ORIGINAL RESEARCH

Determinants of medication adherence among adults with type 2 diabetes mellitus in three Malaysian public health clinics: a cross-sectional study

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Abstract: Medication adherence (MA) in adults with type 2 diabetes mellitus (T2D) is associated with improved disease control (glycated hemoglobin, blood pressure, and lipid profile), lower rates of death and diabetes-related complications, increased quality of life, and decreased health care resource utilization. However, there is a paucity of data on the effect of diabetes-related distress, depression, and health-related quality of life on MA. This study examined factors associated with MA in adults with T2D at the primary care level. This was a cross-sectional study conducted in three Malaysian public health clinics, where adults with T2D were recruited consecutively in 2013. We used the 8-item Morisky Medication Adherence Scale (MMAS-8) to assess MA as the main dependent variable. In addition to sociodemographic data, we included diabetes-related distress, depressive symptoms, and health-related quality of life as independent variables. Independent association between the MMAS-8 score and its determinants was done using generalized linear models with a gamma distribution and log link function. The participant response rate was 93.1% (700/752). The majority were female (52.8%), Malay (52.9%), and married (79.1%). About 43% of patients were classified as showing low MA (MMAS-8 score <6). Higher income (adjusted odds ratio 0.90) and depressive symptoms (adjusted odds ratio 0.99) were significant independent determinants of medication non-adherence in young adults with T2D. Low MA in adults with T2D is a prevalent problem. Thus, primary health care providers in public health clinics should focus on MA counselling for adult T2D patients who are younger, have a higher income, and symptoms of depression.

Keywords: medication adherence, type 2 diabetes mellitus, quality of life, distress, depression, primary care

Introduction

The literature has shown that better medication adherence (MA) is associated with improved disease control (glycated hemoglobin [HbA_{1c}], blood pressure, and lipid profile)[1] and decreased health care resource utilization in patients with type 2 diabetes mellitus (T2D).[2] This has translated into lower health care costs, lower hospitalization rates, fewer diabetes-related complications, increased quality of life, and a lower incidence of death.[2–5] In patients with T2D in Denmark,[6] a greater proportion of variance in HbA_{1c} levels was related to medication (15.6%) when compared with patients' sociodemographic characteristics, behavior, perceptions of care, and diabetes-related distress (DRD), which accounted for only 14% of the total variance. The data also show that for every 25% increase in MA, a patient's HbA_{1c} is reduced by 0.34%.[7]

However, adherence to medical therapy in general and adherence to medication in particular have posed significant challenges to both health care systems and

patients. The prevalence of poor adherence to medication, appointments, screening, diet, exercise, and health behavior is reported to be 30%–40%.[8,9] Common reasons for this include the complexity of the drug regimen, fear of side effects, and misperceptions about T2D as an illness.[10] Other possible reasons include financial constraints and poor social support for refilling prescriptions,[8,11] physical and psychological restrictions affecting daily adherence to prescribed medications, and in particular, increased comorbidity,[12] such as complications of T2D,[11] visual impairment, diabetic foot problems, health literacy,[13] cognitive decline,[14] DRD, and depression.[15] Physician characteristics and health care settings are other potential factors that may affect patient participation in decision-making[16,17] and MA.[18,19]

MA is usually defined as the extent to which patients follow the instructions given for prescribed medications.[20] Methods used to assess MA include pill counts, pharmacy claims, or refill records, as well as subjective assessment of patient-reported adherence.[3] However, there is no consensual standard as to what constitutes adequate adherence; many consider pill count or refill rates >80% to be acceptable.[3] Nevertheless, self-reported measures of MA have been increasingly shown to be reliable and valid,[21] so are being used increasingly in clinical trials.

Realizing the importance of MA as mentioned above, the opportunity for early disease control in patients with T2D, and the need to prioritize our limited health care resources in the face of the rising T2D epidemic, this study examined the determinants of medication non-adherence in adults with T2D attending public health clinics in Malaysia. We addressed the issue of MA taking into account the effects of DRD, depression, and health-related quality of life (HRQoL) in addition to other sociodemographic and clinical variables. To the best of our knowledge, there is a paucity of data on the association between these variables and MA,[2] particularly in an Asian health care setting like Malaysia. Previous similar local studies have not included either DRD or MA,[1,22] or used more general measures for stress or health status (eg, the Short Form-36) and not HRQoL measures.[23,24] It is hoped that this diagnosable condition of medication non-adherence can become more treatable[25] by health care providers based on the findings of this study.

Materials and methods

This study was part of EDDMQoL, a larger cross-sectional study on emotional burden and its effect on disease control, MA, and HRQoL in patients with T2D. The study was conducted from 2012 to 2013. In addition to a questionnaire on demography (age, sex, ethnicity, religion, marital status, educational level, occupation, monthly income), smoking status, and frequency of exercise, we used another structured case record form to capture comorbidity (hypertension and hyperlipidemia/dyslipidemia), diabetes-related complications, duration of diabetes, HbA_{1c}, blood pressure, lipids, number and types of medications used, and MA. In addition to these, we used three additional questionnaires to measure DRD, depression, and HRQoL. These questionnaires were prepared in three languages, ie, English, Malay, and Mandarin.

Setting

Participants were recruited from three public health clinics (Seri Kembangan, Dengkil, and Salak) in Malaysia. These health clinics were specifically chosen because they differ in terms of the characteristics of the patients they serve and the geographical regions in which they are situated. The Seri Kembangan Health Clinic is in an urban area located in the vicinity of Chinese communities, so is visited mainly by Chinese patients. Dengkil Health Clinic is a rural center frequented by larger proportions of Malaysians of Indian origin than for a regular public health clinic. Salak Health Clinic is a rural center in a mainly Malay residential area. The variability of the sites provided a broad range of Asian patients with T2D.

Participants

We consecutively sampled all patients with T2D who came to the clinics for their routine care. The minimum patient age was 30 years and all patients had been diagnosed with T2D more than a year previously. Their records needed to show that they were on regular follow-up, with at least three visits in the past one year and blood tests done within the previous 3 months. We excluded patients who were pregnant or lactating, those who had psychiatric/psychological disorders that could impair judgment and memory, and patients who could not read or understand English, Malay, or Mandarin. Patients who fulfilled the inclusion criteria were approached and informed of the study. Written consent was secured before they answered the questionnaires in the language of their preference. Trained research assistants interviewed patients in their language of preference. Face validity testing in ten patients found the questionnaires to be acceptable and understood without difficulty. This study was approved by the medical research ethics committee at the Ministry of Health, Malaysia.

Medication adherence

The 8-item Morisky Medication Adherence Scale (MMAS-8) enquires about a patient's experiences with medications during the 2 weeks prior to answering the questionnaire.[26] This questionnaire has been translated into different languages so that it can be used with ease among patients in different settings. All the items except item 5 are reverse-coded (no, 0; yes, 1). Item 8 has five options scored in a negative direction from 1 (never) to 5 (always). Items 1–4 and 6–8 are reverse-coded, and item 8 is further divided by 4 when calculating a summated score. The total scale has a range of 0–8, including low adherence (<6), medium adherence (6–7), and high adherence (8). The MMAS-8 scale is reliable (Cronbach's α=0.83), with a sensitivity of 93% and a specificity of 53%, and is available in the Malay and Chinese languages.[26–28] The Malay version of the MMAS-8 showed moderate internal consistency (Cronbach's α=0.675), and had a test–retest reliability of 0.82 $(P<0.001)$. A significant relationship was found between MMAS-8 categories and HbA$_{1c}$ categories (χ^2=20.261; $P\leq0.001$). The Chinese version of the MMAS-8 was also reported to have satisfactory psychometric properties, ie, good internal consistency (Cronbach's α=0.77) and test–retest reliability (r=0.88, $P<0.001$).[28] Following face validity testing in ten patients, some modifications to the wording of items in the questionnaire were done to refine them and improve understanding.

Health-related quality of life

The World Health Organization Quality of Life-Brief (WHOQOL-BREF)[29] produces four HRQoL domains and scores, ie, a physical domain, a psychological domain, a social relationships domain, and an environment domain.[29] This four-domain structure, which has a comparative fit index of 0.901, demonstrates good internal consistency, with Cronbach's α values for each of the four domain scores ranging from 0.66 (for social relationships domain) to 0.84 (for physical domain). There are also two items that are examined separately, ie, question 1, which asks about an individual's overall perception of quality of life, and question 2, which asks about an individual's overall perception of his or her health. Domain scores are scaled in a positive direction (ie, higher scores denote higher quality of life).[30] Where more than 20% of the data are missing from an assessment, the assessment is discarded. Where up to two items are missing, the mean of the other items in the domain is substituted. Where more than two items are missing from the domain, the domain score is not calculated (with the exception of social relationships domain, where the domain should only

be calculated if one or less item is missing). The mean score of items within each domain is used to calculate the domain score. Mean scores are then multiplied by 4 in order to make domain raw scores comparable with the scores used in the WHOQOL-100. The WHOQOL-BREF was shown to be comparable with the WHOQOL-100 in discriminating between ill and well groups. There are high correlations between domain scores based on the WHOQOL-100 and domain scores calculated using items included in the WHOQOL-BREF.[29] These correlations ranged from 0.89 (for social relationships domain) to 0.95 (for physical domain). The Malay and Chinese versions of this questionnaire were previously validated and are reported to have satisfactory psychometric properties.[31,32]

Diabetes-related distress

DRD was measured using the validated 17-item Diabetes Distress Scale (DDS-17).[33–35] This instrument assesses problems and difficulties related to diabetes during the past month on a Likert scale from 1 (not a problem) to 6 (a very serious problem).[33] Internal reliability of the DDS-17 and the four subscales are adequate (Cronbach's α>0.87), and validity coefficients yield significant linkages with the Center for Epidemiological Studies Depression Scale, meal planning, exercise, and total cholesterol.[33] DDS-17 has been found to have adequate and better psychometric properties compared with other similar scales.[34] A mean total score of less than 2.0 indicates little to no distress, a score between 2.0 and 2.9 indicates moderate distress, and 3.0 and greater is considered high distress worthy of clinical attention.[36] Those in the moderate and high distress groups have been found to have poorer behavioral and clinical outcomes. A local translation and validation study of the Malay version of the DDS-17 showed high internal consistency (Cronbach's α=0.94), and the test–retest reliability value was 0.33 (P=0.009). There was a significant relationship between the mean DDS-17 item score categories (<3 versus $\geq$3) and HbA$_{1c}$ categories (<7% versus $\geq$7%); χ^2=4.20; P=0.048). The Chinese version of the DDS contains 15 items and was found to have good psychometric properties; the Cronbach's α for internal consistency was 0.90 and the test–retest reliability coefficient was 0.74.[35] However, we included all the 17 items in this study in accordance with the original author's recommendation.

Depression

Depression was defined using the 9-item Patient Health Questionnaire (PHQ-9), which has been shown to have good construct and criterion validity in making the diagnosis and

assessing the severity of depression.[37–39] The PHQ-9 refers to symptoms experienced by patients during the last 2 weeks (eg, "thoughts that you would be better off dead or of hurting yourself in some way"). The PHQ-9 has nine items that are scored from 0 (not at all) to 3 (nearly every day), giving a total score that ranges from 0 to 27. The PHQ-9 has cut-off points at scores of 5, 10, 15, and 20, representing mild, moderate, moderately severe, and severe depression, respectively. A total score of $\geq$10 indicates a sensitivity of 88% and a specificity of 89% for major depression.[37] The Malay version of the PHQ-9 had been locally validated and found to have a sensitivity of 87% (95% confidence interval [CI] 71–95), a specificity of 82% (95% CI 74–88), a positive likelihood ratio of 4.8 (3.2–7.2), and a negative likelihood ratio of 0.16 (0.06–0.40).[38] The Chinese version of the PHQ-9 is reported to have good psychometric properties, with an internal consistency of 0.82 and test–retest reliability over a 2-week interval of 0.76.[39]

Clinical variables

T2D was defined as present when the patients' case records showed the following criteria: documented diagnosis of diabetes mellitus according to the 1999 World Health Organization criteria,[40] current treatment consisting of lifestyle modification, or on oral antihyperglycemic agents or insulin. Hypertension is diagnosed if systolic blood pressure is $\geq$130 mmHg or diastolic blood pressure is $\geq$80 mmHg on each of two successive readings obtained by the clinic physician.[41] A blood pressure <130/80 mmHg was regarded as controlled, and this was the mean of two readings in the rested position with the arm at heart level, using a cuff of appropriate size. Hyperlipidemia refers to an increase in concentration of one or more plasma or serum lipids, usually cholesterol and triglycerides, and the term dyslipidemia is used for either an increase or decrease in concentration of one or more plasma or serum lipids (low-density lipoprotein cholesterol >2.6 mmol/L, triglycerides >1.7 mmol/L, and high-density lipoprotein cholesterol <1.1 mmol/L). Body mass index is calculated as weight divided by height squared. Low-density lipoprotein-cholesterol $\leq$2.6 mmol/L and HbA$_{1c}$ $\leq$6.5% are regarded as the other treatment targets.[41,42] These clinical data were retrieved from the patient's medical record using a case record form on the day that the patient completed the questionnaires.

Diabetes-related complications

There were five diabetes-related complications in this study; three were classified as microvascular complications, comprising retinopathy, nephropathy, and diabetic foot problems, and two were classified as macrovascular complications, ie,

ischemic heart disease and cerebrovascular disease or stroke. These complications were retrieved from patient records. Diagnoses of these complications were made or confirmed by the attending physician at the clinic based on medical symptoms, laboratory results, radiological evidence, and treatment history at the clinic and other hospitals. Nephropathy was diagnosed as the persistent presence (on two or more occasions at least 3 months apart) of any of the following: microalbuminuria, proteinuria, serum creatinine >150 mmol/L, or estimated glomerular filtration rate <60 mL per minute (calculated using the Cockcroft-Gault formula). Diabetic foot problems comprised foot deformity that is related to the lower limbs muscle weakness and/or as a consequence of the other diabetic foot problems, current ulcer, amputation, peripheral neuropathy, or peripheral vascular disease.

Statistical analysis

The sample size was calculated using G*Power 3.1.2 software,[43] with an estimated effect size of r=0.16 between DRD and HbA$_{1c}$,[44,45] a power of 0.95, and significance at 0.05; the estimated sample size was 500. Taking into consideration about 30% of data being incomplete/missing in patient medical records and 30% of questionnaires returned from patients being incomplete, the sample size needed was 650.

Quantitative data analyses were done using PASW version 21.0 (SPSS Inc, Chicago, IL, USA). Differences in the categorical variables were performed using the Chi-squared test. P<0.05 was considered to be significant at two tails. To analyze the association of the demographic and clinical variables and MA, generalized linear models were used with MMAS-8 total score as the outcome variable. Since the MMAS-8 total score was skewed to the left, a generalized linear model with a gamma distribution and log link function was used. The gamma distribution is a reasonable choice because its flexible distribution accommodates well for positive and continuous variables and it incorporates the assumption that the standard deviation is proportional to the mean. Univariable analyses were done for the independent variables and those that showed significant effects on the MMAS-8 total scores were included in the final multivariable generalized linear model analyses. In the final model, normality of residual was confirmed, as residual plots indicated fulfilment of linearity and homogeneity assumptions, and model fitting encountered no obvious problem as evidenced by the residual deviance being less than the residual degree of freedom.

Results

The participant response rate was 93.1% (700/752). From this number of participants, we had 668 completed

MMAS-8 questionnaires. More than half were female (52.8%) and Malay (52.9%, Table 1). The majority were married or living with a partner (79.1%), had non-tertiary education (89.1%), and were earning <RM 3,000 per month (94.4%); most of the patients were non-smokers and undertook some exercise; about 80% reported having hypertension but antihypertensive usage was almost 90% (Table 1).

Table 1 Patient characteristics according to medication adherence categories

Patient characteristics	Total patients, n (column %)	Medication adherence score, n (row %)		χ^2	*P*-value*
		Low (MMAS-8 <6)	Medium and high (MMAS-8 6–8)		
Health clinic				0.96	0.620
Seri Kembangan	216 (32.3)	94 (43.5)	122 (56.5)		
Dengkil	121 (13.1)	47 (38.8)	74 (61.2)		
Salak	331 (49.3)	145 (43.8)	186 (56.2)		
Age, years				9.18	0.010
≤50	174 (26.1)	88 (50.6)	86 (49.4)		
51–60	260 (39.0)	115 (44.2)	145 (55.8)		
>60	232 (34.8)	83 (35.8)	149 (64.2)		
Diabetes duration, years				2.77	0.251
<5	323 (50.0)	130 (40.2)	193 (59.8)		
5–9.9	183 (28.3)	78 (42.6)	105 (57.4)		
≥10	140 (21.7)	68 (48.6)	72 (51.4)		
Sex				0.24	0.638
Female	359 (54.0)	157 (43.7)	202 (56.3)		
Male	306 (46.0)	128 (41.8)	178 (58.2)		
Ethnicity				7.58	0.023
Malay	351 (53.0)	158 (45.0)	193 (55.0)		
Chinese	155 (23.4)	73 (47.1)	82 (52.9)		
Indian	156 (23.6)	52 (33.3)	104 (66.7)		
Religion				11.45	0.043
No religion	32 (4.8)	11 (34.4)	21 (65.6)		
Moslem	359 (53.9)	161 (44.8)	198 (55.2)		
Buddhist	78 (11.7)	43 (55.1)	35 (44.9)		
Hinduism/Sikh	141 (21.2)	48 (34.0)	93 (66.0)		
Christian/Catholic	21 (3.2)	8 (38.1)	13 (61.9)		
Others	35 (5.3)	13 (37.1)	22 (62.9)		
Religiosity				0.18	0.912
Religious	567 (85.4)	242 (42.7)	325 (57.3)		
Unsure	24 (3.6)	10 (41.7)	14 (58.3)		
Not religious	73 (11.0)	33 (45.2)	40 (54.8)		
Marital status				2.12	0.547
Married/living with a partner	523 (78.8)	227 (43.4)	296 (56.6)		
Widowed	96 (14.5)	36 (37.5)	60 (62.5)		
Divorced/separated	19 (2.9)	10 (52.6)	9 (47.4)		
Single	26 (3.9)	10 (38.5)	16 (61.5)		
Education				9.72	0.008
Never	43 (6.5)	16 (37.2)	27 (62.8)		
Primary and secondary	542 (82.5)	222 (41.0)	320 (59.0)		
Tertiary	72 (11.0)	43 (59.7)	29 (40.3)		
Employment				2.51	0.285
Retired/home manager	356 (53.5)	144 (40.4)	212 (59.6)		
Employed	299 (45.0)	134 (44.8)	165 (55.2)		
Unemployed	10 (1.5)	6 (60.0)	4 (40.0)		
Income (RM)				11.42	0.003
<1,000	310 (47.1)	118 (38.1)	192 (61.9)		
1,000–2,999	310 (47.1)	138 (44.5)	172 (55.5)		
≥3,000	38 (5.8)	25 (65.8)	13 (34.2)		

(*Continued*)

Table 1 (*Continued*)

Patient characteristics	Total patients, n (column %)	Medication adherence score, n (row %)		χ^2	P-value*
		Low (MMAS-8 <6)	Medium and high (MMAS-8 6–8)		
Exercise				19.42	<0.0001
No	283 (42.6)	114 (40.3)	169 (59.7)		
≤3 times in a week	220 (33.1)	119 (54.1)	101 (45.9)		
>3 times in a week	161 (24.2)	52 (32.3)	109 (67.7)		
Smoking				3.20	0.202
Never	509 (76.5)	209 (41.1)	300 (58.9)		
Stopped >5 years	59 (8.9)	27 (45.8)	32 (54.2)		
Stopped ≤5 years and active smoker	97 (14.6)	49 (50.5)	48 (49.5)		
Hypertension				0.48	0.502
No	140 (21.3)	64 (45.7)	76 (54.3)		
Yes	516 (78.7)	219 (42.4)	297 (57.6)		
Dyslipidemia				0.18	0.686
No	381 (59.3)	167 (43.8)	214 (56.2)		
Yes	261 (40.7)	110 (42.1)	151 (57.9)		
Any diabetes complication				0.27	0.635
No	585 (87.7)	253 (43.2)	332 (56.8)		
Yes	82 (12.3)	33 (40.2)	49 (59.8)		
Any microvascular complication				0.22	0.658
No	617 (92.5)	263 (42.6)	354 (57.4)		
Yes	50 (7.5)	23 (46.0)	27 (54.0)		
Any macrovascular complication				0.30	0.628
No	622 (93.8)	270 (43.4)	352 (56.6)		
Yes	41 (6.2)	16 (39.0)	25 (61.0)		
OHA				1.91	0.169
No	58 (8.7)	30 (51.7)	28 (48.3)		
Yes	605 (91.3)	256 (42.3)	349 (57.7)		
Insulin				0.51	0.777
None	403 (60.9)	170 (42.2)	233 (57.8)		
1 type	183 (27.6)	81 (44.3)	102 (55.7)		
≥2 types	76 (11.5)	35 (46.1)	41 (53.9)		
Number of AHA agents				1.22	0.748
None	80 (12.1)	35 (43.8)	45 (56.3)		
1 type	197 (29.8)	90 (45.7)	107 (54.3)		
2 types	191 (28.9)	83 (43.5)	108 (56.5)		
≥3 types	194 (29.3)	78 (40.2)	116 (59.8)		

Note: *Chi-square *P*-value.
Abbreviations: MMAS-8, 8-item Morisky Medication Adherence Scale; OHA, oral hypoglycemic agent; AHA, antihypertensive agent; RM, Ringgit Malaysia.

Figure 1 shows the distribution of the total MMAS-8 score. About 43% and 57% of the patients were classified as low (MMAS-8 score <6) and medium to high (MMAS-8 score 6–8) MA categories, respectively. The mean (± standard deviation) for age was 56.9±10.18 years. The median (interquartile range) scores for the DDS-17, PHQ-9, duration of diabetes, hypertension, and dyslipidemia were 33.0 (24.00 to 47.00), 4.0 (1.00 to 7.00), 4.0 (3.00 to 9.00), 5.0 (3.00 to 9.00) and 3.0 (2.00 to 6.00), respectively.

Table 2 shows the univariable (crude odds ratio) and multivariable (adjusted odds ratio) analyses for the significant variables. It was observed that younger age, Malay ethnicity, higher income, higher education, exercise ≤3 times per week, lower overall HRQoL, higher DRD, and depressive symptoms were associated with poor MA. After adjustment for all these variables, being a younger adult with T2D, higher income, and depressive symptoms were significant independent determinants of non-adherence with medication.

Discussion

This study reports on the determinants of MA in adult T2D patients taking into account DRD, depression, and quality of life, which were not investigated in previous studies.[1,22–24]
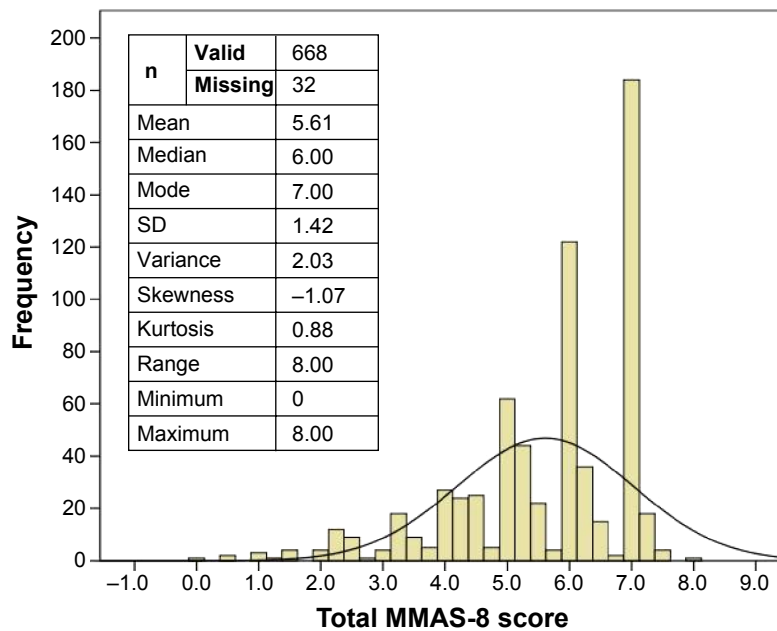
Figure 1 Distribution of MMAS-8 total score.
Abbreviations: MMAS-8, 8-item Medication Morisky Adherence Scale; SD, standard deviation.

We noted a similar prevalence of low MA among adult T2D patients in this study, which is in line with earlier studies, ie, 40%–50% locally,[1,22] and 40%–90% elsewhere, varied by whether the participants were on oral hypoglycemic or insulin medication.[46,47]

Strong determinants for medication non-adherence, such as younger age, higher income, higher education, less adherence to exercise recommendations, poorer HRQoL, having DRD, and depression were expected and have been reported previously.[1,22] However, it was unexpected that those who did

Table 2 Determinants of medication adherence

Parameter	Crude Exp (B)	95% CI for crude Exp (B)		Significance	Adjusted Exp (B), n=597	95% CI for adjusted Exp (B)		Significance
		Lower	Upper			Lower	Upper	
Intercept	NA	NA	NA	NA	4.67	3.519	6.190	<0.0001
Age, n=665	1.004	1.002	1.006	<0.0001	1.003	1.001	1.006	0.019
Ethnicity, n=661								
Indian	1.08	1.017	1.139	0.011	1.05	0.988	1.110	0.118
Chinese	1.004	0.948	1.062	0.900	0.98	0.923	1.046	0.589
Malay	1	NA	NA	NA	1	NA	NA	NA
Income, n=657								
≥3,000	0.83	0.747	0.913	<0.0001	0.90	0.803	0.999	0.048
1,000–2,999	0.95	0.910	0.999	0.046	0.988	0.947	1.051	0.937
<1,000	1	NA	NA	NA	1	NA	NA	NA
Education, n=656								
Tertiary	0.85	0.76	0.95	0.004	0.91	0.804	1.028	0.128
Primary and secondary	0.96	0.879	1.057	0.437	0.99	0.895	1.084	0.759
Never	1	NA	NA	NA	1	NA	NA	NA
Exercise, n=663								
No	0.97	0.916	1.028	0.309	0.99	0.932	1.049	0.705
≤3 times in a week	0.92	0.870	0.982	0.011	0.98	0.915	1.040	0.452
>3 times in a week	1	NA	NA	NA	1	NA	NA	NA
OQOL, n=597	1.004	1.002	1.007	0.001	1.002	0.999	1.004	0.211
DDS, n=639	0.997	0.996	0.999	<0.0001	0.999	0.998	1.001	0.546
PHQ, n=654	0.98	0.978	0.988	<0.0001	0.988	0.981	0.994	<0.0001

Abbreviations: Exp (B), odds ratio; CI, confidence interval; OQOL, overall score for the World Health Organization Quality of Life-Brief 26 items; DDS, Diabetes Distress Scale 17 items; PHQ, Patient Health Questionnaire 9 items; NA, not applicable.

not exercise at all were as adherent to medication as those who exercised more than three times per week. Clustering of healthy behaviors has been reported before, and it would be expected that patients who adhered to exercise recommendations would also adhere to their prescribed medication.[48] However, this finding might be limited by the brevity of this self-reported variable and the lack of simultaneous measurement of other healthy behaviors, such as dietary habits, self-monitoring of blood glucose, and adherence to blood testing.[4]

That adult T2D patients of Indian ethnicity were more adherent to their medication compared with the Malay and Chinese patients was unexpected.[22] Chinese patients are believed to be more health conscious and adherent to health recommendations such as exercise.[49] The Chinese are also often thought to be more adherent to their medication as prescribed by their physicians.[48] However, being in a higher income group and having higher DRD might influence their adherence to prescribed medication. Having higher income possibly enables them to be more resourceful in health-seeking endeavors. In comparison with Indians, Malay patients were more likely to have tried other traditional therapies[50] and the Chinese more often sought further private medical opinions[51] for their T2D. These might have resulted in the observed higher non-adherence among Malay and Chinese patients to their medication when compared with Indians. However, this ethnic disparity in MA became statistically insignificant after adjustment for the stronger influence of income, age, and depression. Higher MA among Indians could also have been due to the lower prevalence of moderate to severe depression (7.5%) compared with the other two ethnic groups (12.0%; data not reported in the study).

Unlike many Western studies that have reported an association of medication non-adherence with DRD instead of depression,[52–54] our results indicated a stronger adjusted effect of depression, rather than DRD, on medication non-adherence. This was probably due to the nature of DRD, which has milder symptomatology[55] or because patients with DRD could manifest a psychological reaction of being successful in coping with MA rather than failing.[56]

The fact that medication use and insulin use did not affect MA is in line with a previous study that was also done in public health clinics,[22] but in contrast with another study showing that patients on insulin and oral hypoglycemic agents were predisposed to medication non-adherence.[1] However, this latter study was conducted in an urban academic hospital, a setting that is different from the studies at the primary care level.[57] Nevertheless, a similar finding was noted with regard to unemployment status in

association with medication non-adherence which reached statistical significance in that study, but not in this study. This could have been due to the higher drug cost required to refill prescriptions in the academic hospital, and thus the patients were predisposed to medication non-adherence.[58] Having comorbidity such as hypertension, dyslipidemia,[22] or diabetes-related complications also did not affect MA in adults with T2D attending public health clinics.[22] On the contrary, after being diagnosed with these comorbidities and complications, there were greater proportions of patients who reported higher MA. This result confirms many primary care physicians' experience and assumption that many of their patients become "better" patients in terms of adhering to therapeutic recommendations and their monitoring schedule after being diagnosed with an additional comorbidity or complication.

For T2D patients who are at risk of medication non-adherence, a poly-pill approach might be a helpful adjunct[59] to other strategies, including reducing treatment complexity, decreasing pill burden, and addressing patient and socioeconomic issues that contribute to the problem.[60,61] Future studies should look into adherence behavior over time and the ability of primary care physician to screen and respond to medication non-adherence.[62]

One of the limitations of this study lies in the use of a single measure for MA assessment, ie, the MMAS-8. This might predispose to recall bias or a biased response in the presence of significant others during the interview. However, since this was part of a larger study and used a locally validated MMAS-8 in a large sample size, we believe the design was able to produce a valid evaluation of determinants of MA. It would be desirable in a future study to have more than one measure for MA, such as pill count in addition to a self-report measure. The strength of the study was its representative sample of patients, in terms of their sociodemographic background being similar to the adult T2D patients in public health clinics throughout the whole country.[63]

Conclusion

Low MA is a serious problem in adult patients with T2D, and its downstream effects will be multiplied in increased complication rates, psychological burden, and health care costs if left unaddressed. Primary health care providers in public health clinics should focus on MA counselling for adult T2D patients of younger age, with a higher income, and who report more depressive symptoms. This study provides further evidence regarding the characteristics of patients who may be at risk for medication non-adherence. This

behavior did not differ according to ethnic groups, number and types of medication prescribed, or duration of diabetes and comorbidities/complications.

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Disclosure

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