.54****
Adjusted R^2 (%) (95 CI)	9 (5 to 14)	6 (2 to 10)	5 (2 to 10)	4 (1 to 8)	5 (2 to 10)	8 (4-13)
Individual factors F-values[b]						
Age group	4.53***	4.29***	4.39***	4.68***	2.76*	5.63****
Comparison[b]	*C, J, M, O*	*C, J*	*B, C*	*C, D*		*C, D, O*
Gender	1.44	0.00	0.52	0.58	0.70	1.05
Education level	1.35	0.66	0.15	0.79	0.24	0.19
Household income	1.72	3.90*	1.04	3.15*	2.07	3.47*
Comparison[b]		*Q*		*Q*		*Q*
Duration	0.67	0.05	0.00	0.05	0.04	0.00
BMI group	5.13**	0.22	1.94	0.74	0.80	2.17
Comparison[b]	*T, U*					
Race/Ethnicity	0.55	1.86	1.70	1.09	0.50	0.85
Smoking status	2.54	0.79	0.58	0.78	0.69	0.75
TRIAD center	1.12	2.10	0.58	0.69	3.04*	1.37
Comparison[b]					*Z*	

[a] Analysis of covariance (ANCOVA) models. [b] only significant comparisons of post-hoc simulation results are shown. % denotes percent. CI denotes confidence interval. BMI denotes body mass index. TRIAD is Translating Research Into Action for Diabetes.

Age (in years) comparisons: A = 40 to 49 vs. 18 to 39 ; B = 40 to 49 vs. 50 to 59 ; C = 40 to 49 vs. 60 to 69 ; D = 40 to 49 vs. 70 to 79 ; E = 40 to 49 vs. ≥80 ; F = 50 to 59 vs. 18 to 39 ; G = 50 to 59 vs. 60 to 69 ; H = 50 to 59 vs. 70 to 79 ; I = 50 to

59 vs. ≥80 ; J = 60 to 69 vs. 18 to 39 ; K = 60 to 69 vs. 70 to 79 ; L = 60 to 69 vs. ≥80 ; M = 70 to 79 vs. 18 to 39 ; N = 70 to 79 vs. ≥80 ; and O = ≥80 vs. 18 to 39 .
Household annual income comparisons: P = high income ($75,000 or more) vs. middle income ($40,000 to < $75,000); Q = high income ($75,000 or more) vs. low income (less than $40,000); and R = middle income ($40,000 to < $75,000) vs. low income (less than $40,000).
BMI group comparisons: S = morbidly obese vs. obese; T = morbidly obese vs. overweight; U = morbidly obese vs. normal weight; V = obese vs. overweight; W = obese vs. normal weight; and X = overweight vs. normal weight.
TRIAD research center comparisons: Y = Kaiser Northern California vs. Indiana University; Z = University of Michigan vs. Indiana University; A1 = Kaiser Northern California vs. University of Michigan; A2 = Kaiser Northern California vs. UCLA; A3 = University of Michigan vs. UCLA; and A4 = UCLA vs. Indiana University.
* P<0.05. ** P<0.01. *** P<0.001. **** P<0.0001.

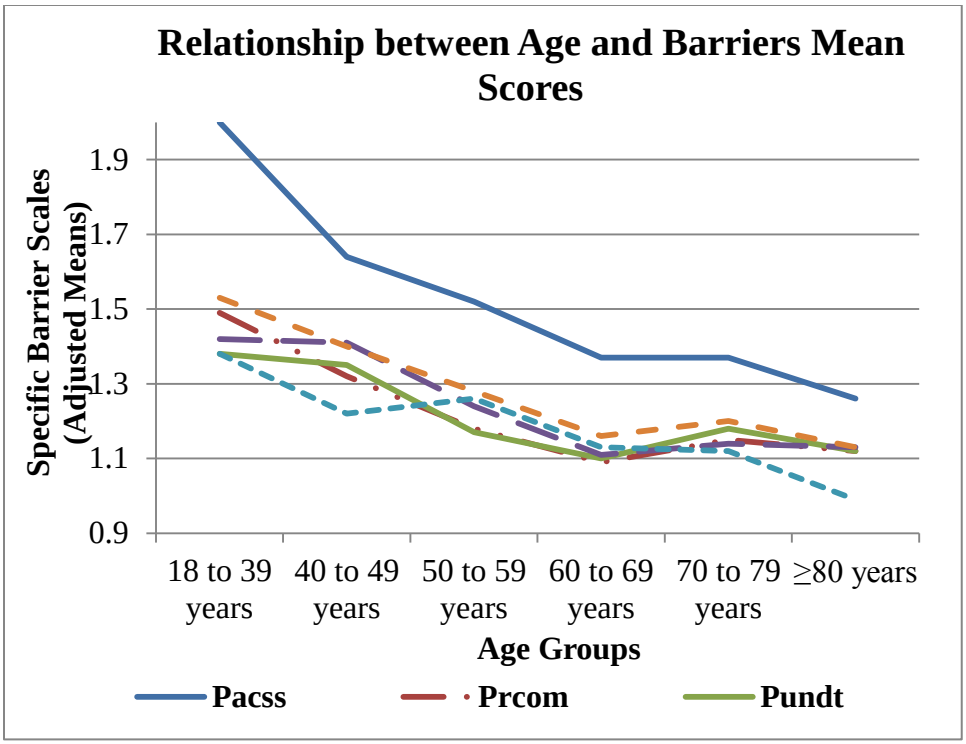


Figure 3.1.Relationship between age and barriers mean scores.
"Pacss" denotes poor provider access barrier; "Prcom" denotes poor communication with providers barrier; "Pundt" denotes poor understanding and/or difficulty taking medicine; "Sdeft" denotes side effects barrier; "Sybrs" denotes system access barrier; and "Overall" denotes overall total barriers mean score.

The poor communication with providers barrier score, the side effects barrier score and the overall barrier score differed by annual household income. All three barrier mean scores decreased with increasing annual household income (Figure 3.2). Patients from low annual household income (less than $40,000) had on average significantly higher mean scores than those from high household income ($75,000 or more) on the three barriers: poor communication with providers barrier, mean difference 0.15, 95% CI, 0.02 to 0.27; side effects barrier, mean difference 0.15, 95% CI, 0.01 to 0.29; and overall barrier experience, mean difference 0.12, 95% CI, 0.01 to 0.23.

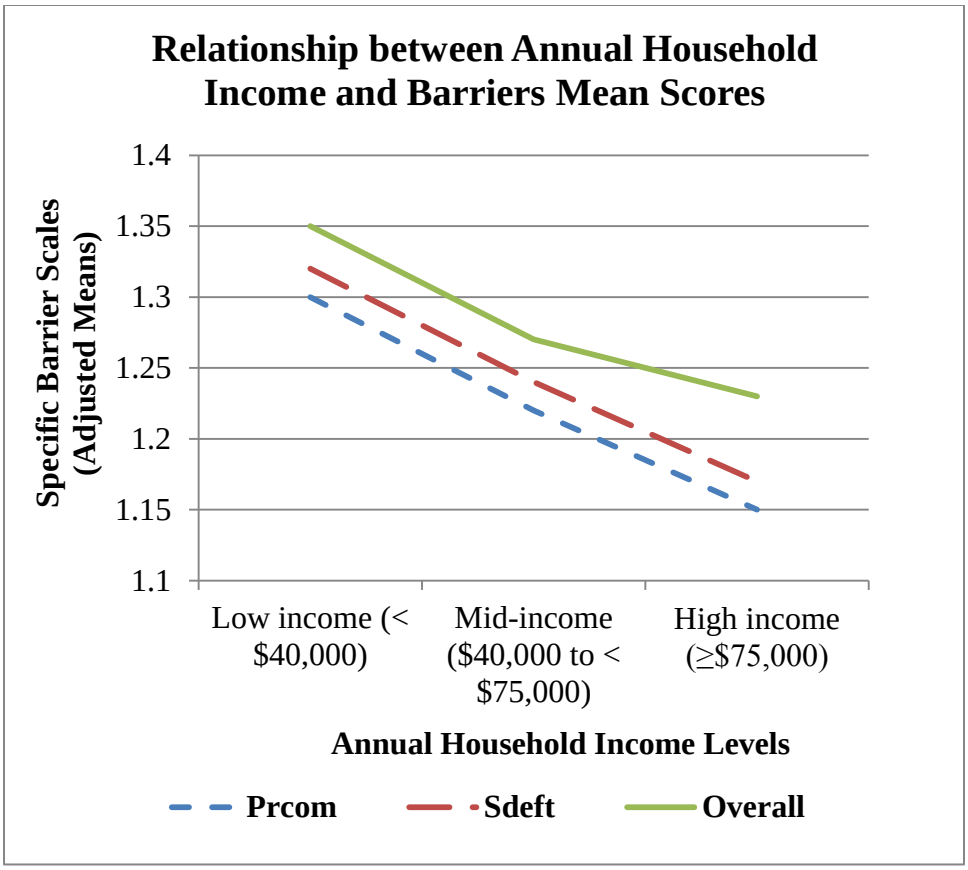


Figure 3.2. Relationship between annual household income and barriers mean scores. "Prcom" denotes poor communication with provider barrier; "Sdeft" denotes side effects barrier; and "Overall" denotes overall total barriers mean score.

Two covariates also were significant: the poor personal access barrier score increased with increasing BMI status. Morbidly obese patients had a significantly higher poor personal access mean score than overweight patients, mean difference 0.25, 95% CI, 0.05 to 0.44; and normal weight patients, mean difference 0.32, 95% CI, 0.08 to 0.57. Additionally, the system barriers to access score differed by the participant's TRIAD research center. System access barriers were significantly more common among Indiana University patients than University of Michigan patients (mean difference 0.20, 95% CI, 0.02 to 0.37). The system access barrier mean score was highest among Indiana

University (1.28) patients, then UCLA (1.21) followed by Kaiser Northern California (1.15), and University of Michigan (1.09) had the lowest score.

Potential interactions were identified between the primary demographic factors (Table 3.4). For the poor personal access barrier model only annual household income and race/ethnicity interaction was significant.

In the poor communication with providers barrier model, the age and education interaction and the age and race/ethnicity interaction were separately significant. However, when both interactions were simultaneously included in the model only the age and race/ethnicity interaction ($F=2.50$, $p=0.003$) remained significant, suggesting the age and race/ethnicity interaction influenced the communication with providers barrier more than the age and education interaction.

Similarly, for the poor understanding of and/or difficulty taking medicine barrier model, the age and education interaction, age and race/ethnicity interaction, and race/ethnicity and gender interaction were separately significant. But when simultaneously included in the model only the age and education ($F=3.17$), $p=0.008$) interaction remained significant. This suggests that the age and education interaction strongly influenced the poor understanding of and/or difficulty taking medicine barrier.

For the side effects barrier model, the age and education interaction, age and race/ethnicity interaction, and age and gender interaction were separately significant. When included in the model together, both the age and race/ethnicity interaction ($F=2.27$, $p= 0.0080$) and the age and gender interaction ($F=2.33$, $p=0.0411$) remained significant. However, all interactions remained significant when any pair of the three interactions was included in the model simultaneously. This suggests all three interactions were

contributing unique explanation of the variation of the side effects barrier. In the system barriers to access model, only the age and education interaction was significant.

Finally, on the overall barrier experience model, the age and education interaction, age and race/ethnicity interaction, and age and gender interaction were significant separately. When all three were included in the model, none was significant. However, the age and education interaction remained significant when included in the model with either the age and race/ethnicity interaction or the age and gender interaction. Also, when the age and race/ethnicity interaction and the age and gender interaction are concurrently included in the model both maintained significance. The finding suggests the age and education interaction influenced the overall barrier experience more than the other two interactions.

Table 3.4. Interactions between the primary demographic factors (age, race/ethnicity, education level and household income level) evaluated in separate ANCOVA models and their specific F-values. [a]

Possible interactions	Poor personal access	Poor communication with providers	Poor understanding of and/or difficulty taking medicine	Side effects	System barriers	Overall Barrier Score
Age and Education	2.09	2.65*	3.61**	4.31***	2.61*	4.33***
Age and Race/ethnicity	0.90	2.91***	1.93*	2.74**	1.10	2.25**
Income and Race/ethnicity	2.31*	0.20	0.36	0.61	1.21	0.47
Age and Income	0.51	0.92	0.70	0.64	0.36	0.54
Education and Income	0.59	0.38	0.42	0.21	0.66	0.34
Education and Race/ethnicity	2.25	0.59	0.02	1.09	1.44	0.69
Age and Gender	1.49	1.70	1.88	4.12**	1.60	2.81*
Education and Gender	0.26	0.00	0.32	0.06	0.17	0.01
Race/ethnicity and Gender	2.13	1.19	2.80*	2.12	1.07	1.44
Income level and Gender	2.09	0.05	0.33	0.87	0.95	0.88

* P<0.05. ** P<0.01. *** P<0.001.

3.5 Discussion

Our study found that age and household income are independently associated with barriers to using medications as prescribed. Age was inversely associated with all barriers. This finding is consistent with studies by Rolnick et al., Yang et al. and others that found older patients had higher medication adherence than younger patients (60, 61, 70, 71). Unlike younger patients, perhaps older patients are likely to take their treatment seriously, because they have more experience with the benefits of treating chronic conditions using medication. Also, the relationship may be attributed to older patients having greater understanding and acceptance that body immunity weakens with increasing age. It is also possible that older patients are less distracted by competing responsibilities such as job or children and thus, can focus more on complying with therapeutic interventions.

Income was also inversely associated with two specific barriers, poor communication with providers and side effects. This finding agrees with existing literature that adherence increases with income, implying that barriers to medication use would be inversely related to income (60, 70, 72). It is likely that low income patients may be constrained with time from multiple jobs or less flexible work environment resulting in lack of adequate time to visit and discuss medication details with their providers. It also is likely that they are financially constrained, even with coverage, to continuously purchase their prescriptions as required.

The observed interactions reveal an extended interplay between socio-economic status (SES) measures, plus age, gender and race/ethnicity in influencing the barriers (73). Education and income, two of the three cardinal measures of SES interact with age

and race/ethnicity, respectively. In turn, age and race/ethnicity interact with each other and separately with gender. The interactions reveal important insights on how these demographic factors influence the barriers to using medication as prescribed by a healthcare provider.

To interpret the significant interactions in this study, the adjusted means for barrier scores were examined descriptively within subgroups of factors. The age and education interaction suggests that younger patients with less than college education experienced the four barriers more frequently than younger patients with moderate to high education and all older patients.

The age and race/ethnicity interaction indicate that younger minority patients had greater challenges with communication with providers, understanding of and/or difficulty taking medicine and side effects barriers than younger Caucasian patients. This may reflect the impact of poor language congruence between patients and providers. In situations where English is not the patient's primary language, it is plausible that instruction about how to take medications or cautions about possible side effects may not be fully understood and thus, result in use disruption. Furthermore, the interaction agrees with previous findings that younger patients and minority patients have lower adherence (60, 61, 70, 71, 74-76).

The age and gender interaction revealed that younger females report experiencing side effect barrier more often than their younger male counterparts and all older patients. Finally, the race/ethnicity and gender interaction further pointed that female minorities, in particular Hispanic/Latino and non-Hispanic African Americans, tend to have higher experience of poor understanding of and/or difficulty taking medicine barrier than female

non-Hispanic Caucasians and males in general. The observation agreed with previous findings on medication adherence (60, 61). Again this finding is potentially attributable to poor language congruence.

Our study is not immune to limitations inherent in cross-sectional designs. First, there could be unidentified confounding factors that were not measured, which may influence the observed associations even though an attempt was made to adjust for all important confounders. Recall bias also could have been introduced when completing the surveys.

Our findings are generalizable to patients with Type-2 diabetes and provide a foundation for higher level studies exploring the barriers as precursors of medication adherence. Specifically, development of models that predict each specific barrier would contribute to significant advancements in the clinical application of the barriers. Likewise, determining a threshold of the barriers score that would distinguish non-adherent from adherent patients would also contribute significantly to the practical use of identified barriers toward improving medication adherence.

3.6 Conclusion

Age and income are inversely associated with patients' perceived barriers to using medication as prescribed. Therefore, they should be considered when evaluating barriers to using medications as prescribed. Specifically, while age should be considered with all barriers identified by the 4M scale, income should be considered when the focus is communication with providers and/or side effects barriers. Nonetheless, both

demographic factors are important considerations when evaluating the overall barrier experience.

Additionally, education, race/ethnicity and gender interact with age and/or income variably in influencing the identified barriers. Hence, they should be considered together with age and income in evaluating barriers. Our finding that age and income are associated with barriers is consistent with the finding of previous research that showed that both demographic factors are associated with medication adherence, which suggests a potential inverse relationship between barriers and medication adherence.

Therefore, understanding the influence of these demographic factors on the barriers provide insight for developing tailored interventions with a greater likelihood of success.

CHAPTER 4

PATIENT PERCEIVED BARRIERS TO MEDICATION USE AND CARDIOVASCULAR DISEASE RISK

4.1 Abstract

Background

Medication non-adherence among patients with diabetes is associated with poor control of cardiovascular disease (CVD) risk factors. This study examines whether patient's perceived barriers to using medications as indicators of medication adherence are associated with CVD risk factor control among Type 2 diabetes (T2D) patients treated for CVD.

Method

A cross-sectional study of T2D patients treated for CVD in the Translating Research into Action for Diabetes (TRIAD) study was conducted. From 964 patients who completed the Murage-Marrero-Monahan Medication barrier scale (4M scale) – a measure of perceived barriers to using medications as prescribed – 405 had poor control of at least two CVD risk factors ("cases") and 559 had good control of all three CVD risk factors: glucose, lipids, and blood pressure ("controls"). Association between perceived barriers and CVD risk factors control was evaluated using multivariable logistic regression.

Results

A unit increase in overall mean score on the 4M scale was associated with a 92% increase in the odds of having poor control of at least two CVD risk factors compared to good control of all three CVD risk factors (adjusted OR=1.92, 95% CI: 1.16 – 3.17). Analysis of specific perceived barriers revealed that poor personal access, side effects, and system access barriers were significantly associated with increased odds of poor control of CVD risk factors.

Conclusion

Increased barriers are associated with greater likelihood of having poorly controlled CVD risk factors. Assessing patient's perception of barriers should be considered in the clinical care of T2D patients as indicators of medical utilization.

4.2 Introduction

Diabetes is an established risk factor for cardiovascular disease (CVD) (19), the leading cause of death in the United States (15). Cardiovascular disease risk attributable to diabetes has increased from 5.4% to 8.7% of the U.S. population over the last half a century (16), and so has the enormous economic burden engendered by the two chronic and avoidable conditions (4, 17). Progression to CVD among diabetes patients has increased despite availability of medications with proven efficacy in controlling the three main precursors of CVD: hyperglycemia, hypertension and dyslipidemia (18, 20).

It has been shown that less than 13% of patients with diabetes attained recommended goals on the three CVD risk factors: glycosylated Hemoglobin A1c (HbA1c), systolic blood pressure (SBP) and low density lipoprotein cholesterol (LDL-c) (19, 21). Medication non-adherence among patients with diabetes is one reason that has been postulated to explain the less than optimal targets on the three CVD risk factors (13). Research has shown that many persons with diabetes do not reliably take medication as prescribed (22).

For interventions to improve medication adherence to be successful, understanding behaviors leading to non-adherence is essential. This study postulates that understanding patients' perception of barriers to using medication as prescribed can indicate possible issues with medication adherence. With this premise, we sought to assess the association between patients' perceptions of barriers to taking medications in general as prescribed and CVD risk. These findings will help in determining specific interventions to address medication adherence challenges (67). Additionally, the findings will provide evidence supporting the need to consider patient perceived barriers to

medication use in clinical care of diabetic patients, for example when considering treatment intensification (77).

4.3 Methods

4.3.1 Study population

We conducted a cross-sectional study of patients with Type 2 diabetes (T2D) treated for CVD from the Translating Research into Action for Diabetes (TRIAD) cohort. Details of the TRIAD prospective study are described elsewhere (63). The survey administered between 2005 and 2006 included a written survey and chart reviews to determine CVD risk factor control. The written survey assessed barriers to medication use, patient activation, CVD risk perception, lifestyle behaviors, cost of medications, and participatory decision-making style among others. The chart review was used to abstract medical history and specific diabetes related health information for the past 18 months. Data used in this study are responses to barriers to using medication as prescribed (4M scale items) on the survey and CVD risk factor status from chart reviews.

Participants were adult (18 years or older) patients with Type 2 diabetes that were enrolled in a managed care health plan for more than 12 months and spoke either English or Spanish. They had to have been diagnosed with hypertension and dyslipidemia. In addition, they were required to have had at least one laboratory test for diabetes, hypertension, and dyslipidemia within the past 12 months. Participants were recruited from one of four TRIAD research centers: Indiana University, Kaiser Northern California, University of Michigan and University of California Los Angeles (UCLA). Pregnant women and patients who did not meet the good and poor CVD risk control

criteria were excluded from the analysis for this paper. Approval for secondary analysis of the data was obtained from the Indiana University Purdue University Indianapolis institutional review board (IRB). For the original TRIAD study, approval was obtained from IRBs at each participating site and informed consent obtained from each participant (78).

4.3.2 Outcome measure

CVD risk was defined as good or poor based on criteria set forth by the American Diabetes Association that defines cut-points for three risk factor measures: glycosylated Hemoglobin A1c (HbA1c) for diabetes glycemic control, systolic blood pressure (SBP) for hypertension, and Low density lipoprotein cholesterol (LDL-c) for dyslipidemia (64, 66). Poor diabetes control was defined as having an HbA1c ≥ 8 and the opposite was good control. Poor hypertension control was defined as either a chart diagnosis of hypertension and an SBP ≥ 140 mm Hg, or two recent SBPs ≥ 160 mm Hg, while good hypertension control was defined as a chart diagnosis of hypertension and a most recent SBP < 140 mm Hg. Poor dyslipidemia control was defined as a most recent LDL-c ≥ 130 plus a chart diagnosis of dyslipidemia, or a Statin prescription and most recent LDL-c ≥ 130, or simply a most recent LDL-c ≥ 160, while good dyslipidemia control was defined as a chart diagnosis of dyslipidemia and a recent LDL-c < 130.

Cases were defined as patients having poor control on at least two of the three CVD risk factors, whereas controls had values within the good control range on all the three CVD risk factors. Classification was conducted and adjudicated by a panel of four

physicians who reviewed the chart data. Based on the criteria 405 patients met the criteria for poor control and 559 patients met the criteria for good control.

4.3.3 Main Exposure

Barriers were defined as obstacles that, from the respondent's perspective, hinder compliance with recommendations for using medications as prescribed by their healthcare provider. Barriers were measured using the Murage-Marrero-Monahan Medication barriers scale (4M scale), an instrument for assessing patients' perceived barriers to using medications as prescribed (67). The 19-item scale has demonstrated acceptable validity and reliability in assessing overall barriers experience or five specific barrier domains, namely poor personal access, poor communication with providers, poor understanding of and/or difficulty taking medicine, side effects, and system barriers to access. The items assess whether and how often the patient experiences a series of possible barriers to taking medication as prescribed. A five-category response scale is used for all items: "Never", "Rarely", "Sometimes", "Usually" and "Always". The score for each item ranged from 1 to 5, respectively (67). The instrument was designed to reduce false positive reporting of medication use resulting from social desirability bias, a common drawback of direct assessment methods of medication adherence. This is accomplished by assessing experiences with barriers to using medications in general without asking about specific medications during the encounter. Rather, the respondents are asked if they have ever run out or ever missed a dose of any of their medicines within the past 6 months and how often they experience the barriers listed. The overall mean score, the mean of the five subscale means, was intended as a measure of the frequency

of overall barriers experience. Higher scores on the 4M subscales and overall mean barrier score indicated increased frequency of experiencing barriers to medication use.

4.3.4 Other measures

Age, gender, race/ethnicity, education level, smoking status, income level, body mass index (BMI), duration with diabetes, and participant's TRIAD research center (TRC) were collected as potential confounders or important adjusting covariates. Age was categorized into ten-year intervals, except the first and last age groups that had wider age ranges to avoid sparse categories in response, and for the same reason income responses were grouped in the survey and further compressed into three groups for analysis. BMI was grouped into four groups: normal (BMI $\leq 24 kg/m^2$), overweight (BMI 25 to $< 30 kg/m^2$), obese (BMI 30 to $<40 kg/m^2$), and morbidly obese (BMI $\geq 40 kg/m^2$). Except for duration with diabetes, all other covariates were categorical.

4.3.5 Statistical analysis

Descriptive characteristics of cases and controls were calculated using frequencies and proportions for categorical variables, and means and standard deviations for continuous variables. Continuous variables were examined for normality. Only duration with diabetes was skewed and was log-transformed.

To improve completeness of domain mean scores, missing items were imputed to the domain mean if at least 50% of items in a domain had responses. When computing the overall barriers score, all five domain scores were required to be non-missing. Missing scores were distributed across the five domains. Without imputation of domain

scores, the overall mean barrier score were missing in 20% of cases and 17% of controls. After imputation of domain scores, missing data on the overall barrier scores were reduced to 6% among cases and by 4% among controls.

Unadjusted odds ratios (ORs) and adjusted ORs for the association between identified barriers and CVD risk control were computed using logistic regression. The unadjusted OR was computed by entering a single barrier scale score into the model as the sole independent variable without other covariates. Adjusted ORs for the barriers score were controlled for age, gender, race/ethnicity, education level, smoking status, income level, BMI group, duration with diabetes and participant's TRC. All are either confounders or important covariates of CVD risk. Each barrier domain and overall score was entered in separate models because the correlated domain scored would have created a multicollinearity problem if all domain scores were entered into the same model.

Analysis of the association between specific barriers and CVD risk control was examined by computing unadjusted and adjusted ORs of each barrier separately. A p-value of 0.05 was considered significant. All analyses were performed using SAS software (Version 9.4, SAS Institute, Cary, NC).

4.4 Results

4.4.1 Participants

From the 1,137 surveys mailed out and chart reviews, 964 (85%) eligible participants responded to the survey and met the criteria for cases and controls (Table 4.1). Except for CVD risk control classification that was obtained from chart reviews, all other variables were obtained from the survey. Cases were on average slightly, but significantly, younger and had longer duration living with diabetes than controls. Also cases reported a slightly higher proportion of low household income (<$40,000) than controls.

Table 4.1. Characteristics of participants by CVD risk control group: poor control (cases) vs. good control (controls).

Patients Characteristics	**Cases: Patients with poor control of CVD risk factors (N=405) n (%)**	**Controls: patients with good control of CVD risk factors (N=559) n (%)**	**Chi-square and Significance level**
Duration with diabetes[†]	14 (10.4)	12 (10.5)	2.51*
Age			19**
18 to 39 years	11 (3)	8 (1)	
40 to 49 years	48 (12)	34 (6)	
50 to 59 years	113 (28)	154 (28)	
60 to 69 years	127 (31)	191 (34)	
70 to 79 years	91 (22)	126 (22)	
80 years and older	14 (3)	42 (8)	
Unknown	1 (1)	4 (1)	
Gender			6*
Female	250 (62)	302 (54)	
Male	155 (38)	257 (46)	
Race/ethnicity			39***
Non-Hispanic Caucasian	164 (41)	321 (58)	
Non-Hispanic African American	114 (28)	82 (15)	
Other races	50 (12)	47 (8)	
Hispanic/Latino	60 (15)	79 (14)	
Unknown	17 (4)	30 (5)	
Education			3
Up to high school graduate or GED	202 (50)	251 (45)	
Some college or higher education	197 (49)	302 (54)	
Unknown	6 (1)	6 (1)	

Table 4.1. Continued.

Patients Characteristics	Cases: Patients with poor control of CVD risk factors (N=405) n (%)	Controls: patients with good control of CVD risk factors (N=559) n (%)	Chi-square and Significance level
BMI group			7
Normal (BMI ≤ 24kg/m^2)	33 (8)	62 (11)	
Overweight (BMI 25 to < 30kg/m^2)	92 (23)	153 (27)	
Obese (BMI 30 to <40kg/m^2)	186 (46)	233 (42)	
Morbidly obese (BMI ≥ 40kg/m^2)	62 (15)	77 (14)	
Unknown	32 (8)	34 (6)	
Household Income			10*
Low income (less than $40,000)	209 (52)	249 (45)	
Middle income ($40,000 to < $75,000)	64 (16)	126 (22)	
High income ($75,000 or more)	70 (17)	112 (20)	
Unknown	62 (15)	72 (13)	
Triad Research Centers			41***
Kaiser Northern California	201(50)	214 (38)	
Indiana University	116 (29)	119 (21)	
University of Michigan	34 (8)	117 (21)	
UCLA	54 (13)	109 (20)	
Smoking Status			4
Current Smoker	67 (17)	85 (15)	
Former Smoker	127 (31)	204 (36)	
Non-Smoker	184 (45)	244 (44)	
Unknown	27 (7)	26 (5)	

† Summary presented as mean and standard deviation, and the statistical test value is the T value from two-sided t test. CVD denotes Cardiovascular Disease. n denotes frequency by specified characteristic. % denotes percentage. GED denotes General Educational Development. BMI denotes body mass index. UCLA denotes University of California, Los Angeles. * $p<0.05$, ** $p<0.01$ and *** $p<0.001$.

Cases had a higher overall barrier score on the 4M scale than controls and the difference was statistically significant (Table 4.2). A similar trend was observed on all specific subscale barriers mean scores, indicating that the barriers were more common among cases than among controls.

Table 4.2. Overall barrier mean score and subscale barriers mean scores by CVD risk control group: poor control (cases) vs. good control (controls).

Overall and specific subscale barriers	**Cases: Patients with poor control of CVD risk factors. mean (SD)**	**Controls: patients with good control of CVD risk factors. mean (SD)**	**Mean difference (95% CI)**
Overall barrier score	1.3 (0.4)	1.2 (0.3)	0.1 (0.08-0.19)***
Poor personal access	1.6 (0.7)	1.4 (0.5)	0.2 (0.11-0.28)***
Poor communication with providers	1.2 (0.5)	1.1 (0.4)	0.01 (0.03-0.15)**
Poor understanding of and/or difficulty taking medicine	1.2 (0.5)	1.1 (0.3)	0.1 (0.06-0.18)***
Side effects	1.3 (0.6)	1.2 (0.5)	0.2 (0.08-0.23)***
System barriers to access	1.3 (0.5)	1.2 (0.4)	0.1 (0.04-0.17)**

CVD denotes cardiovascular disease. SD denotes Standard Deviation. CI denotes confidence interval. ** $p<0.01$ and *** $p<0.001$.

Table 4.3. Unadjusted and adjusted odds ratios from logistic regressions modeling the probability of poor control of CVD risk factors from patients' perceived barriers to medication use.

Overall and specific subscale barriers	**Unadjusted ORs**	**(95% CI)**	**Adjusted ORs**	**(95% CI)**
Overall barrier score	2.25***	(1.48-3.41)	1.92*	(1.16-3.17)
Poor personal access	1.58***	(1.22-2.05)	1.52*	(1.11-2.07)
Poor communication with providers	1.63**	(1.13-2.35)	1.42	(0.93-2.19)
Poor understanding of and/or difficulty taking medicine	1.75**	(1.21-2.54)	1.43	(0.91-2.26)
Side effects	1.78***	(1.24-2.46)	1.57*	(1.06-2.30)
System barriers to access	1.70**	(1.22-2.35)	1.47*	(1.01-2.14)

CVD denotes cardiovascular disease. CI denotes confidence interval. OR denotes odds ratio. Adjusting factors are age group, gender, education level, household annual income level, duration with diabetes, BMI status group, race/ethnicity, smoking status and participants TRIAD research center. * $p<0.05$, ** $p<0.01$ and *** $p<0.001$.
Note: For all adjusting factors only duration of living with diabetes ($p=0.0001$), race/ethnicity ($p=0.003$) and Triad research center ($p<0.0001$) were significant.

The overall barrier score remained significant even after adjusting for other factors (Table 4.3). A one-unit increase in the 5-point overall mean of patients' perceived barriers to using medication as prescribed by their healthcare provider was associated with a 92% increase in the odds of having poor control of two or more of the three cardiovascular disease risk factors as opposed to good control of all three CVD risk factors, after adjusting for all other covariates in the model (adjusted OR=1.92, 95% CI: 1.16 – 3.17; $p<0.05$). Duration with diabetes (OR=4.77, 95% CI: 3.47-7.13; $p=0.0001$), race/ethnicity ($p=0.0013$) and participant's Triad research center ($p<0.0001$) were significant adjusting factors in the model.

For subscale analyses, even though all unadjusted associations between the five specific barriers on the 4M scale and probability of poor control of CVD risk were significant, only poor personal access, side effects and system barriers to access specific barriers maintained significance after adjusting for all other covariates (Table 4.3). A unit increase in poor personal access barrier mean score was associated with a 52% increase in the odds of having poor control on at least two or the three CVD risk factors (OR=1.52, 95% CI: 1.11-2.07; $p<0.01$). A unit increase in side effects barrier mean score was associated with a 57% increase in the odds of having poor control on at least two or the three CVD risk factors (OR=1.57, 95% CI: 1.06-2.30; $p<0.05$). A unit increase in system barriers to access mean score was associated with a 47% increase in the odds of having poor control on at least two of the three CVD risk factors (OR=1.47, 95% CI: 1.01-2.14; $p<0.05$).

4.5 Discussion

Our study illustrates that patients' perceptions of barriers that interfere with taking their medication as prescribed are associated with poor CVD risk factor control. Specifically, on average, patients with diabetes who experienced barriers more frequently as measured by the 4M scale had higher odds of having poorly controlled HbA1c, SBP, or LDL-c compared to those who experienced barriers less frequently. The findings agreed with previous research relating medication non-adherence to increased CVD hospitalization (59) and medication adherence to reduced vascular events (79, 80). These previous research when taken together with our findings, suggests that patients' perceived barriers are specific determinants or drivers of medication adherence issues. Our findings are important not only in confirming that patients' perceived barriers helps to explain CVD risk control but also in identifying barriers on which specific interventions can be designed (67). The association corroborates the need to first consider barriers to medication use before commencing treatment intensification among patients with diabetes (13, 77, 81, 82).

Race/ethnicity, duration of living with diabetes and participants recruitment site were significant correlates of poor CVD risk control in the overall barrier score model. They agreed with previous research that duration of diabetes increases cardiovascular mortality (83). Additionally, minorities, particularly non-Hispanic African Americans, have higher odds of poor CVD risk compared to non-Hispanic Caucasians (84). Significance of the participant recruitment site suggested that regional differences, perhaps socio-economic or clinical practice, may affect CVD risk control.

Analysis of the 4M subscales revealed three specific barriers – poor provider access, side effects and system barriers to access – were significantly associated with poor CVD risk factor control. Therefore, focusing interventions to this population on the three barriers is likely to yield improvement in medication adherence, control of CVD risk factors, and eventually improvement in CVD risk factor control.

The study also had unique strengths. First, it minimized social desirability bias by indirectly focusing on barriers of the 4M scale rather than inquiring about adherence to specific medications. The 4M scale is a unique measure in that it can identify specific sources of barriers that can inhibit appropriate utilization of medications. This is a necessary step in developing interventions to improve medication utilization. Second, the study was conducted on a large, national multisite sample of well characterized patients from wide regional, clinical, racial-cultural backgrounds. Therefore, the study findings can be generalized to adult patients who have Type 2 diabetes, CVD and healthcare access.

Similar to other cross-sectional studies there may be potentially uncontrolled confounders not adjusted for in the study. The potential for recall bias is introduced by retrospectively assessing the barriers using the 4M scale. Also, the potential for misclassification bias may have been introduced by lack of information whether patients were seated or standing during SBP measurement, and lack of information whether patients were fasting before the laboratory measures. Finally, inherent in cross-sectional study design, the study could not establish temporal relationships between the barriers and CVD risk factors control.

Critical to the importance of these findings in addressing medication adherence through clinical care and public health interventions, there is need for future studies to prospectively establish the temporal relationships between patients' perceived barriers to using medication as prescribed, as drivers of medication adherence, and CVD risk factors. Also, there is need for a randomized clinical intervention study to assess the effectiveness of interventions targeting barriers identified by the 4M scale.

4.6 Conclusion

This study demonstrated that increased experiences of barriers to using medication as prescribed is associated with greater likelihood of having poor control of CVD risk factors. The association provides scientific evidence supporting the need to consider assessing patient's perception of barriers to medication use as indicators of medical utilization in the clinical care of Type 2 diabetes patients treated for CVD. For practical importance, the finding suggests that targeted interventions against identified barriers to medication use would contribute to slowing or stopping progression to CVD.

CHAPTER 5

DISCUSSIONS AND CONCLUSIONS

Findings from the three studies provide important insights into the role of barriers on medication adherence among Type-2 diabetes patients. First, the developed 19-item Murage-Marrero-Monahan Medication barriers scale (4M scale) was established as a valid and reliable instrument for assessing patients' perceived barriers to using medication as prescribed by a healthcare provider. The frequencies of the barriers measured by the instrument were found to be associated with age and income. Additionally, education, gender, race/ethnicity and geographic location of patients modified the association of age and income on barriers. Finally, greater barriers were associated with poorer CVD risk control. Comparing these findings with those of medication adherence from previous research illuminates several important implications on the adequacy of assessing barriers to using medication as prescribed by a healthcare provider as an alternate to assessing medication adherence.

The association between barriers and control of CVD risk factors agreed with previous studies which found poor medication adherence was also associated with CVD (59, 79, 80). This agreement and the understanding that poor control of CVD risk factors is an intermediate stage in the natural history of CVD implies that barriers can indicate issues with medication adherence as conceptualized.

Additionally, the finding that barriers were associated with age and income also agreed with other studies that have demonstrated medication adherence is associated with

both age and income (60, 61, 70-72). By further examining the direction of associations for both barriers and medication adherence with respect to CVD and the two demographic factors separately, the postulated counter-directional relation becomes evident. When barriers increase, CVD risk increases, while when medication adherence decreases, CVD risk increases and vice versa. For the demographic factors, when age increases barriers are fewer whereas medication adherence is higher. Likewise, when income increases, barriers are fewer whereas medication adherence is higher. The observed counter-directional associations imply existence of a plausible link between barriers and medication adherence and suggest that the two are possibly inversely related.

Barriers may potentially influence medication adherence. Because previous studies have shown that medication adherence is a modifiable behavior, the potential influence between barriers and medication adherence presents an opportunity for using tailored interventions on identified barriers to improve medication adherence (29). Consequently, the personalized interventions on identified barriers through a cascade of responses have a higher likelihood of success in improving health outcomes, for example slowing down or reducing CVD outcomes.

Finally, the fact that the association of barriers and both age and income agrees with the association of medication adherence and both demographic factors, underscores the need for considering age and income when assessing and interpreting barriers as an alternate to medication adherence.

Overall, findings from this study, that patients' perceived barriers to medication use are a potential alternative to directly measuring medication adherence, expose many opportunities for future research studies. To broaden evidence in using the 4M scale for

assessing barriers will require the following: psychometric evaluation of the tool among other patient populations and in other regions for a wider application, criterion validity evaluation for evidence that it is a reasonable proxy for adherence, and responsiveness evaluation for evidence on its ability to detect change in patients' perceived barriers following an intervention. Furthermore, studies to establish temporal relationship between reported barriers to medication use and the cardiovascular outcome would provide additional indication on the interrelationship between the barriers and medication adherence. Likewise, a randomized controlled trial on the effectiveness of interventions targeting identified barriers on the 4M scale would also corroborate the clinical importance of considering perceived barriers during clinical encounters. Equally important, studies to develop models that include readily observable demographic characteristics in predicting specific barriers in the 4M scale would enhance interpretation and generalizability of the 4M scale scores. Additionally, future studies to determine a threshold on the 4M scale score that distinguish potentially non-adherent patients from adherent patients would enhance interpretation of the 4M scale and its practical use for measuring patients' perceived barriers to medication use as prescribed.

In conclusion, the developed 19-item Murage-Marrero-Monahan Medication barriers scale (4M scale) has acceptable psychometric properties as an adequate assessment instrument for assessing patients' perceived barriers to medication use as prescribed by their healthcare provider. The tool provides novel information that can facilitate discussions between patients and their providers during clinical encounters.

Most importantly, comparisons of findings from this dissertation associating barriers to demographic factors and CVD risk control and those of previous studies

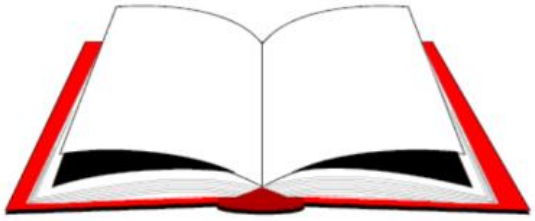
associating medication adherence to demographic factors and CVD risk corroborate the hypothesis that barriers indicate possible issues with medication adherence. Therefore, assessing patient's perceived barriers to using medications as prescribed by their healthcare provider is a plausible alternative for assessing medication adherence. By assessing barriers in a generalized context, the 4M scale circumvents social desirability bias introduced by directly confronting patients about their medication use, and captures information beyond the immediate use which could be confounded by other prevailing factors, for example, closeness to an appointment. Additionally, by identifying specific barriers to medication use, care providers have the added opportunity of personalizing interventions to reduce or eliminate the barriers. Thus, the tailored interventions will have increased likelihood of success.

APPENDIX A

DIABETES MEDICINES SURVEY

Note: Select sections extracted from the diabetes medicines survey used to collect data for development and psychometric evaluation study discussed in chapter 1.

Diabetes Medicines Survey



Understanding
Your Experiences With Medicines
for Your Diabetes

NOTE: When answering questions below about your diabetes medicines, please think about any oral medicines, injectable, or other medicines you take for your diabetes to control your blood sugar.

The first few questions ask some general information about your diabetes and the medicines you take for diabetes.

1. Which of the following statements best describes the medicines you take for your diabetes?

(circle one)

I do not take any oral or injectable medicines for my diabetes 1

I take a single oral medicine for my diabetes 2

I take two or more different oral medicines for my diabetes 3

I take *only* insulin for my diabetes 4

I take both oral medicines and insulin for my diabetes 5

I take injections other than insulin for my diabetes 6

If you take oral medicines,

how many *different kinds* of oral medicines do you take? (circle one)

1) one kind 2) two kinds 3) three or more kinds

how many *times a day* do you take your oral medicines? (circle one)

1) one time a day 2) two times a day 3) three or more times a day

If you take insulin,

a) how do you take it? (circle all that apply)

1) syringe 2) insulin pen 3) insulin pump

b) how many times do you inject insulin each day? (circle one)

1) one time 2) two times 3) three times 4) four times 5) more than 4 times

21. From time to time, many people have trouble taking the diabetes medicines their doctors prescribe. **I sometimes don't take my diabetes medicines because ...**

(circle one number on each line)

	Never	Rarely	Some-times	Often	Very Often
The pharmacy could not fill my prescription.	1	2	3	4	5
My doctor or nurse forgot to write a new prescription for my medicine.	1	2	3	4	5
I had to cancel or put off a visit to my doctor or nurse and ran out of medicine.	1	2	3	4	5
I don't know what dose to take.	1	2	3	4	5
I am not sure exactly what each medicine is for.	1	2	3	4	5
I don't feel my medicines are helping me.	1	2	3	4	5
They are unpleasant to take (e.g., hard to swallow, bad tasting, painful).	1	2	3	4	5
My medicines make me feel bad or have side effects that I don't like.	1	2	3	4	5
I have heard about side effects that I am afraid I might get.	1	2	3	4	5
It's too hard to keep track of what I am supposed to take when.	1	2	3	4	5
There are too many doses to take each day.	1	2	3	4	5
I just forget to take them.	1	2	3	4	5
I forget to refill my prescription in time.	1	2	3	4	5
I can't afford them.	1	2	3	4	5
I don't have enough time to talk with my doctor or nurse about problems that I'm having with my medicines.	1	2	3	4	5
I sometimes forget to ask my doctor or nurse about problems that I am having with my medicines.	1	2	3	4	5
I sometimes find it hard to ask my doctor or nurse questions about my medicines.	1	2	3	4	5
Getting to the pharmacy to pick up my medications is difficult.	1	2	3	4	5
I just don't like taking medicine in general.	1	2	3	4	5
Taking medicines means my health will get worse.	1	2	3	4	5

Now we'd like to ask you a few questions about your overall health. Please think about your health in general and not any specific problem or condition you may have.

YOUR HEALTH IN GENERAL

22. **In general,** would you say your health is: *(circle one)*

Excellent 1

Very good 2

Good 3

Fair 4

Poor 5

23. How much bodily pain have you had during the **past month**?

(circle one)

None 1

Very mild 2

Mild 3

Moderate 4

Severe 5

Very severe 6

24. During the **past month**, how much did pain interfere with your normal work (including both outside the home and housework)?

(circle one)

Not at all 1

A little bit 2

Moderately 3

Quite a bit 4

Extremely 5

These questions are about how you feel and how things have been with you during the past month.

25. How much of the time during the **past month** …

(circle one number on each line)

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
Did you feel full of pep?	1	2	3	4	5	6
Have you been a very nervous person?	1	2	3	4	5	6
Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
Have you felt calm and peaceful?	1	2	3	4	5	6
Did you have a lot of energy?	1	2	3	4	5	6
Have you felt downhearted and blue?	1	2	3	4	5	6
Did you feel worn out?	1	2	3	4	5	6
Have you been a happy person?	1	2	3	4	5	6
Did you feel tired?	1	2	3	4	5	6

26. How often during the **past month**…

(circle one number on each line)

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
Were you discouraged by your health problems?	1	2	3	4	5	6
Did you feel weighed down by your health problems?	1	2	3	4	5	6
Was your health a worry in your life?	1	2	3	4	5	6
Were you frustrated about your health?	1	2	3	4	5	6

APPENDIX B

TRIAD FOCUSED SURVEY CHART REVIEW INSTRUMENT

VERSION 2.0

Note: Extracted sections of the original chart review instrument used for studies in chapter 3 and 4. The complete instrument is available online at http://www.triadstudy.org/instruments_tools/pdf/focused_surv_chart_review.pdf

TRIAD FOCUSED SURVEY CHART REVIEW INSTRUMENT

VERSION 2.0

Please refer to the TRIAD Medical Chart Abstraction Instructions for detailed information regarding use of this instrument.

Study Subject ID Number:	_____ _____ _____ _____ _____ _____
Date of TRIAD Patient Survey Interview:	___ ___/___ ___/___ ___ ___ ___ (month) (day) (4 digit year)
Review Period End Date:	___ ___/___ ___/___ ___ ___ ___ (month) (day) (4 digit year)
18-Month Review Period Start Date:	___ ___/___ ___/___ ___ ___ ___ (month) (day) (4 digit year)

Date of Medical Chart Abstraction:	___ ___/___ ___/___ ___ ___ ___ (month) (day) (4 digit year)
Reviewer's ID Number: _____ _____ _____ _____ _____	

PATIENT MEDICAL HISTORY

Abstractors should consider medical documentation over an 18-month interval. Based on these records, check 'Yes' or 'No' to indicate if the patient has a record of EVER having the listed condition, treatment, or risk factor.

1. Chart evidence of a history of each of the following risk factors: *(answer all items)*

a. Diabetes mellitus	❑ 1 No ❑ 2 Yes
b. Hypertension (HTN)	❑ 1 No ❑ 2 Yes
c. Hyperlipidemia/Hypercholesterolemia	❑ 1 No ❑ 2 Yes
d. Cigarette Smoking	❑ 1 No ❑ 2 Yes

2. Did the patient have Outpatient Visits to a PCP, Nurse Practitioner, Endocrinologist, or Diabetologist during the review period? ❑ 1 No ❑ 2 Yes

If No, go to Q.4

a. Was Weight recorded at a visit included in #13a? ❑ 1 No ❑ 2 Yes

If No, go to Q.3

b. Most recent recorded Weight ___ ___ ___ • ___ **kg** or **lbs**.
(IMPORTANT: circle unit of measure)

3. Was a blood pressure reading taken at any visit included in any outpatient visit in the review period? ❑ 1 No ❑ 2 Yes

If No, go to Q.4

a. Values for the **3 most recent** systolic pressure measures:

___ ___ ___ mmHg
Date: __ __/__ __/__ __ __ __

___ ___ ___ mmHg
Date: __ __/__ __/__ __ __ __

___ ___ ___ mmHg
Date: __ __/__ __/__ __ __ __

4. Was an HbA1c test performed during the review period? ❑ 1 No ❑ 2 Yes

If No, go to Q.5

a. Value of **most recent** HbA1c test: ___ ___ ___ %
Date: __ __/__ __/__ __ __ __

b. Upper limit of normal range for **most recent** HbA1c test: ___ ___ ___ %

Check if unavailable ❑

5. Was LDL-Cholesterol measured during the review period? ❑ 1 No ❑ 2 Yes

If No, go to Q.6

a. Value of **most recent** LDL-C test: ___ ___ ___ mg/dl
Date: __ __/__ __/__ __ __ __

CURRENT MEDICATIONS

6. Were any of the medications listed on pages 4-5 prescribed or taken during the review period with no indication that they were stopped or discontinued prior to the end of the review period?

❑ 1 No ❑ 2 Yes

If Yes, indicate these current medications in the spaces below. Record in the spaces below the ***number*** *that corresponds to each current medication as it is listed on the following pages.*

Note: Medications are listed alphabetically. Trade names are capitalized and generics are in lower case. Generic equivalents to trade name medications are shown within brackets.

_____	_____	_____	_____	_____
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____

END OF DATA ENTRY

APPENDIX C

CVD RISK FACTOR PATIENT WRITTEN SURVEY

VERSION 0206

Note: Extracted sections of the original survey used for studies in chapter 3 and 4. The complete survey is available online at http://www.triadstudy.org/instruments_tools/pdf/cvd_risk_patient_written_survey.pdf

Many people tell us that there are reasons why they can't take every one of their medicines every day.

84. In the past **6 months**, did you **EVER** ***RUN OUT*** of ***ANY*** of the medicines that were prescribed by your doctor or another health provider?

- ☐ 0 No *(If no, SKIP TO question 92)*
- ☐ 1 Yes
- ☐ 2 I have not been prescribed ***ANY*** medicines in the last **6 months** *(SKIP TO question 109)*
- ☐ 8 Don't know *(SKIP TO question 92)*
- ☐ 9 Refuse *(SKIP TO question 92)*

The following are some reasons why people *RUN OUT* of medicines. For each reason, please check the box if it happens "never," "rarely," "sometimes," "usually," or "always."

I have RUN OUT of my medicines because…	Never	Rarely	Some-times	Usually	Always	Not Applicable	Don't know	Refuse
85. The doctor or nurse forgot to write a new prescription for my medicine.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 7	☐ 8	☐ 9
86. I had to cancel or put off a visit to my doctor or nurse and ran out of medicine.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 7	☐ 8	☐ 9
87. I forgot to refill my prescription in time.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 7	☐ 8	☐ 9
88. I could not afford them (they cost too much).	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 7	☐ 8	☐ 9
89. The pharmacy could not fill my prescription.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 7	☐ 8	☐ 9
90. It was hard to get to the pharmacy to pick up my medicines.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 7	☐ 8	☐ 9

92. In the past **6 months**, did you ***EVER MISS A DOSE*** of ***ANY*** of your medicines, even just one pill or shot?

0 ☐	No	***(If no, SKIP TO question 108)***
1 ☐	Yes	
8 ☐	Don't know	***(SKIP TO question 108)***
9 ☐	Refuse	***(SKIP TO question 108)***

The following are some reasons why people may have trouble taking their medicines, even when they have enough of it. For each reason, please check the box if it happens "never," "rarely," "sometimes," "usually," or "always."

I sometimes DON'T TAKE my medicines because…	**Never**	**Rarely**	**Some times**	**Usually**	**Always**	**Don't know**	**Refuse**
93. I don't know what dose to take.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
94. I am not sure exactly what each medicine is for.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
95. I don't feel they are helping me.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
96. They are unpleasant to take (e.g., hard to swallow, bad tasting, painful).	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
97. They make me feel bad or have side effects that I don't like.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
98. I have heard about side effects that I am afraid of.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
99. It's too hard to keep track of what I am supposed to take and when.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
100. There are too many doses to take each day.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
101. I just forget to take them.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
102. I don't have enough time to talk with my doctor of nurse about problems that I'm having with my medicines.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
103. I sometimes forget to ask my doctor or nurse about problems that I'm having with medicines.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
104 I sometimes find it hard to ask my doctor or nurse questions about my medicines.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
106. I just don't like taking medicines in general.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9
107. Taking medicines means my health will get worse.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 8	☐ 9

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CURRICULUM VITAE

Mwangi James Murage

EDUCATION

Indiana University	Ph.D. in Epidemiology	2014
	Minor in Biostatistics	
Indiana University	M.P.H. in Health Policy and Management	2005
Moi University	B.Sc. in Environmental Health	1999

FURTHER EDUCATION

African Virtual University	Certification in computer applications	2000 to 2001

APPOINTMENTS AND WORK EXPERIENCE

LOCAL

Indiana University Health	Epidemiologist	2011 to present
Indiana Minority Health Coalition	Director, Training and Evaluation	2007 to 2011
Indiana University Purdue	Research Assistant	2007
University Indianapolis (Nursing), IN U.S.A.		
Indiana University Purdue	Research Assistant	2007
University Indianapolis (Bioethics), IN U.S.A.		
Indiana University Purdue	Grader	2007
University Indianapolis (Mathematical sciences), IN U.S.A.		
Indiana University Purdue	Tutor	2007

University Indianapolis (Mathematical sciences), IN U.S.A.		
Indiana Minority Health Coalition	Lead Consultant/ Coordinator	2006
Velociti Integrated Systems	Executive Director, Health Policy and Management	2005
Indiana University Purdue University Indianapolis (SPEA), IN U.S.A.	Associated Faculty	2004
Indiana University Purdue University Indianapolis (Dental), IN U.S.A.	Research Assistant	2004 to 2005
Indiana University Purdue University Indianapolis (Biostatistics), IN U.S.A.	Data Entry Specialist	2003 to 2005

INTERNATIONAL

Kenya Medical Research Institute (KEMRI),	Assistant Research Officer	2000 to 2002
Kenya National Health Research and Development Center (NHRDC),	Program Assistant	2000 to 2002
Kenya African Medical and Research Foundation (AMREF), Kenya	Lead Consultant	2002
African Medical and Research Foundation (AMREF), Kenya	Lecturer/Consultant	2000 to 2002
Kenya Medical Research Institute / Japan International Cooperation Agency (KEMRI/JICA), Kenya	Intern/Supervisor	1999

PROFESSIONAL ORGANIZATION MEMBERSHIP

Delta Omega Honorary Society of Public Health	2009 to present
American College of Healthcare Executives	2014 to present
AcademyHealth	2013 to present
National Association of Health Services Executives	2007 to 2010
American Public Health Association	2005 to 2006

PROFESSIONAL HONORS AND AWARDS

Delta Omega	Honorary Society of Public Health Professionals	2009
Bachelor's Honors	Moi University	1999
Honorary member	Environmental Health Student's Association	1999
Doctoral scholarship	Indiana University Purdue University Indianapolis	2010
International student scholar	Indiana University Purdue University Indianapolis	2005
International student scholar	Indiana University Purdue University Indianapolis	2004

SUMMARY OF SELECTED PROFESSIONAL EXPERIENCE

<u>Program management and leadership</u>

Directing several statewide training grants with budgets ranging from $25,000 to $500,000

- Division of Mental Health and Addiction $500,000 cultural competency training grant, *2007 to 2011*.
- Health Resources and Services Administration $25,000 health disparities training grant for healthcare professionals, *2008 to 2010.*

- Indiana State Department of Health, Environmental health division $211,000 grant for cultural competency training of its statewide employees, *2009*.

Serving as a leader in several community initiatives

- Chaired the Mid-American Public Health Training Center as it transitioned to be the Indiana Public Health Training Center after securing a $130,000 renewable grant from HRSA, *2009*.
- Lead a team of local organizations in Indiana in organizing four annual statewide conferences on cultural competency in healthcare, *2007 to 2011*.

Program evaluation and analytics

- Provided measurement and analytics support on healthcare quality improvement. Making sense of clinical, administrative and claims data to improve healthcare provision, *2011 to present*.
- Lead the evaluation team of a federally supported statewide program designed to increase diversity in healthcare professions in Indiana, with a cumulative funding of over $630,000, *2007 to 2008*.
- Coordinated evaluation of the Indiana Tobacco Prevention and Control (ITPC) statewide program, *2006*.

SERVICE

Indiana State Lead-Safe Housing Advisory Council	Member (Governor Appointee)	2008 to 2011
Indiana Division of Mental Health and Addiction (DMHA) Workforce Development Taskforce	Member	2009 to 2011
Indiana Public Health Training Center	Chair	2011

Mid-American Public Health Training Center Advisory Board	Chair	2007 to 2010
IU Health/IUPUI Institutional Review Board (IRB)	Member	2007 to 2011
IUPUI School of Public Health Ph.D. Curriculum Committee	Student Representative	2010 to 2011
IUPUI Master of Public Health Alumni Association	Board Director	2008 to 2010
International Students Health Insurance Task Force, IUPUI	Student Representative	2006
Adolescent Substance Abuse Program (ASAP)	Member	2004 to 2005
IUPUI Master of Public Health Community Practice Committee	Student Representative	2003 to 2005
National Health Research and Development Center (NHRDC)	Research Assistant	1999 to 2000

TEACHING

Teaching assignment:

Indiana University	A316	Environmental Health Science	Lecture	Associate Faculty	Spring 2004	40 students

Other Selected Teaching/Training Assignments

INTERNATIONAL

1.	African Medical and Research Foundation International Training Center	*Introduction to Problem Based Learning (PBL) teaching/learning method*	Consultant	Spring 2002	20 Lecturers
2.	African Medical and Research Foundation International Training Center	*Problem based learning*	Lecturer	Spring 2002, Spring 2001, and Spring 2000	25, 20 and 20 students, respectively
3.	African Medical and Research Foundation International Training Center	Curriculum review of the community health program	Lecturer	Spring 2001	All faculty

LOCAL

4.	Wishard Hospital	*Cultural competency: Why? and How?*	Training Director / instructor	Fall 2010	15 employees

5.	Methodist Hospital	*Healthcare and Cultural Competency: The Bafa` Bafa` Simulation*	Training Director / instructor	Fall 2010	25 employees
6.	IUPUI Public Health graduate students	*Public Health and Cultural Competency*	Invited lecturer	Spring 2009 & Spring 2010	30 students
7.	Indiana State: Marion, Howard, Lake, Allen and Vanderburgh counties	*Cultural Awareness: The Bafa` Bafa` Experience*	Training Director / instructor	Fall 2009	35 participants each
8.	Indiana State: Marion, Howard, Lake, Allen and Vanderburgh counties	*Cultural Competency: Scenario- Based*	Training Director / instructor	Spring 2009	35 participants each
9.	Indiana State Department of Health (ISDH), Environmental	*Cultural Competency and Migrant Outreach*	Training Director / instructor	Spring 2009	40 state employees each of 6 counties

	Health				
10.	Indiana State: Marion, Howard, Lake, Allen and Vanderburgh counties	*Understanding Cultural Competency: A Strength's Perspective.*	Training Director / instructor	Fall 2008	35 participants each
11.	Indiana State: Marion, Howard, Lake, Allen and Vanderburgh counties	*Developing Cultural Competency: A Strength's Perspective.*	Training Director / instructor	Spring 2008	35 participants each
12.	HealthNet	*Understanding and Developing Cultural Competency: A Strength's Perspective.*	Training Director / instructor	Summer through Fall 2008	25 members of the leadership team
13.	Centurion Clinical Research LLC.	*Research and Cultural Competence*	Consultant/ instructor	Spring 2008	16 participants

INVITED PRESENTATIONS

Community Entry and Cultural Competency	Indiana Kids Environment Conference	2010

Cultural Competency Training Standards	Moffit Cancer Center: Cancer, Culture and Literacy Conference, Florida	2010
Cultural Competency	Office of Public Health Practice breakfast café	2009
Cultural Awareness: The Bafa` Bafa` Experience	Indiana Statewide HIV Prevention Community Planning Group (CPG)	2009
Why Cultural Competence is Important	Indiana Public Health Week Conference	2008
Overcoming barriers to HIV/AIDS stigma and discrimination among women in Kenya	American Public Health Association conference	2005

PUBLICATIONS

1. Murage JM, Monahan PO, Lane KA, et al. *Development and Psychometric Evaluation of the Murage-Marrero-Monahan Medication Barriers scale (4M scale)* [Dissertation]. Unpublished, Manuscript in preparation: Indiana University, Purdue University, Indianapolis; 2014.
2. Murage JM, Monahan PO, Wessel J, et al. *Patient Demographic Characteristics Associated with Perceived Barriers to Using Medications as Prescribed: The Translating Research into Action for Diabetes (TRIAD) Study.* [Dissertation]. Unpublished, Manuscript in preparation: Indiana University, Purdue University Indianapolis; 2014.

3. Murage JM, Wessel J, Monahan PO, et al. *Patient Perceived Barriers to Medication Use and Cardiovascular Disease Risk* [Dissertation]. Unpublished, Manuscript in preparation: Indiana University, Purdue University Indianapolis; 2014.