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# Examining Factors of Intervention Lost to Follow-up as a Prerequisite to Improving Medication Adherence among Adults with Diabetes

**Robert M. Mayberry, MS, MPH, PhD[1,2#], Fengxia Yan, MD, MS[1,2], Pamela V. Daniels, MPH, MBA, PhD[2], Robina Josiah Willock, MPH, PhD[1,2]**

[1]Department of Community Health and Preventive Medicine, Morehouse School of Medicine, Georgia, USA
[2]Clinical Research Center, Morehouse School of Medicine, Georgia, USA

[#]**Corresponding author:** Robert M. Mayberry, PhD, Professor and Vice Chair, Department of Community Health and Preventive Medicine, Morehouse School of Medicine, 720 Westview Drive, SW (A-330), Atlanta, Georgia 30310-1495, USA

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## Abstract

**Introduction:** Lost to follow-up for patients with diabetes precludes the benefits of diabetes care interventions, including efforts to improve medication adherence. It is also not an uncommon observation in diabetes care interventions and often unexplained in interventional studies.
**Objective:** The primary objective of this study was to examine factors associated with lost to follow-up among predominately African American adults with type 2 diabetes and low adherence to diabetes medication, who participated in an intervention study to improve adherence to prescribed diabetes medications.
**Methods:** We reexamined our previous multicomponent randomized controlled intervention, conducted at a local community health center, in which lay persons trained as Community Health Workers (CHWs) delivered customized educational content on evidence-based diabetes medications to adults with type 2 diabetes and supported patients in self-care through monthly one-on-one in-person and telephone educational and counseling sessions over a 12-month period. Lost to follow-up was defined as not having a scheduled in-person clinic visit for diabetes care at the 6-month or 12-month intervention follow-up. Logistic regression modelling was used in final analyses to examine socio-demographic, psychosocial, behavioral, and clinical risk factors associated with the 6-month lost to follow-up and 12-month lost to follow-up.
**Result:** Of 460 participants recruited into this study, 290(63%) and 330(72%) was lost follow-up at the 6-month and 12-month intervention period, respectively. Participants lost to follow-up did not differ from those not lost to follow-up on most socio-demographic, psychosocial, behavioral, and clinical factors examined. Younger participant age, younger age at diabetes diagnosis, and unknown hypertension status were associated with lost to follow-up.
**Conclusions:** Understanding lost to follow-up in diabetes care interventions in local primary care settings is necessary to improve diabetes medication adherence among populations with low adherence.

**Keywords:** Adherence; Diabetes care; Diabetes medication; Intervention; Lost to follow up

## Summary Message of the Paper

Lost to follow-up in diabetes care interventions in local primary care settings needs to be better understood to best improve medication adherence. Low medication adherence among persons with diabetes is a common problem and an enormous challenge to achieving the benefits of evidence-based diabetes care [1,2]. Low adherence or non-adherence is also a significant contributor to diabetes progression to severe (eye, kidney, nerve, and heart) complications, hospitalizations and overall diabetes care costs [3]. This is especially true for low-income, racial/ethnic populations who shoulder a disproportionate diabetes burden and its severe complications and poorer treatment outcomes.

The prevalence of diabetes medication adherence varies considerably according to how it is measured and by frequency, dosing, number of medications taking for comorbid conditions and other socio-cultural and economic factors [1]. It ranges from less than 40% to more than 90% depending on these factors and the population in which it is studied [4]. African Americans with newly diagnosed diabetes had an initially medication adherence rate (over 90%), i.e., filled their first prescription for oral diabetes medication within 30 day of the diabetes diagnosis; the rate was comparable to Whites in a diverse, inner-city multispecialty practice [5]. A subsequent adherence rate assessment showed a significant racial disparity in adherence sustainability in a 24-month follow-up; 50% of African Americans versus 60% adherence of Whites were adherent at follow-up. In a Medicaid enrollee population with type 2 diabetes, oral medication adherence rates were also slightly lower for African Americans (54%) compared to Whites (59%) [6]. In our previous work, [7] we observed an unusually low prevalence rate of diabetes medication adherence in a predominately inner-city African American population, lower than reported in other inner-city practices [5,8] and low-income Medicaid enrollees with type 2 diabetes [6].

There is considerable continuing interest in improving diabetes medication adherence [9]. However, the best strategy for improving medication adherence among adults with type 2 diabetes in what setting and what population remains undetermined [10]. Many simple strategies and multicomponent interventions have been tested to improve adherence with varying results [1]. Yet, given our poor understanding of medication adherence behavior, it is understandable that most interventions to improve medication adherence are not predictably effective; others are only modestly effective, at best [10]. Making matters more complex in efforts to improve diabetes medication adherence is intervention lost to follow-up [11,12].

Lost to follow-up and low participation are not uncommon observations for diabetes clinical care and self-care interventions that require frequent engagement of the participant for an extended period to affect behavior change, such as a one-year intervention period [11,13-15]. Low participation in Diabetes Self-Management and Support (DSME/S) is notoriously well documented, though DSME/S is widely available and provide a context for improving medication adherence [11,12]. Participating rates for DSME/S ranged from 5% to 14% regardless of subgroups (older adults, those enrolled in fee-for-service health plans, those residing in a metropolitan area or those residing outside urban areas) [11]. Lost to follow-up, or attrition rates, among patients enrolled in these self-management educational interventions, while under 20% in most studies, have been reportedly over 70% in a 6-month to 12-month follow-up periods in some studies [16,17]. Few of these studies with low or modest rates have investigated the factors associated with lost to follow-up [15].

The primary question that we wanted to answer in this investigation was “What are the factors associated with intervention lost to follow-up among adults with type 2 diabetes who are poorly adherent to prescribed diabetes medications?” We also wanted to know whether the factors we previously identified to be associated with baseline diabetes medication adherence in this population were also associated with participant lost to follow-up [7]. We reported here the results of our investigation of lost to follow-up among adults with type 2 diabetes receiving care in a local Community Health Center (CHC) who participated in a multicomponent-community health worker (CHW) intervention to improve adherence to evidence-based prescribed diabetes medications. Not unlike follow-up in previous CHW studies [13,18] and often common in longitudinal interventions of diabetes self-management [16], patient follow-up was problematic. In general, intervention lost to follow-up is problematic as patients who are lost to follow-up may differ significantly for those who were not lost to follow-up on important factors related to diabetes medication adherence. This differential, or potential attrition bias, cautions the interpretation of intervention results. From the perspective of improving diabetes medication adherence in which active patient engagement is essential, understanding the barriers to patient follow-up is also a critical prerequisite to adherence intervention effectiveness, especially among poorly adherent and healthcare vulnerable populations.

## Methods

Our previous intervention was entitled “Adaptation, Education, and Motivation: Improving Evidence-Based Medication Adherence among Adults with Type 2 Diabetes” and promoted as the “iADAPT” Project. The iADAPT Project was planned and implemented as a randomized controlled intervention in which lay persons trained as CHWs by certified diabetes educators were central to its implementation. We trained and deployed CHWs in this intervention because they had demonstrated effectiveness in previous studies in chronic disease and, specifically, diabetes care, such as helping patients keep appointments, increasing patient satisfaction with care, increasing disease knowledge, improving self-care behavior and glycemic control [13,19]. CHWs in this study delivered customized educational contents on evidence-based diabetes medications to adults with type 2 diabetes and supported patients through monthly one-on-one in-person and telephone educational and counseling sessions over a 12-month period. The iADAPT Project was also aided by the adaptation of Agency for Healthcare Research and Quality (AHRQ) educational materials and recommendations of Comparative Effectiveness Research Summary Guides (CERSGs) for Consumers and Clinicians: Consumer Guides “Pills for Type 2 Diabetes” and “Premix Insulin for Type 2 Diabetes” and Clinician Guides “Comparing Oral Medications for Adults with Type 2 Diabetes” and “Premixed Insulin Analogues” [20], incorporating CERSGs for providers into the Electronic Medical Record (EMR) system, an interactive website for clinic providers and CHWs, audits of medications and diabetes care problems, and feedback discussions of diabetes care, medication adherence and patient-provider communication issues, e.g., during “Lunch and Learn” for the diabetes care team inclusive of CHWs. The previous intervention study project period was 2010-2013. The study was approved by the Morehouse School of Medicine Institutional Review Board for the Protection of Human Subjects.

## Target Population and Primary Care Setting

Persons eligible for this study were existing patients 18 years of age and older with a diagnosis of type 2 diabetes, according to the International Classification of Disease Clinical Modification, ninth revision (ICD-9-CM codes 250.0-259.9). Patients with diabetes who lacked English proficiency, or were visually, hearing or otherwise cognitively impaired, as assessed by the clinic's nursing staff, were not eligible to participate in this study.

The local CHC, a Federally Qualified Health Center (FQHC), had more than 62,000 medical encounters annually at its three neighborhood locations at the time this study started, of which approximately 10% were diabetes related. Nearly 600 patients with diabetes were documented in the Electronic Medical Record (EMR) system with at least one clinic visit in the last two years. Most adults with diabetes (95%) were seen at the main clinic because of the weekly "Diabetes Day" and the extended hours on Mondays-Fridays and on Saturdays. The CHC is the primary health provider for the area high disparity neighborhoods. This area has a high-poverty rate and a median income well below the national average [21]. Diabetes-related hospitalization is also one of the most common causes of hospitalization in these neighborhoods [22].

## Participant Recruitment

Eligible patients for the study were identified prior to scheduled appointments through the healthcare center's scheduling system. Patients were then recruited to the study during regularly scheduled visits. As in a previous study at this CHC, the nurses served as the first point of patient recruitment. After triage, the nurse introduced eligible patients to the study according to a project-specifically prepared script. Patients who agreed to participate were then introduced to the CHW who elaborated his/her introduction regarding the study, described the purpose of the study, obtained voluntary consent, and completed the study baseline patient assessment. We recruited as study participants 460 of the 524 (87.8%) seeking treatment for type 2 diabetes in a 12-month period.

## Intervention Design

The intervention deployed the Randomized Controlled Trial (RCT) design. Adults with type 2 diabetes recruited at baseline were randomly assigned to one or the other of two groups of CHWs: one group trained in Diabetes Self-Management Education (DSME) only (GE-CHW), based on the six standard content areas recommended by the American Diabetes Association (ADA) [23]. The other group of CHWs (MI-CHW) were trained in DSME and also in Motivational Interviewing (MI), a directive counseling approach for behavior change, by a certified motivational interviewing network trainer [24]. Study participants were randomized after recruitment, the baseline assessments of diabetes medication adherence, and assessment of psychosocial and behavioral needs by the CHWs [7]. Participants were followed by CHWs during schedules monthly one-on-one in-person and phone-administered DSME or the DSME/MI directive counseling sessions, respectively, over a 12-month intervention period. CHWs were also accessible by phone if participants had self-care questions in between monthly sessions. In addition, a uniquely customized CERSGs one-page module (information) sheet was discussed with the patient at each session to increase oral and insulin medication knowledge, address medication problems, and other issues of adherence to prescribed medication use. CHWs also encouraged participants, during monthly sessions, to keep scheduled diabetes care clinic visit, which were expected to be every 6 months. All monthly sessions were 20-30 minutes in duration [25,26]. Each CHW was responsible for 45-50 participants initially randomly assigned to him/her over the 12-month intervention period. Diabetes medication adherence for each study participants were to be again assessed at the 6-month and 12-month intervention period during the in-person clinic visit or shortly thereafter. Improvement in diabetes medication adherence was compared between the MI-CHW intervention group participants and the GE-CHW intervention control group participants at the 6-month and 12-month intervention period.

## Data Collection

Two major sources of data collection were used for this intervention: specifically designed self-administered questionnaires and the Electronic Medical Record (EMR) system. The EMR system at the CHC was utilized for capturing HbA1c and other clinical measures including cholesterol, blood pressure, Body Mass Index (BMI) and prescribed medications. The study questionnaires, used successfully in our previous research, were adopted from widely and validated instruments currently used in diabetes research [27,28]. The Patient Assessment (PA) Questionnaire, assessed demographic (e.g., age, gender, race/ethnicity, education, and marital status), self-management behaviors (e.g., blood glucose monitoring frequency, diet, and meal planning, physical activity, and self-foot care), medication (i.e., insulin, other drugs, adherence to prescription), medical history, general health behavior, social support, and other relevant information to diabetes education and self-care at the study enrollment.The Psychological Needs Assessment and Behavioral Needs Assessment (PBNA) was designed to assess diabetes knowledge and attitudes, self-efficiency, locus of control, and stage of change in the context of evidence-based self-management behaviors for diabetes [28]. A Behavioral Goal Assessment Form was also used to assess the participant' response to the "Importance" and "Confidence" to achieve desired behavioral change [27]. To assess medication adherence among the study participants, we utilized the well-validated medication adherence assessment tool developed by Morisky [29] and adapted by Hill-Briggs [30]. The 5-item scale was scored 0 to 5; participants with a score of 0 (patients had none of the behaviors) were defined as adherers and participants with scores of 1 to 5 (patients had one or more of the behaviors) were defined as non-adherers.

## Statistical Analysis

In previous analysis, no statistically significant difference was observed in diabetes medication adherence over time by intervention group status (i.e., GE-CHW or MI-CHW). (No significant association was observed between intervention group status and lost to follow-up at the six-month (p=0.1234) or the 12-month (p=0.1187) follow-up periods.) Thus, in reexamining the data for this study on lost to follow-up, all participants were combined as one study group and intervention group status was included in the analyses as a covariate. Lost to follow-up was defined as not having a scheduled in-person clinic visit for diabetes care at the 6-month or 12-month intervention follow-up period. Descriptive statistics were performed in exploring socio-demographic, psychosocial, behavioral, and clinical risk factors and lost to follow-up; mean with standard deviation for numerical variables and frequency with percentage and the 95% confidence interval for categorical variables were used to describe analytical results. The comparison of possible risk factors on lost to follow-up at 6 months and at 12 months of the intervention were also constructed using two samples t-test for numerical variables and chi-square for categorical variables. To select possible risk factors for the 6-month lost to follow-up and 12-month lost to follow-up, logistic regression modelling was performed. The purposeful selection process was used to select possible risk factors for modelling analyses. The process began by a univariate analysis and bivariate analysis of each variable. Any variable with a p-value less than 0.30 were selected to be included in the final logistic model selection; this p-value was used because the traditional p-value 0.05 can fail in identifying variables known to be important [31]. The backward selection method in logistic regression was used to select the final risk factors [32]. The 6-month lost follow-up status also was considered as one input risk factor for the 12-month lost to follow-up status.

## Results

## Patient Characteristics

Socio-demographic and other baseline characteristics of the patients participating in the iADAPT intervention are indicated in (Table 1). This was a predominantly Black (i.e., African American) patient population (80%) with a mean age of 52.2 years. The mean age at diabetes diagnosis was 42.6 years. Most of study participants were female (64%), not currently married (44%) or never married (32%), had a personal doctor (88%), had no insurance (60%), considered themselves to be in good to excellent health (51%), and indicated not feeling depressed (63%). Forty-four percent of the study participants had some college education. More than half of the study participants (51%) also reported having "High Cholesterol" and 75% of the participants reported having hypertension. Only 23% of the study participants were assessed as adherent to diabetes medications at baseline.

| | | 6-Month Follow-Up | | | 12-Month Follow-Up | | |
|---|---|---|---|---|---|---|---|
| | **Total Baseline (N=460)** | **No (n=170)** | **Yes (n=290)** | **p value** | **No (n=130)** | **Yes (n=330)** | **p value** |
| **Age** | 52.22(11.06) | 55.08(9.52) | 50.54 (11.58) | <0.0001 | 55.53(9.88) | 50.92(11.25) | **<0.0001** |
| **Age at Diabetes Diagnosis**** | 42.6(14.05) | 45.73(13.80) | 40.74(13.90) | 0.0002 | 46.98(14.29) | 40.86(13.61) | **<0.0001** |
| **Race** | | | | 0.7339 | | | 0.1026 |
| Black | 367(80) | 132(79) | 235(82) | | 106(83) | 261(80) | |
| White | 52(12) | 21(13) | 31(11) | | 17(13) | 35(11) | |
| Other | 37(8) | 15(9) | 22(7) | | 5(4) | 32(9) | |
| **Marriage status** | | | | 0.006 | | | **0.0205** |
| Married | 110(24) | 40(24) | 70(24) | | 26(20) | 84(25) | |
| Divorced/Widowed/Separated | 204(44) | 90(53) | 112(39) | | 71(55) | 133(40) | |
| Never married/Unmarried couple | 146(32) | 40(24) | 106(37) | | 33(25) | 113(35) | |
| **Highest level of education** | | | | 0.7724 | | | 0.5548 |
| < High school | 87(19) | 35(21) | 52(18) | | 26(20) | 61(18) | |
| High school graduate | 168(37) | 61(36) | 107(37) | | 51(40) | 117(36) | |
| At Least Some college | 203(44) | 73(43) | 130(45) | | 52(40) | 151(46) | |
| **Gender** | | | | 0.2675 | | | 0.9488 |
| Male | 167(36) | 67(40) | 100(34) | | 47(36) | 120(36) | |
| Female | 292(64) | 102(60) | 190(66) | | 83(64) | 209(64) | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Personal doctor** | | | | 0.0436 | | | 0.1902 |
| Yes | 405(88) | 157(92) | 248(86) | | 119(92) | 286(87) | |
| No | 53(12) | 13(8) | 40(14) | | 11(8) | 42(13) | |
| Yes | 228(51) | 94(56) | 134(49) | | 71(56) | 157(50) | |
| No | 216(49) | 73(44) | 143(51) | | 56(44) | 160(50) | |
| **High Blood Pressure** | | | | <0.0001 | | | **<0.0001** |
| yes | 129(28) | 56(33) | 71(24) | | 45(34) | 84(25) | |
| no | 163(35) | 73(43) | 90(31) | | 62 (48) | 101(31) | |
| unknown | 168(37) | 39(23) | 129(44) | | 23(18) | 145(44) | |
| **High Cholesterol** | | | | 0.0028 | | | **0.0185** |
| Yes | 27(6) | 9(5) | 18(6) | | 6(5) | 20(6) | |
| No | 130(28) | 64(38) | 66(23) | | 49(38) | 81(25) | |
| unknown | 303(66) | 97(57) | 206(71) | | 74(57) | 229(69) | |
| **HbA1c** | | | | 0.0002 | | | **<0.0001** |
| <7 | 42(9) | 24(14) | 18(6) | | 24(19) | 18(6) | |
| 9-Jul | 44(10) | 25(15) | 19(7) | | 21(16) | 23(7) | |
| >9 | 41(9) | 17(10) | 24(8) | | 11(9) | 30(9) | |
| Unknown | 333(72) | 104(61) | 229(79) | | 74(57) | 259(78) | |
| **Type of Anti-Diabetes Medication** | | | | 0.7334 | | | 0.6557 |
| Insulin and oral medication | 97(21) | 39(23) | 58(20) | | 29(22) | 68(21) | |
| Insulin only | 75(16) | 28(16) | 47(16) | | 18(14) | 57(17) | |
| Pill only | 288(63) | 103 (61) | 185(64) | | 83(64) | 205(62) | |
| **Medication adherent** | | | | 0.8069 | | | 0.3369 |
| yes | 103(23) | 39(23) | 64(22) | | 33(26) | 70(21) | |
| no | 353(77) | 129(77) | 224(78) | | 96(74) | 257(79) | |

*Data are presented as frequency (percent) or mean (SD).
**For some individual variables, the total may not add up to 460 because of missing value. The self-reported high cholesterol level had 3.5% missing and self-reported hypertension had 2.0%. All other variables had less than 1% missing value. We used the complete data to perform all the analyses.
***Self-reported

**Table 1:** Socio-Demographic, Psychosocial, Behavioral, and Clinical Factors* Associated with Intervention Lost to Follow-Up.

## Observed Medication Adherence over Time

Observed increases in diabetes medication adherence is indicated in Figures 1. We observed an increase in adherence from 22.6% (95% CI =18.8-26.4) at baseline to 40.0% (95% CI = 32.6-47.4) among participants who completed the diabetes medication adherence interview at the 6-month follow-up period (n=170). We also observed an increase in diabetes medication adherence to 49.2% (95% CI = 40.6-57.8) among participants who completed the diabetes medication adherence interview at the 12-month intervention follow-up period (n=130). When we restricted adherence assessment to participants who completed both the 6-month and the 12-months intervention follow-up (n=115), diabetes medication adherence increased to 37.9%, 95% CI (29.1-46.8) and 50.9%, 95% CI (41.8-60.0), respectively. More salient here for this report and analyses was the observation that, of 460 participants with type 2 diabetes recruited into this study, 290(63%) and 330(72%) was lost follow-up at 6-month and 12-month intervention period, respectively. We note, however, that this "lost to follow-up" is best described as a not keeping the scheduled in-person diabetes clinic care appointment and refusal to complete the biannual, 20-30 minutes medication adherence follow-up interview in-person or by telephone. CHWs were instructed to document monthly contact with study participants. Our monthly log indicated that 60-80% of study participants were reached by telephone at any given month over the 12-month intervention period.

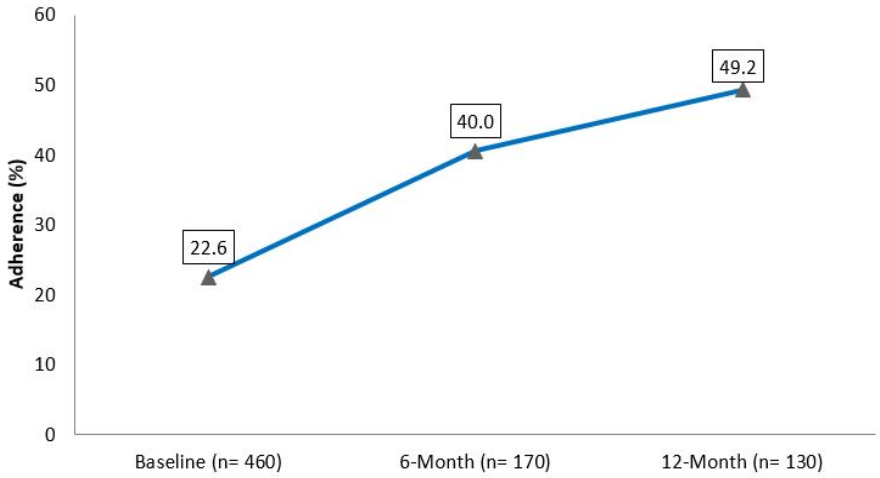


**Figure 1:** Improvement in Medication Adherence among Adults with Type 2 Diabetes: All Participants.

## Factors Associated with Lost to Follow-Up

Factors associated with lost to intervention follow-up in bivariate analyses are indicated in the Table 1. Participants who were lost to follow-up at 6 or 12 months were significantly younger than those were completed the 6- and 12-month follow-ups, 50.5 years versus 55.1 years ($p<0.0001$) and 50.9 years versus 55.5 years ($p<0.0001$), respectively. A significantly larger proportion of participants who were lost to intervention follow-up at 6 months and 12 months were also not married. The participants who had missing blood pressure, blood cholesterol and hemoglobin A1C (HbA1C) measures were also more likely to be lost follow-up at both 6 months and 12 months.

Baseline diabetes medication adherence was similar among study participants "Who Were" and "Who Were Not" lost to follow-up at the 6-month intervention period ($p=0.8069$) (Table 1). Likewise, baseline diabetes medication adherence was similar among participants "who were" and "who were not" lost to follow-up at the 12-month intervention ($p=0.3369$). That is, we observed no statistically significant association in baseline medication adherence between those lost to follow-up and not lost to follow-up at neither of the assessed time periods during intervention.

The significant factors in bivariate analyses were further evaluated in multiple logistic regression analyses according to our selection criteria as described in the Methods section. The final multiple logistics regression modelling results are indicated in (Table 2). The results indicated that older participants were significantly less likely to be lost to follow-up at the six-month intervention period (odds ratio (OR) = 0.96, 95% CI = 0.94-0.98). The results also indicated that compared to hypertensive participants, the participants without blood pressure measurements were more than 2 times more likely to be loss to follow-up (odds ratio=2.59, 95% CI=1.54-4.35) at the 6-month intervention period.

| | Odds Ratio | 95% Confidence Interval |
|---|---|---|
| 6-Month Follow-Up | | |
| **Age** | 0.96 | 0.94-0.98 |
| **Hypertension** | | |
| Yes | 1 | |
| No | 0.98 | 0.61-1.59 |
| Unknown | **2.59** | 1.54-4.35 |
| 12-Month Follow-Up | | |
| **Age at Diabetes Diagnosis*** | | |
| | 0.97 | 0.94-0.99 |
| **Race** | | |
| Black | 1 | |
| White | 1 | 0.37-2.65 |
| Other | **6.71** | 1.63-27.67 |
| **Lost follow up at 6 months** | | |
| No | 1 | |
| Yes | **26.94** | 13.00-55.80 |
| *Self-reported | | |

**Table 2:** Factors Associated with Lost-follow-up: Final Multiple Logistics Regression Results.

At the 12-month intervention completion period, the final logistic regression results indicated that the older participants were at diabetes diagnosis, the less likely they were lost to follow-up (OR =0.97 (95% CI = 0.94-0.99) (Table 2). The results also indicated that there was no significant difference in lost to follow-up among the study's predominately Black patient participants and the White patient participants. "Other Race" participants were limited in number to make any meaning interpretation of lost to follow-up (n= 2 Native Americans, n=4 Asian, and n =32 other). The final results also indicated that the 6-month lost to follow-up status was the strongest predictor for the 12-month intervention lost follow-up; participants who was lost to follow-up at 6 months were 27 times more likely to be lost to follow-up at 12 months compared with those who was not lost to follow-up at 6 months (OR = 26.9 (95% CI = 13.00 - 55.80).

## Discussions

By way of summary, this investigation found that study participants lost to follow-up differed from those not lost to follow-up only by age, age at diabetes diagnosis, and hypertension as a comorbid condition, among the many factors investigated. Chronologically older participants and those who were relatively older at diabetes diagnosis were less likely lost to follow-up. Those with a diagnosis of hypertension were less likely to be lost to follow-up; participants with an unknown hypertension status were more likely to be lost to follow-up. It was significantly observed that participants who were lost to follow-up at the 6-month intervention follow-up period were definitively most likely to be lost to follow-up at 12-month intervention follow-up. We also observed that baseline diabetes medication adherence was similar among study participants "Who Were" compared to those "who were not" lost to follow-up at the 6-month and the 12-month intervention follow-up periods. So, the answer to the primary question that we wanted to answer is that participants who were lost to follow-up were characteristically similar to those not lost to follow-up and had a similar rate of baseline adherence of diabetes medication. While lost to follow-up and low participation are not an uncommon observations for diabetes interventions, few studies have attempted to explain this lack of continuous participant engagement [15]. In a study in which 44% of newly diagnosed patients with type 2 diabetes withdrew before completing the one-year period of self-management education, this attrition was associated with being older than 65 years of age, working full or part-time, having a regular primary care physician and fewer diabetes symptoms [33]. In another study of newly diagnosed patients with type 2 diabetes, only 59% of these participants completed the six-month program when randomly assigned to one of three diabetes self-care management approaches: CHW, case management, and standard provider care. Lost to followup was greatest in the standard provider care group (50%); it was 43% in the case management group and 28% in the CHW group [7]. In other studies involving CHWs or interventions led by CHWs, lost to follow-up was associated with the participants educational level, literacy level [34] income, physical activity, and previous DSME/S class attendance [35].

In this investigation, we observed chronologically older age was inversely associated with medication adherence, contrasting with the results of a previous study among a Hispanic patient population [33]. We did not observe any significant association between educational level and adherence in this study of a predominately African American patient population, in contrast to previous findings [34]. We also observed that older age at diabetes diagnosis and diagnosis of hypertension to be inversely associated with lost to follow-up; unknown hypertension status was directly associated with lost to follow-up. These are unique observations for this investigation and not previous reported elsewhere. Another unique observation for this study is that short-term lost follow-up of 6 months is significantly strongly associated with lost to follow-up for a longer intervention period of 12 months [36].

Lost to follow-up, or attrition, in medication adherence interventions is significantly underexplored and specific factors associated with lost to follow-up in medication adherence interventions are generally unknown or fully explicated. In general, and in addition to factors indicated above, there is likely a constellation of qualitative, quantitative, distal, and proximal factors to intervention participation, and better understood will help mitigate lost to follow-up. These factors have been broadly categorized as follows: patient demographic and psychosocial characteristics, clinical staff characteristics (including patient-provider communication), social support, research design and practice settings (e.g., complexity of treatment, duration of treatment, reminders, and degree of required behavioral change), and healthcare policy (e.g., professional norm, quality and benchmarks of care) [39]. There may be other sociocultural factors of particular important to healthcare vulnerable groups that do not fit neatly within these categories, including scheduling conflicts and perceived benefits of participation among other factors [37].

Lost to follow-up is a prerequisite to determine the effectiveness of evidence-based interventions since these interventions are predicated on our abilities to facilitate intervention participation and completion of the planned intervention. Non-random or systematic differences between those lost to follow-up and those participating through the completion the intervention would signify attrition bias and a potential threat to the validity of intervention study findings. That is, persons with diabetes who do not complete the intervention and are not engaged over time with their provider, diabetes care educator, or the CHW as educator, self-care facilitator, and social supporter, as the intervention is designed, may be less conscientious of or not able to actualize diabetes self-care behavior and adherence to prescribed medication [1,17]. These similarities observed in this study among those lost to intervention follow-up and those not lost to intervention followup argues well for the overall inference that attrition bias is not a major factor in explaining the diabetes medication adherence increase observed in this study population as a result of the multicomponent CHW intervention we previously implemented at a local CHC.

In our previous work, we approached medication adherence from the perspective of the clinical care and patient self-care in implementing a multicomponent intervention to improve diabetes medication adherence. One of our cursory observations in this CHC was that physicians and nurses have limited time for counseling and patient education in self-care. We had also observed diabetes medication adherence to be poor; patient follow-up clinic visits over a 12-month period were also observed to be poor.

In the previous investigation, we had found that having maintained a desired level of glycemic control, self-perceived health status, self-reported comorbidities (heart attack and high cholesterol) and diagnosed hypertension were associated with baseline diabetes medication adherence. A number of other common sociodemographic and psychosocial behavioral factors were also investigated and not observed to be associated with adherence. The previous results indicated that adult patients with type 2 diabetes and a comorbid diagnosis of hypertension were less likely to adhere to diabetes prescribed medication; patients with unknown diagnosed hypertension were also less likely to adhere. While less likely to adhere, only the subset of study participants with an unknown hypertension status were more likely to be lost to followup. That is, only this subset of participants would result in attrition bias, indicating a likely modest underestimation of diabetes medication adherence achieve through the intervention in this study population. In all, the findings of this study indicate that, with the exception of unknown hypertension status, none of the factors associated with diabetes medication adherence at baseline in this population were associated with participant lost to intervention follow-up. In other words, these study findings indicate that diabetes medication adherence and lost to follow-up are explained by different factors.

Non-adherence to prescribed diabetes medication continues to challenge providers and patients in the evidence-based benefits of medication treatment, i.e., glycemic control and opportunities to stave off diabetes' severe complications [1]. Many factors contribute to adherence to medication [1,25]. Some of the more common factors identified in the literature regarding medication adherence for persons with type 2 diabetes are regimen complexity of more than one drug or more than one dose daily and remembering doses and refills
[38]. Complexity of treatment or the intervention and forgetfulness or need for reminders are common factors of lost to follow-up and adherence. Other common factors include perceived benefits [39], social support, and the nature of doctor-patient relationship [40]. Nevertheless, the scientific evidence is relatively limited regarding the determinants of diabetes medication adherence in healthcare vulnerable populations, defined by race/ethnicity, income, socio-economic status, or geography and community [30,39]. And while there may be some common factors of lost to follow-up and adherence, our study indicates that the factors associated with lost to follow-up are not the same factors associated with diabetes medication adherence. That this study population was poor adherers, receiving diabetes

## Limitations

We investigated many factors in relationship to lost to follow-up. Nevertheless, lost to follow-up was the major limitation for this study. That is, it precluded intervention efforts to achieve a greater improvement in adherence to prescribed diabetes medication than observed. CHWs were able to document that most study participants could be reached by telephone for monthly self-care education and counseling sessions, reminders, and social support. However, these patients did not want to complete the follow-up assessments, and we were not able to explore in more detail the patients' explanation of why they did not continue to participant in the intervention, even though most accepted the phone calls from the CHWs. This study was also limited in capturing data on medication adherence in-person because these participants did not return to the clinic for scheduled diabetes care during the intervention period. We also do not know why participants did not complete the brief five-item self-assessment of medication adherence in light of their willingness to receive the phone calls from the CHWs.

## Applicability of Findings

Regarding the applicability of these findings, this local community population of adults with type 2 diabetes had an unusually low prevalence rate of diabetes medication adherence, lower than that reported in other inner-city practices [5] and low-income Medicaid enrollees with type 2 diabetes [6]. We believe this poor adherence is partly explained by the strict dichotomized measure of adherence we used. We assessed diabetes medication adherence most appropriately as a dichotomized variable (adherent vs non-adherent), although any items in the five-item adherence scale would provide some measure of adherence [30]. The study population was also comprised of prevalent or existing diabetes cases which have a lower rate of medication adherence than observed among newly diagnosed cases [5]. Prevalent diabetes cases are less likely to lost to follow-up; new cases, especially those with fewer symptoms, are more likely to lost to intervention follow-up [7]. In any case, the results of the study is limited in its applicability, yet relevant to other inner-city high diabetes-disparities patient population receiving care in community-based clinics [41] and our ability to engage and retain participants in evidence-based intervention to improve diabetes medication adherence.

## Conclusions

Factors associated with lost to follow-up may not be the same factors associated with diabetes medication adherence. Understanding intervention participation and lost to follow-up is a prerequisite to intervention effectiveness for diabetes medication adherence and to better understand what adherence intervention works best in what diabetes care setting.

## Author Contributions

RMM drafted the manuscript. RMM, FY, PVD, and RJW reviewed and edited the manuscript and contributed to the discussion. PVD and FY take responsible for data collection and integrity. FY and RMM take responsibility for data analyses.

## Conflict of Interest

None of the authors have any conflict of interests.

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