

Medication adherence and direct treatment cost among diabetes patients attending a tertiary healthcare facility in Ogbomosho, Nigeria

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Abstract

Background

Diabetes mellitus (DM) is now prevalent in many countries in sub-Saharan Africa, with associated health and socioeconomic consequences. Adherence to antidiabetic medications has been shown to improve glycaemic control, which subsequently improves both the short- and long-term prognosis of the disease. The main objective of this study was to assess the level of adherence to antidiabetic drugs among outpatients in a teaching hospital in southwestern Nigeria.

Methods

A cross-sectional study was carried out using the eight-item Morisky Medication Adherence Scale (MMAS-8) among diabetic patients attending the medical outpatients' diabetes clinic of Ladoke Akintola University Teaching Hospital, in Ogbomosho, Oyo State in southwestern Nigeria, during a three-month period (October to December 2013).

Results

A total of 129 patients participated in the study with a male-to-female ratio of 1:1.5. Seventy-eight (60.5%) patients had systemic hypertension as a comorbid condition while the remaining were being managed for diabetes mellitus alone. Only 6 (4.7%) of the patients had type 1 DM while the remaining 123 (95.3%) were diagnosed with type 2 DM. Metformin was the most prescribed oral hypoglycaemic agent ($n = 111$, 58.7%) followed by glibenclamide ($n = 49$, 25.9%). Medication adherence was classified as good, medium, and poor for 52 (40.6%), 42 (32.8%), and 34 (26.6%) patients, respectively.

Medication costs accounted for 72.3% of the total direct cost of DM in this study, followed by the cost of laboratory investigations (17.6%).

Conclusion

Adherence of diabetes patients in the study sample to their medications was satisfactory. There is a need for the integration of generic medicines into routine care as a way of further reducing the burden of healthcare expenditure on the patients.

Introduction

Diabetes mellitus (DM) is now one of the most common non-communicable diseases affecting the global population, with increasing incidence in many emerging countries of the world¹⁻³. In developing countries like Nigeria, the incidence of DM, especially the type 2 variant, is on the increase, with its attendant complications. According to the International Diabetic Federation (IDF), the prevalence of DM will increase by as much as 54% globally between 2010 and 2030 with projections for countries in sub-Saharan Africa close to 100%⁴. In Nigeria, studies from different parts of the country have recorded prevalence rates between 1% and 8%⁵⁻⁸.

The management of DM consists of lifestyle and dietary changes and pharmacotherapy. For patients with type 1 DM, insulin remains the mainstay of treatment while the different groups of oral hypoglycaemic agents (OHA) and insulin are used in treating patients with type 2 DM. Studies have shown that adequate glycaemic control will slow down or prevent

the development of microvascular and macrovascular complications of both types of DM⁹⁻¹². Adherence to anti-diabetic medications has been shown to improve glycaemic control, which augurs well for the long-term prognosis of the disease^{13,14}. Medication adherence to antidiabetic agents has also been shown to be more cost-effective, as it may reduce hospitalization frequency and costs associated with both short- and long-term complications^{15,16}. Some of the reasons or predictors of poor adherence found in the literature include high pill burden, complexity of drug regimens forgetfulness, high cost of medications, presence or perceived fear of adverse effects, and poor knowledge about the disease condition¹⁷⁻¹⁹.

Worldwide, studies on medication adherence among diabetes patients have shown a wide variation. Ahmad et al. reported 53% non-adherence among diabetics in Malaysia; similar studies in India and Ethiopia have reported non-adherence rates of 42.3% and 25.4%, respectively¹⁹⁻²¹. Recent Nigerian studies using different instruments revealed non-adherence rates between 27.5% and 50%²²⁻²⁴. These Nigerian studies investigated medication adherence among diabetes patients and its association with the number of prescribed medications and glycaemic control. The relationship between cost of medications and adherence is well established in the literature^{15,25}. The issue of cost of medications and indeed healthcare expenditure is especially germane in developing countries like Nigeria, where the majority of patients pay out of pocket²⁶. The national health insurance scheme (NHIS), which has been operational for about a decade now, covers less than 10% of the country's population: mainly those in the formal sectors of the economy^{27,28}.

The principal objective of the study was to assess the level of adherence to OHAs and insulin among diabetes patients attending the medical outpatient clinics of a tertiary hospital in Nigeria. Secondary objectives included: the prescription pattern for OHAs, some components of direct costs, and the effects of various factors on medication costs.

Methods

Study setting

The study was carried out in the medical outpatients' diabetes clinic of a tertiary-level healthcare facility in Nigeria during a three-month period (October to December 2013). The study centre was Ladoke Akintola University Teaching Hospital in Ogbomosho, Oyo State in southwestern Nigeria. This site caters for the population of Oyo and its surrounding states. This teaching hospital is the major referral hospital in the northern part of Oyo State and draws its patient population from numerous private hospitals and primary and secondary healthcare facilities in the region. The medical outpatients' clinic is manned by a consultant endocrinologist physician, registrars (senior and junior) in internal medicine, and medical interns. The centre runs a weekly clinic with an average attendance between 30 and 60 patients.

Study population

Consecutive patients who had been diagnosed with type 1 and type 2 DM and who had been on treatment in the study centre were invited to participate in the study. Patients older than 18 years of age, who had been on medication for at least six months, and gave informed consent were included in the study. Patients younger than 18 years, those who refused to consent, and those with acute symptomatology were excluded from the study. All participating patients were paying out of pocket, as they were not enrolled under the national health insurance scheme of the country.

Sampling

Sample size

The number of patients needed for this study was calculated using the formula for descriptive studies:

$$\text{Sample size (n)} = [\text{DEFF} * N p(1-p)] / [(d^2 / Z_{1-\alpha/2}^2 * (N-1) + p*(1-p))]$$

Where, N = Population size (600)

p = prevalence of poor adherence (0.4)

d = Precision (0.1)

DEFF = Design effect (1.5)

$Z_{1-\alpha/2} = 1.96$

The estimated prevalence of poor adherence of 40% was chosen based on results from two similar Nigerian studies with values of 27.5% and 50% respectively^{22, 24}. An estimated minimum sample size of 129 was obtained using the aforementioned assumptions. A convenience sampling method was used, as consecutive patients presenting at the clinic were recruited.

Study Instrument

A cross-sectional study was done using a validated self-reported adherence tool (the eight-item Morisky Medication Adherence Scale (MMAS-8))²⁹. The MMAS-8, a validated instrument with high reliability and validity, has been used for studies on medication adherence among diabetes patients in many countries^{19,30,31}. In Nigeria, the MMAS has been used for studies on medication adherence among hypertensive and psychiatric patients^{32,33}. A previous Nigerian study on medication adherence among diabetes patients used the modified MMAS-4 instrument³⁴. It collects information on how frequently patients may forget to take their medications and the reasons for this using a binary (Yes/No) and a five-option response version (never/rarely/sometimes/often/always). The summary of the scoring interpretation is as follows: 0 (for high adherence), 1-2 (medium adherence) and > 2 (poor adherence). An additional questionnaire for collection of sociodemographic details, diagnoses, a list of prescribed medications, some components of direct costs (cost of medications, laboratory investigations, transportation to and from hospital, and consultation) and factors that may affect adherence was also administered. The additional questionnaire, a mixture of open- and closed-ended statements was developed by the authors for the purpose of this study and was pre-tested among ten diabetes patients who were attending another tertiary healthcare facility in Ekiti State, southwestern Nigeria. Necessary adjustments were made in the contents and structure before its administration. The questionnaires were administered by medical interns during clinic encounters after informed consent was obtained. Glycaemic control was

assessed using the average of the two most recent fasting plasma glucose and/or glycosylated haemoglobin (HbA1c) measurements available. The blood glucose was done with capillary blood taken from the patients' finger and analyzed using a glucometer in the clinic early in the morning before consultation starts. The investigators ensured that there was no discrimination against those that refused participation in the study by attending to them promptly and professionally. Six months of medication use was chosen as the cut-off for inclusion into the study because most patients had appointments either monthly or every other month and would have had between three and six clinic appointments by the time they were recruited into the study. The monthly cost of the prescribed medications was calculated using the price list of the hospital pharmacy, while patients gave an estimate of their individual transport fares to and from the hospital. The consultation fee is a constant one charged by the hospital for a consulting encounter with a physician. Written consent was obtained from each patient during study recruitment. Ethical approval was obtained from the Research Ethics Committee of the hospital before commencement of the study.

Statistical Analysis

The information obtained from the general questionnaire was coded and entered using IBM SPSS version 19 (IBM Corporation, Armonk, NY, USA). The information from the MMAS-8 was interpreted using its keys and entered. General characteristics of the patients were analyzed using descriptive statistics. Demographic variables that were normally distributed were described by mean and standard deviation. The median and range were calculated for other demographic variables that were not normally distributed. Categorical variables are reported as frequency distributions and proportions with 95% confidence intervals and were compared using the chi-square test or Fisher's exact test. Comparisons of the means of some variables (age, fasting plasma glucose, HbA1c, monthly income, monthly medication cost) were done using analysis of variance (ANOVA) with a p-value of < 0.05 taken as the level of statistical significance.

Results

A total of 129 patients participated in the study with a male-to-female ratio of 1:1.5. The sociodemographic variables of the participants are shown in Table 1. Seventy-eight patients (60.5%) had systemic hypertension as a comorbid condition, while the remaining were being managed for DM alone. Only six (4.7%) of the patients had type 1 DM, while the remaining 123 (95.3%) were diagnosed with type 2 DM. The median duration of disease (time since initial diagnosis was made) was seven years, while the median duration of clinic attendance was three years. The average of the previous two fasting plasma glucose measurements (done on the morning of clinic appointments) of the patients was 8.2 ± 3.4 mmol/L while the mean HbA1c (done within the previous three months) was $7.5 \pm 2.4\%$. On further analysis, only 45.9% (n = 50) of the patients had their fasting plasma glucose within the normal range (4 to 6.9 mmol/L), while 50% of those who had HbA1c done in the previous three months recorded values within normal range. Five hundred five medications were prescribed for the patients, with a mean number of 4.1 ± 1.4 prescribed per patient. The frequency distribution of number of prescribed drugs is shown in Figure 1. The breakdown of

the drugs is as follows: 220 antidiabetic agents prescribed (43.6%), 163 antihypertensives (32.3%), 23 antilipemics (4.5%), and 42 anti-platelets (8.3%). Insulin usage either alone or in combination with oral hypoglycaemic agents was observed in 14.1% of patients, while the majority of patients (85.9%) had OHAs alone as antidiabetic agents. Metformin, with 111 prescriptions (58.7%), was the most prescribed oral hypoglycaemic agent followed by glibenclamide (49 prescriptions, 25.9%). Glimepiride, vildagliptin and pioglitazone were prescribed for 26 (13.8%), 2 (1.1%) and 1 (0.5%) of the patients respectively. Combination therapy of oral hypoglycaemic agents was prescribed in 74 (57.4%), oral hypoglycaemic agents and insulin in 18 (14%) and metformin alone 15 (11.6%). Lisinopril (37.4%) was the most prescribed antihypertensive, followed by nifedipine (16.6%) and hydrochlorothiazide (14.1%). The groups of prescribed antihypertensives are shown in Figure 2.

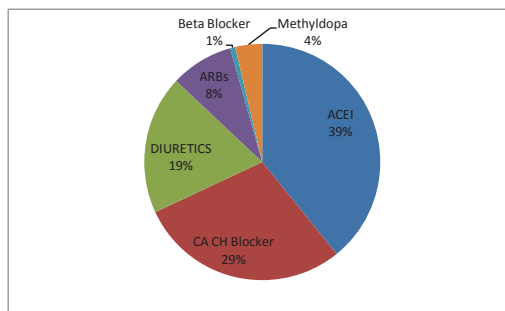


Figure 2. Percentages of prescribed antihypertensives by drug class at LAUTECH Teaching Hospital diabetes clinic

ARB = Angiotensin Receptor Blocker
 ACEI = Angiotensin-Converting Enzyme Inhibitor
 CA CH Blocker = Calcium Channel Blocker

Medication adherence among the patients was grouped as follows: 52 good (40.3%), 43 medium (33.3%), and 34 poor (26.4%). The mean monthly cost of medications was N6557 ± N4463 Nigerian Naira (NGN) while the median monthly amount spent on transportation, investigations and consultations was NGN N400, N800 and N250, respectively (165 Nigerian Naira = 1 US Dollar, USD, at the time of data collection). The total amount (direct cost) expended monthly by patients was NGN N1,096,668, of which medications, laboratory investigations, transportation and consultation fees accounted for 72.3%, 17.6%, 7% and 3.1%, respectively. The descriptive statistics of the means of the different components of direct cost is shown in Table 4.

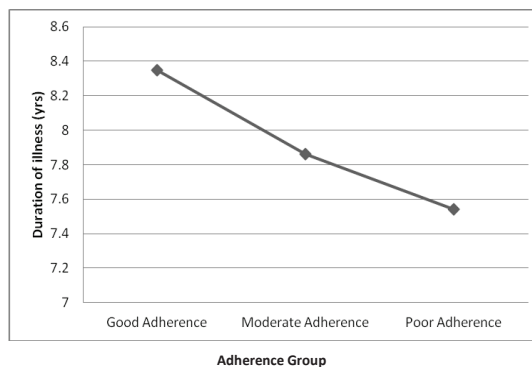


Figure 3. Relationship between duration of DM and the three levels of adherence at LAUTECH Teaching Hospital diabetes clinic

Duration of Illness = time since first diagnoses of diabetes mellitus (DM) was made
 Adherence groups were defined based on the level of diabetes patient adherence to medications according to the Morisky Medication Adherence Scale (MMAS-8) questionnaire results

The relationship between medication adherence, sex, level of education, monthly income and other categories was explored using the chi-square test (Table 2). The variation of the mean HbA1c levels among the three adherence groups was statistically significant ($p = 0.003$). Details of the comparison are shown in Table 3. The relationship between average duration of illness and the three adherence groups is shown in Figure 3, and Figure 4 depicts the the mean HbA1c levels of the three groups. The most common factors, according to the study participants, that may affect adherence to medications were cost of treatment (20.2%), lack of family support (11%), high pill burden (11%), cultural and religious beliefs (10%), inadequate information about therapy (10%) and non-availability of prescribed medications (10%).

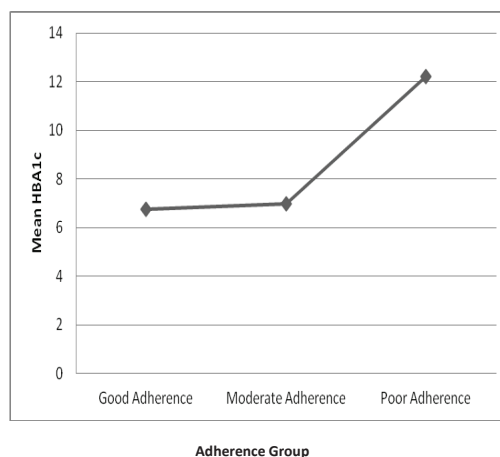


Figure 4. Relationship between mean HbA1c and three levels of adherence at LAUTECH Teaching Hospital diabetes clinic

HbA1c = blood glycosylated haemoglobin concentration
 Adherence groups were defined based on the level of diabetes patient adherence to medications according to the Morisky Medication Adherence Scale (MMAS-8) questionnaire results

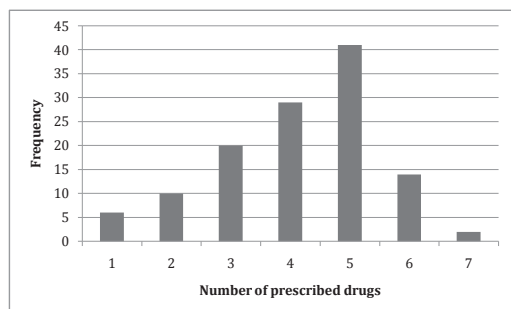


Figure 1. Number of drugs prescribed to individual study participants at diabetes clinic at LAUTECH Teaching Hospital

Table 1. Sociodemographic data of study participants attending diabetes clinic at LAUTECH Teaching Hospital

	Frequency (n)	Percentage (%)
SEX		
Male	51	39.5
Female	78	60.5
EDUCATIONAL LEVEL		
No Education	22	17.6
Primary Education	30	24
Secondary Education	20	16
Tertiary Education	53	42.4
EMPLOYMENT STATUS		
Unemployed	8	6.5
Employed	115	93.5
AGE GROUP		
< 30yrs	2	1.6
31 – 44yrs	5	4.1
45 – 64yrs	61	49.6
> 65yrs	55	44.7
MONTHLY INCOME		
< 20,000 Naira	50	43.1
20 – 50,000 Naira	37	31.9
50 – 100,000 Naira	22	19
> 100,000 Naira	7	6

₦165 Nigerian Naira = \$1 US Dollar at the time of data collection

Table 2. Associations between study participant drug adherence and other variables at LAUTECH Teaching Hospital diabetes clinic

Adherence level	X ²	df	p-value
Monthly Income	5.25	2	0.51
Sex	3.39	2	0.18
Level of Education	6.2	6	0.40
Age group	5.06	6	0.54
Fasting Plasma Glucose (Normal/Elevated)	0.05	2	0.98
HbA1c (Normal/Elevated)	3.2	2	0.20

X² = chi-square statistic
df = degrees of freedom
HbA1c = blood glycosylated haemoglobin concentration

Table 4. Descriptive statistics of components of direct costs for study participants at LAUTECH Teaching Hospital diabetes clinic

	n	Mean	Std. Deviation	Median	95% Confidence Interval for Mean		Minimum	Maximum	p-value	
					Lower Bound	Upper Bound				
Monthly medication cost	Good	49	6772.45	4804.102	5000	5392.55	8152.35	1000	20000	.64
	Moderate	39	6900.00	4140.303		5557.87	8242.13	1300	20000	
	Poor	32	5965.62	4353.390		4396.06	7535.19	1000	16500	
	Total	120	6598.75	4457.614		5793.00	7404.50	1000	20000	
Monthly cost of investigations	Good	44	1498.64	1891.121	800	923.68	2073.59	200	10000	.81
	Moderate	38	1772.89	2603.174		917.25	2628.54	150	10000	
	Poor	32	1807.81	2633.595		858.30	2757.32	200	11000	
	Total	114	1676.84	2345.813		1241.57	2112.12	150	11000	
Monthly transportation cost	Good	48	609.79	709.232	400	403.85	815.73	60	3000	.92
	Moderate	42	641.19	869.853		370.13	912.26	10	4000	
	Poor	30	682.33	663.105		434.73	929.94	60	3000	
	Total	120	638.92	753.217		502.77	775.07	10	4000	
Consultation fees	Good	34	223.53	105.339	250	186.77	260.28	100	500	.24
	Moderate	37	400.09	498.259		233.96	566.21	3	3000	
	Poor	26	404.05	737.844		106.03	702.07	5	4000	
	Total	97	339.26	495.978		239.30	439.22	3	4000	

Prices in Nigerian Naira, ₦ (₦165 Nigerian Naira = \$1 US Dollar at the time of data collection)

Table 3. Comparison of means of some variables between the three levels of adherence among study patients at LAUTECH Teaching Hospital

		Sum of Squares	df	Mean Square	F	p-value
HbA1c	Between Groups	50.519	2	25.260	9.049	.003
	Within Groups	36.290	13	2.792		
	Total	86.809	15			
Mean number of drugs	Between Groups	2.846	2	1.423	.785	.458
	Within Groups	213.848	118	1.812		
	Total	216.694	120			
Fasting Plasma Glucose	Between Groups	10.580	2	5.290	.486	.616
	Within Groups	1109.207	102	10.875		
	Total	1119.787	104			
Cost of medications	Between Groups	1.784E7	2	8922409.439	.445	.642
	Within Groups	2.347E9	117	2.006E7		
	Total	2.365E9	119			
Duration of illness	Between Groups	12.259	2	6.130	.161	.851
	Within Groups	4061.705	107	37.960		
	Total	4073.964	109			
Monthly income	Between Groups	.798	2	.399	.462	.631
	Within Groups	96.733	112	.864		
	Total	97.530	114			
AGE	Between Groups	377.306	2	188.653	1.741	.180
	Within Groups	12893.317	119	108.347		
	Total	13270.623	121			

HbA1c = blood glycosylated haemoglobin concentration
df = degrees of freedom
F = F-ratio

Discussion

The results above have described, in detail, the prescribing pattern of antidiabetic drugs, some direct costs, and adherence of patients to treatment. Female patients made up the larger proportion of patients in our study; this reflects the general trend from similar studies among diabetes patients worldwide³⁵⁻³⁷. The mean age of 61.4 ± 10.5 years found in this study is close to the 58.15 ± 9 .16 years and 61 ± 12.3 years recorded in work from Malaysia and the USA^{31,38}.

Achieving and keeping good glycaemic control (fasting plasma glucose < 110mg/dl or 6.1 mmol/L) is the goal of pharmacotherapy among diabetes patients, though this is not possible in a large percentage of them. Less than 50% of the study participants had good glycaemic control, similar to the 40.3% in another Nigerian study³⁴. Studies conducted in Ethiopia and Nepal found glycaemic control rates of 41.8% and 49.5% respectively^{39,40}. Of the 16 patients (12.4%) who were able to obtain (afford) HbA1c as a biomarker for glycaemic control, 50% of them had their values within normal limits. The mean plot for HbA1c (Figure 3) reveals

a trend of higher values of HbA1c in poorly adherent patients. This supports the statistical significant difference found when the average HbA1c was compared between the three adherence groups. Though HbA1c was tested in a small number of patients (because of financial constraints), this trend shows the importance of HbA1c as a useful tool for monitoring medication adherence among diabetes patients.

The number of drugs prescribed for patients has been found to affect adherence to treatment. The

average number of prescribed medications in this study was 4.1 ± 1.4 ; this is close to the 4.6 found in another Nigerian study and less than the 5.56 ± 2.52 in an Indian study^{24,41}. Oral hypoglycaemic agents were the most prescribed drugs in our study, with metformin either alone or in combination with other hypoglycaemic agents. Yusuff et al. found that oral hypoglycaemic agents were prescribed in 86% of cases while a similar study involving 384 type 2 diabetes patients had over 91% of these patients prescribed oral hypoglycaemic drugs^{23,40}. Oral agents from the thiazolidinedione and DPP4-inhibitor groups were prescribed for only three patients during the duration of this study; this is likely because of the higher cost of these drugs, their availability and potential safety issues. The cost of drugs formed a substantial part (72.3%) of the calculated direct costs in this study; this was higher than the 42.4% and 46% reported in studies from India and Pakistan^{42,43}. The aggressive development and marketing of generic medicines in these two Asian countries may account for the significantly lesser medication costs. Taking a cue from the Asian examples, it may be necessary for authorities in Nigeria to aggressively promote the use of cheap and effective generic medicines to increase access and adherence to these medications. The mean cost of monthly medications of about NGN N6556.60 (USD \$39.70) found in this study indicates that a large chunk of the patients' income is spent on drugs: over 70% of the patients in this study earned less than NGN N50,000 (USD \$303) monthly. This mismatch obviously has the potential to negatively impact patients' medication adherence; however, the communal way of life in Nigerian society means that the family usually supports or sponsors healthcare expenditures of any ill member.

Using the MMAS-8, medication adherence was recorded as good (40.6%), moderate (32.8%), or poor (26.6%). Using the same study tool, Jamons et al. identified only 16.9% of patients as poorly adherent in a study among 131 Palestinian diabetic patients, while Abebe et al. recorded 45.9%, 28.7% and 25.4% with high, medium and low adherence, respectively^{19,44}. A Nigerian study using another tool, the Adherence and Self-Management Monitoring Tool (ASMMT), found 59% of its sample diabetes patients to be non-adherent²³. Ahmad et al. in a study among Malaysian diabetic patients found 53% to be non-adherent using the Medication Compliance Questionnaire, while a study using pill count and other self-reporting methods found adherence to be adequate in only 29% of patients^{20,45}. The predictors of medication non-adherence shown in previous studies include disease and medication beliefs, poverty, service dissatisfaction, and using traditional medicines^{19,31,40,46,47}. This study, in addition to some of these aforementioned factors, identified inadequate information about the pharmacotherapy of diabetes, high pill burden and non-availability of prescribed drugs as obstacles to medication adherence among diabetes patients.

Conclusion

This study identified a satisfactory level of adherence to diabetes medications in the population evaluated. There is a need for the integration of generic medicines into routine care as a way of further reducing the burden of healthcare expenditure on the patients. The role or influence of healthcare insurance on medical expenditure among diabetes patients in the Nigerian setting is a potential research topic for the future.

Study Limitations

The relatively small sample size and the fact that only one centre was used for the study were major limitations. This would mean that results of the study might not be representative of other regions of the country. Additionally, some respondents refused to disclose some sensitive information such as income level and age because of fear about possible use of their information for tax-related or other official purposes. Though bias could arise from participant self-reporting and patients' recall ability, the standardization and validation of the data collection instruments used in the study act to mitigate such biases. Measuring adherence for all medications being taken by diabetes patients and not anti-diabetic agents alone may pose some questions. DM is a multi-system disease, however, with a myriad of complications, and it therefore might not have been as practical to analyze only adherence to anti-diabetic agents.

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