Therapeutics and Clinical Risk Management

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Association of diabetes-related distress, depression, medication adherence, and health-related quality of life with glycated hemoglobin, blood pressure, and lipids in adult patients with type 2 diabetes: a cross-sectional study

This article was published in the following Dove Press journal:
Therapeutics and Clinical Risk Management
29 April 2015
Number of times this article has been viewed

Boon-How Chew[1]
Mohd-Sidik Sherina[2]
Noor-Hasliza Hassan[3]

[1]Department of Family Medicine, [2]Department of Psychiatry, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang; [3]Klinik Kesihatan Dengkil, Jalan Dengkil, Malaysia

Video abstract

Point your SmartPhone at the code above. If you have a QR code reader the video abstract will appear. Or use:
http://youtu.be/Nyq75N30tYU

Correspondence: Boon-How Chew
Department of Family Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia
Tel +60 3 8947 2520
Fax +60 3 8947 2328
Email chewboonhow@gmail.com

Abstract: This study examined the associations of diabetes-related distress (DRD), depressive symptoms, health-related quality of life (HRQoL), and medication adherence with glycemia, blood pressure (BP), and lipid biomarkers in adults with type 2 diabetes mellitus (T2D). This cross-sectional study was conducted in three Malaysian public health clinics in 2012–2013, recruited adult patients (aged ≥30 years) with T2D who had been diagnosed for more than one year, were on active follow-up, and had recent blood test results. Univariable and multivariable analyses were performed to identify significant associated factors for glycated hemoglobin (HbA_{1c}) BP, and lipids. The response rate was 93.1% (700/752). The majority were females (52.8%), Malay (52.4%), and married (78.7%). DRD correlated with systolic BP (r= –0.16); depressive symptoms correlated with low-density lipoprotein cholesterol (r=0.12) and total cholesterol (r=0.13); medication adherence correlated with HbA_{1c} (r= –0.14) and low-density lipoprotein cholesterol (r= –0.11); and HRQoL correlated with casual blood glucose (r= –0.11), high-density lipoprotein cholesterol (r= –0.13), and total cholesterol (r= –0.08). Multivariable analyses showed that HRQoL was significantly associated with casual blood glucose (adjusted B= –0.06, P=0.024); DRD was associated with systolic BP (adjusted B= –0.08, P=0.066); depressive symptoms were associated with low-density lipoprotein cholesterol (adjusted B=0.02, P=0.061), and medication adherence was associated with HbA_{1c} (adjusted B= –0.11, P=0.082) and total cholesterol (adjusted B= –0.06, P=0.086). There were significant and distinctive associations of DRD, depressive symptoms, HRQoL, and medication adherence with glycemia, BP, and lipid biomarkers. Unexpected beneficial therapeutic effects of DRD on BP require further study. A multidisciplinary approach may be needed for risk management in adults with T2D at the primary care level.

Keywords: distress, depression, medication adherence, quality of life, type 2 diabetes mellitus, glycated hemoglobin, blood pressure, lipids

Introduction

It is widely known that patients living with type 2 diabetes (T2D) carry a high burden of psychosocial problems[1] and psychological disorders.[2–4] Worrying about the future, the possibility of complications, and feelings of guilt or anxiety when "off-track" with diabetes management are reported to be sources of significant distress.[5,6]

Emotional distress in people with diabetes mellitus mainly comprises diabetes-related distress (DRD) and depression.[7] Among adults with T2D, DRD and depression

were reported to be more prevalent and persistent than other affective disorders (anxiety, panic disorders, and dysthymia) over a period of 18 months.[3] DRD is defined as patient concerns about disease management, support, emotional burden, and access to care, and is distinctively different from depression, which is not disease-specific or context-specific to diabetes care.[8–10] It was suggested from previous studies that DRD could progress to depression,[11] a more severe form of emotional distress, which in turn causes poor self-care activity, disease control, morbidity, and mortality.[7,12] Fisher (β=0.026)[10] and Aikens (adjusted β=0.34)[13] reported a cross-sectional relationship between DRD and control of glycated hemoglobin (HbA_{1c}).

Since the introduction of DRD-specific scales such the Diabetes Distress Scale (DDS-17) in 2005[8] and the Problem Areas In Diabetes in 1995,[14] there have been increasing numbers of studies looking into the relationship between DRD and disease control in adults with T2D.[15] Nevertheless, reports of patient self-reported outcome measures, such as DRD, depression, health-related quality of life (HRQoL), and medication adherence (MA) have been few in non-Western countries. As these aspects of patient are important in self-management and disease control,[15–17] it is paramount that their associations are studied in patients of other cultural backgrounds. The Asia-Pacific region including Malaysia has reported an increasing prevalence of T2D.[18] Abundant local data have shown that poor disease control and suboptimal clinical management are hard to overcome.[19–21] This would inevitably lead to increased patient suffering and health care costs from diabetes-related complications.[22,23]

This study examined the associations of DRD, depression, MA, and HRQoL with the three main biomarkers of risk, namely glycemia, blood pressure (BP), and lipids in adults with T2D. As part of a larger study of emotional burden and its effect on disease control, MA, and quality of life in patients with T2D (EDDMQoL), it is hoped that this study would be informative regarding the associations between these variables to improve existing therapeutic strategies or provide grounds for a potential risk management intervention in these patients.

Materials and methods

This cross-sectional study was conducted from 2012 to 2013. In addition to a questionnaire on demography (age, gender, ethnicity, types of religion, degrees of religiosity, marital status, educational level, employment status, monthly income), exercise, and smoking status, we used a structured case record form to capture comorbidity (hypertension and hyperlipidemia/dyslipidemia), diabetes-related complications, duration of diabetes, glycemic status, and BP and lipid control, along with number and types of medication used. We also used another four questionnaires to evaluate DRD, depressive symptoms (DS), MA, and HRQoL. These questionnaires were prepared in three languages, ie, English, Malay, and Mandarin.

Setting

Participants were recruited from three public health clinics (Klinik Kesihatan Seri Kembangan, Klinik Kesihatan Dengkil, and Klinik Kesihatan Salak) in Malaysia. These health clinics were chosen because they are different in terms of patient sociodemographic characteristics and the geographical regions that they are situated in. The variability of the sites provided a broad range of patients in which to assess the relationships between the study variables.

Participants

We consecutively sampled all patients with T2D who came to the clinics. They were at least 30 years old and had to have been diagnosed more than one year earlier. Patients were on regular follow-up, had made at least three visits in the past year, and had recent blood results within the previous 3 months. We excluded patients who were pregnant or lactating, patients who had a psychiatric/psychological disorder that could impair judgment and memory, and patients who could not read or understand English, Malay, or Mandarin. Patients who fulfilled the criteria were approached and informed of the study, and written consent was secured before answering the questionnaires in the language they preferred. This cross-sectional study was approved by the Medical Research Ethics Committee, Ministry of Health, Malaysia.

Definitions of disease

The definition of T2D in this study was based on the following: either a documented diagnosis of T2D according to 1999 World Health Organization criteria[24] or current treatment recorded in the patient's card as consisting of lifestyle modification, oral hypoglycemic agents, or insulin. This information was obtained from patient case records.

Glycemic status comprised HbA_{1c} and casual blood glucose (CBG). Hypertension was diagnosed if systolic BP was $\geq$130 mmHg or diastolic BP was $\geq$80 mmHg on each of two successive readings obtained by the clinic physicians.[25]

Lipid profile consisted of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and total cholesterol. Dyslipidemia refers to either an increase or decrease in concentration of one or more plasma or serum lipids (LDL-C >2.6 mmol/L, triglycerides >1.7 mmol/L, and HDL-C <1.1 mmol/L).[25,26] These clinical data were retrieved from the patient's medical record using a case record form on the same day as the patient completed the questionnaires.

Definitions of diabetes-related complications

There were five diabetes-related complications in this study; three were classified as microvascular complications, ie, retinopathy, nephropathy, and diabetic foot problems; another two were classified as macrovascular complications, ie, ischemic heart disease and cerebrovascular disease or stroke. These complications were retrieved from patients' records. Diabetic foot problems comprised foot deformity, current ulcer, amputation, peripheral neuropathy, or peripheral vascular disease.

Diabetes-related distress

DRD was measured using the validated DDS-17.[8] This instrument assesses problems and difficulties concerning diabetes during the previous month on a Likert scale from 1 (not a problem) to 6 (a very serious problem).[8,27] The DDS-17 yields a total diabetes distress scale score plus four subscale scores that address different types of distress, ie, emotional burden, physician-related distress (PD), regimen-related distress, and diabetes-related interpersonal distress.[8] 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 association between mean DDS-17 item score categories (<3 versus ≥3) and HbA_{1c} categories (<7% versus ≥7%, χ^2=4.20; P=0.048). [under a journal's review].

Depressive symptoms

Symptoms of depression were measured using the 9-item Patient Health Questionnaire (PHQ-9), which has been shown to have good construct and criterion validity in diagnosing and assessing the severity of depression.[28] The PHQ-9 refers to symptoms experienced by patients during the 2 weeks prior to answering the questionnaire. As a severity measure, the PHQ-9 scores range from 0 to 27. A PHQ-9 score of 0–4 suggests none to minimal depression, 5–9 indicates mild depression, 10–14 indicates moderate depression, 15–19 indicates moderately severe depression, and 20–27 indicates severe depression. The Malay version of the PHQ-9 had been locally validated, with acceptable psychometric properties.[29] The reported sensitivity was 87% (95% confidence interval [CI] 71–95), the specificity was 82% (CI 74–88), the positive likelihood ratio was 4.8 (CI 3.2–7.2), and the negative likelihood ratio was 0.16 (CI 0.06–0.40).[29]

Medication adherence

The 8-item Morisky Medication Adherence Scale (MMAS-8) was used to measure MA. The MMAS-8 is reliable (Cronbach's α=0.83), with a sensitivity of 93% and a specificity of 53%,[30] and the Malay version of the MMAS-8 has been locally validated, showing a significant relationship between MMAS-8 categories and HbA_{1c} categories (χ^2=20.261; $P\leq$0.001).[31] The MMAS-8 enquires about patient's experiences with medications during the 2 weeks prior to answering the questionnaire. The total scale has a range of 0–8, including low adherence (<6), medium adherence (6–7), and high adherence (8).

Health-related quality of life

The World Health Organization Quality of Life-Brief (WHOQOL-BREF) produces four HRQoL domains and scores,[32] ie, a physical domain, a psychological domain, a social relationships domain, and an environment domain.[32] There are two items that examine overall HRQoL separately: question 1 asks about an individual's overall perception of quality of life and question 2 asks about an individual's overall perception of his or her health. Higher scores denote higher quality of life. We arbitrarily categorized this variable into three using a 0–100 score, ie, 0–49.99 (low), 50.01–74.99 (medium), or 75–100 (high, Figure 1).

Statistical analysis

The sample size was calculated using G*Power 3.1.2 software.[33] Using an estimated relationship effect of r=0.16 between DRD and HbA_{1c},[10,34] a power of 0.95, and significance at 0.05, the estimated sample size was 500. Taking into consideration 30% of incomplete/missing data in the patient medical record and incomplete questionnaires returned from patients, the sample size needed to be increased to 650.

The data analyses were done using PASW version 21.0 (SPSS, Chicago, IL, USA). Descriptive analyses were conducted to characterize the sample, and distributions were visually and quantitatively examined for normality of distribution.

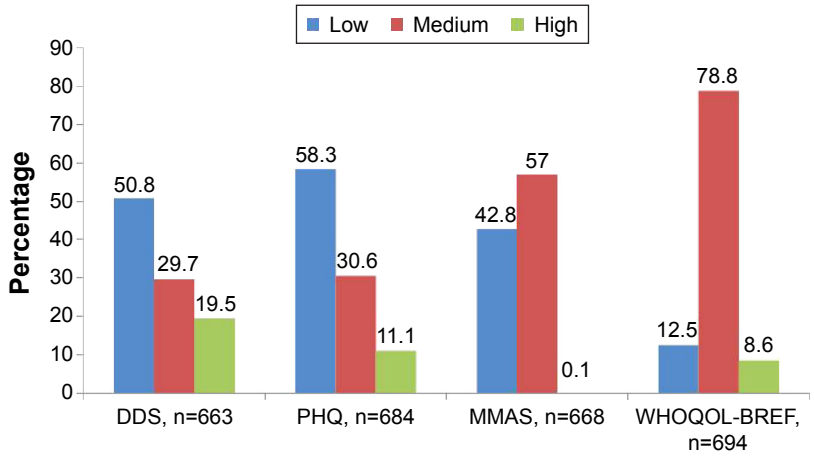

Figure 1 Proportion of patients according to the categories of diabetes-related distress, depressive symptoms, medication adherence, and health-related quality of life.
Abbreviations: DDS, Diabetes Distress Scale 17 items (low, no distress, mean DDS score <2; medium, moderate distress, mean DDS score 2–2.9; high, distress worthy of clinical attention, mean DDS score ≥3); PHQ, Patient Health Questionnaire 9 items (depression severity: low, no depression; PHQ score 0–4; medium, mild depression, PHQ score 5–9; high, moderate to severe depression, PHQ score 10–27); MMAS, Morisky Medication Adherence Scale 8 items (low, low adherence, MMAS score <6; medium, medium adherence, MMAS score 6–7; high, high adherence, MMAS score 8); WHOQOL-BREF, World Health Organization Quality of Life-Brief (low, 0–49.99; medium, 50.01–74.99; high, 7–100. WHOQOL-BREF categories are arbitrarily set).

Table 1 Sociodemographic characteristic according to the health clinics

		Total	HbA_{1c} (%)		CBG (mmol/L)		SBP (mmHg)	
			Mean (SD)	*P*	Mean (SD)	*P*	Mean (SD)	*P*
			8.5 (2.1)		**9.4 (3.7)**		**136.9 (17.7)**	
Gender	Female	368	8.4 (2.0)	0.253	9.4 (3.6)	0.638	137.0 (17.6)	0.902
	Male	329	8.6 (2.3)		9.5 (3.8)		136.8 (17.8)	
Ethnicity	Malay	367	8.4 (2.2)	0.138	9.5 (3.9)	0.753	138.6 (17.9)	**0.020**
	Chinese	162	8.3 (1.8)		9.3 (3.2)		136.1 (16.0)	
	Indian	165	8.8 (2.2)		9.6 (3.7)		134.2 (18.5)	
	Aborigine	3	7.8 (1.6)		8.3 (1.8)		125.7 (7.4)	
	Others	3	7.1 (0.9)		5.5 (1.1)		130.7 (13.3)	
Religion	No religion	33	8.7 (1.8)	0.494	8.6 (3.2)	0.457	133.0 (14.6)	0.053
	Moslem	375	8.4 (2.2)		9.5 (3.9)		138.6 (17.9)	
	Buddhist	82	8.3 (2.0)		9.9 (3.5)		137.0 (16.4)	
	Hindu/Sikh	149	8.7 (2.7)		9.4 (3.6)		133.6 (18.5)	
	Christian/ Catholic	22	8.8 (2.7)		9.1 (3.2)		134.5 (14.7)	
	Others	37	8.1 (1.7)		8.7 (2.6)		136.5 (16.3)	
Religiosity	Very agree	294	8.6 (2.2)	0.586	9.5 (3.5)	0.334	137.5 (18.5)	0.744
	Agree	301	8.3 (2.2)		9.5 (3.9)		137.1 (17.6)	
	Not sure	25	8.6 (1.5)		10.0 (3.0)		133.4 (16.0)	
	Disagree	73	8.4 (1.8)		8.6 (3.2)		135.4 (15.6)	
	Very disagree	3	9.5 (0.9)		9.6 (2.0)		133.0 (2.6)	
Marital status	Married	548	8.6 (2.2)	0.067	9.5 (3.7)	0.123	136.8 (17.7)	0.942
	Living with a partner	3	8.1 (2.7)		11.0 (4.3)		128.3 (14.6)	
	Divorced	13	8.9 (2.5)		8.6 (3.1)		138.2 (16.0)	
	Widowed	98	8.0 (1.9)		9.1 (3.6)		138.0 (18.8)	
	Separated	8	10.2 (2.4)		11.2 (3.0)		135.5 (23.1)	
	Single	26	7.9 (1.6)		7.9 (2.6)		137.3 (15.1)	
Educational level	Primary	259	8.4 (2.2)	0.807	9.4 (3.4)	0.870	137.2 (19.6)	0.673
	Secondary	310	8.6 (2.2)		9.5 (4.0)		136.2 (16.9)	
	Tertiary	75	8.5 (1.8)		9.3 (3.3)		136.8 (15.8)	
	Others	45	8.5 (2.0)		9.8 (3.9)		139.5 (14.9)	

Since all the independent variables included were based on past studies, we further selected potential demographic and medical confounders from the univariable analyses. The dependent variables were HbA_{1c}, CBG, systolic BP, diastolic BP, LDL-C, HDL-C, triglycerides, and total cholesterol. The associations of these disease control variables were analyzed using multivariable regression analyses, with potential confounders included in the model and using the criterion of two-tailed $P<0.05$. Missing data were not imputed because the available data and sample size were deemed adequately powered as evidence by the normal distributions of all the dependent variables as well as the main independent variables (DRD, DS, MA, and HRQoL). As the DDS-17 and PHQ-9 scores were moderately correlated ($r=0.51$, $P<0.0001$), they were evaluated both alone and when the other was adjusted for, because their multicollinearity could distort their individual regression coefficients. Outliers were checked with std (standardized) residual, making sure that the minimum and maximum values did not exceed ±3. There were fewer than five outliers identified in the analyses, and as all the outliers were validated, we included all of them in the analyses. All statistical assumptions were checked and confirmed within acceptable limits.

Results

The participants' response rate was 93.1% (700/752). The majority were females (52.8%), Malay (52.9%), married or living with partners (79.2%), had non-tertiary education (89.1%), and were earning <RM 3,000 per month (94.5%); most of the patients had some exercise and were non-smokers (Table 1). About 80% were reported to have hypertension, but use of antihypertensives was almost 90%. A similar observation was noted for dyslipidemia, with almost doubled percentage use of lipid-lowering agents compared to the prevalence of dyslipidemia (Table 1). Use

DBP (mmHg)		LDL-C		HDL-C		TG		Total-C	
Mean (SD)	***P***	**Mean (SD)**	***P***	**Mean (SD)**	***P***	**Mean (SD)**	***P***	**Mean (SD)**	***P***
79.2 (12.2)		**3.0 (1.0)**		**1.0 (0.3)**		**1.9 (1.3)**		**4.8 (1.2)**	
78.8 (12.0)	0.381	3.0 (1.0)	0.084	1.0 (0.3)	**<0.0001**	1.8 (1.0)	**0.003**	4.9 (1.1)	0.119
79.6 (12.3)		2.9 (1.0)		0.9 (0.3)		2.1 (1.6)		4.7 (1.2)	
81.0 (12.8)	**<0.0001**	3.1 (1.0)	0.136	0.9 (0.3)	**<0.0001**	2.0 (1.3)	0.214	4.9 (1.2)	0.587
75.6 (11.5)		2.9 (0.9)		1.1 (0.4)		1.8 (0.9)		4.8 (1.0)	
78.5 (10.6)		2.9 (1.0)		0.9 (0.3)		2.0 (1.5)		4.8 (1.1)	
77.7 (2.1)		1.6 (0.5)		0.7 (0.2)		2.0 (1.0)		3.2 (0.5)	
77.0 (14.1)		2.3 (0.6)		0.9 (0.2)		1.4 (0.5)		3.8 (0.6)	
73.5 (9.2)	**<0.0001**	2.8 (0.8)	0.147	1.2 (0.4)	**<0.0001**	1.6 (0.7)	0.066	4.7 (0.8)	0.223
80.9 (12.9)		3.1 (1.0)		0.9 (0.3)		2.0 (1.3)		4.9 (1.2)	
76.4 (12.1)		3.0 (1.0)		1.1 (0.5)		1.9 (1.1)		5.0 (1.0)	
78.1 (10.2)		3.0 (1.1)		0.9 (0.2)		2.1 (1.5)		4.8 (1.2)	
80.0 (13.2)		2.5 (0.6)		1.0 (0.3)		1.3 (0.6)		4.3 (0.7)	
75.2 (10.4)		2.7 (1.0)		1.1 (0.3)		1.7 (0.7)		4.6 (1.1)	
80.4 (12.9)	0.065	3.1 (1.1)	0.404	1.0 (0.3)	**<0.0001**	2.0 (1.5)	0.272	4.9 (1.3)	0.542
78.7 (10.9)		2.9 (0.9)		0.9 (0.3)		2.0 (1.2)		4.7 (1.0)	
78.0 (11.3)		2.8 (0.9)		1.0 (0.3)		2.1 (1.2)		4.9 (1.0)	
75.9 (14.0)		3.0 (0.9)		1.2 (0.4)		1.6 (0.6)		4.9 (1.0)	
80.0 (6.1)		2.9 (1.7)		1.0 (0.2)		2.0 (1.1)		4.8 (1.4)	
79.9 (12.1)	**0.024**	3.0 (1.0)	0.642	1.0 (0.3)	**0.039**	2.0 (1.3)	0.216	4.8 (1.2)	0.152
73.7 (6.7)		2.5 (0.2)		1.0 (0.1)		1.3 (0.8)		4.9 (1.3)	
77.8 (9.5)		3.2 (1.3)		1.1 (90.3)		2.7 (2.4)		5.7 (1.7)	
75.3 (12.3)		3.0 (0.9)		1.0 (0.4)		1.7 (0.9)		4.8 (1.0)	
79.8 (15.0)		3.0 (1.1)		1.0 (0.2)		2.2 (1.4)		5.0 (1.0)	
80.5 (12.2)		2.7 (0.8)		1.1 (0.6)		1.9 (1.3)		4.5 (0.8)	
77.3 (12.4)	**0.003**	2.9 (1.0)	0.466	1.0 (0.3)	**<0.0001**	1.8 (1.2)	0.206	4.7 (1.1)	0.181
80.2 (11.9)		3.0 (1.0)		1.0 (0.3)		2.0 (1.4)		4.9 (1.2)	
82.2 (11.7)		3.1 (1.0)		0.9 (0.20)		2.2 (1.5)		4.9 (1.3)	
77.1 (11.9)		2.9 (1.0)		1.2 (0.6)		1.9 (0.7)		4.9 (1.0)	

(*Continued*)

Table 1 (*Continued*)

		Total	HbA_{1c} (%)		CBG (mmol/L)		SBP (mmHg)	
			Mean (SD)	*P*	Mean (SD)	*P*	Mean (SD)	*P*
			8.5 (2.1)		**9.4 (3.7)**		**136.9 (17.7)**	
Employment status	Employed	315	8.7 (2.3)	0.166	9.4 (3.7)	0.632	135.3 (17.8)	0.054
	Unemployed	11	8.7 (1.3)		9.7 (3.3)		130.5 (21.2)	
	Retired	172	8.3 (1.9)		9.7 (3.7)		137.5 (18.4)	
	Home manager	199	8.3 (2.1)		9.2 (3.6)		139.3 (16.5)	
Income (RM)	No income	157	8.3 (2.1)	0.703	9.2 (3.2)	0.742	138.0 (17.9)	0.405
	<1,000	170	8.5 (2.1)		9.5 (4.0)		138.2 (919.4)	
	1,000–2,999	235	8.5 (2.3)		9.3 (3.5)		135.3 (17.1)	
	3,000–4,999	87	8.7 (2.1)		9.9 (3.8)		135.5 (14.6)	
	≥5,000	38	8.3 (1.6)		9.6 (3.3)		136.8 (15.5)	
Exercise	No	295	8.6 (2.2)	0.443	9.5 (3.9)	0.481	137.7 (17.8)	0.309
	≤3 times/week	232	8.4 (2.2)		9.6 (3.6)		137.2 (17.5)	
	>3 times/week	169	8.3 (2.0)		9.1 (3.4)		135.1 (17.8)	
Smoking	Never	532	8.4 (2.1)	0.177	9.4 (3.5)	0.983	137.0 (917.6)	0.808
	Stopped ≤5 years	22	9.1 (2.8)		9.3 (5.6)		139.8 (23.2)	
	Stopped >5 years	60	8.1 (2.3)		9.5 (4.0)		136.1 (15.7)	
	Yes	83	8.7 (2.0)		9.6 (3.7)		135.9 (18.0)	
Alcohol consumption	Never	607	8.5 (2.2)	0.359	9.5 (3.7)	0.692	137.0 (17.9)	0.615
	Yes	45	8.4 (1.8)		9.3 (3.7)		134.5 (17.8)	
	Stopped drinking	46	8.0 (1.8)		9.0 (3.5)		137.8 (15.1)	
Hypertension	No	149	8.9 (2.1)	**0.024**	10.1 (4.6)	**0.014**	130.3 (15.4)	**<0.0001**
	Yes	539	8.4 (2.1)		9.3 (3.3)		138.9 (17.8)	
Dyslipidemia	No	408	8.4 (2.1)	0.465	9.6 (3.9)	0.199	139.3 (18.4)	**<0.0001**
	Yes	265	8.6 (2.2)		9.2 (3.2)		133.5 (16.0)	
Stroke/TIA	No	681	8.5 (2.1)	0.288	9.4 (3.7)	0.790	136.8 (17.7)	0.239
	Yes	14	7.8 (2.0)		9.2 (3.0)		142.4 (16.1)	
Ischemic heart disease	No	662	8.5 (2.2)	0.816	9.4 (3.6)	0.488	136.8 (17.8)	0.430
	Yes	31	8.4 (1.6)		9.9 (5.1)		139.3 (15.7)	
Retinopathy	No	680	8.4 (2.1)	**0.013**	9.4 (3.7)	0.858	136.9 (17.8)	0.986
	Yes	19	9.7 (2.2)		9.6 (3.5)		136.8 (14.5)	
Nephropathy	No	670	8.5 (2.2)	0.350	9.4 (3.7)	0.689	136.8 (17.7)	0.807
	Yes	23	8.9 (1.7)		9.7 (3.5)		137.7 (17.3)	
Diabetic foot problems	No	672	8.5 (2.1)	0.994	9.5 (3.7)	0.065	137.1 (17.7)	0.071
	Yes	22	8.5 (2.0)		8.0 (3.1)		130.2 (15.3)	
OHA	No	61	9.0 (2.5)	**0.041**	10.1 (4.3)	0.128	144.1 (20.2)	**0.001**
	Yes	634	8.4 (2.1)		9.4 (3.6)		136.2 (17.3)	
Insulin	Nil	423	7.7 (1.7)	**<0.0001**	8.6 (3.0)	**<0.0001**	136.1 (16.9)	0.075
	1 type	191	9.6 (2.1)		10.5 (3.4)		136.6 (19.0)	
	2 types	69	10.2 (2.3)		11.7 (5.5)		141.1 (18.5)	
	≥3 types	11	8.8 (1.7)		10.8 (5.6)		144.8 (10.6)	
Number of AHA agents	Nil	82	8.7 (2.1)	0.530	10.1 (4.6)	**0.038**	125.7 (14.0)	**<0.0001**
	1 type	206	8.6 (2.1)		9.3 (3.5)		132.8 (14.5)	
	2 types	204	8.3 (2.1)		8.9 (93.3)		137.3 (16.4)	
	3 types	144	8.3 (2.3)		9.8 (3.5)		143.8 (18.5)	
	≥4 types	58	8.5 (2.0)		9.9 (4.0)		148.2 (21.5)	
Number of LLA agents	Nil	156	8.5 (2.1)	0.773	9.7 (4.1)	0.417	137.4 (17.8)	0.125
	1 type	534	8.5 (2.1)		9.3 (3.5)		136.6 (17.6)	
	2 types	4	9.3 (1.0)		11.2 (93.9)		154.3 (15.5)	
Number of APA agents	Nil	616	8.4 (2.1)	0.656	9.5 (93.7)	0.686	137.1 (17.8)	0.644
	1 type	74	8.7 (2.3)		9.2 (93.6)		135.1 (16.6)	
	2 types	2	8.0 (0.6)		7.9 (3.2)		140.5 (20.5)	

Note: *P*-values were for the independent *t*-test and analysis of variance. The bold *P*-values signify those that were below the significant cut-off value of <0.05.

Abbreviations: CBG, casual blood glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; OHA, oral hypoglycemic agent; AHA, antihypertensive agent; LLA, lipid-lowering agent; APA, antiplatelet agent; SD, standard deviation; TG, triglycerides; TIA, transient ischemic attack.

DBP (mmHg)		LDL-C		HDL-C		TG		Total-C	
Mean (SD)	***P***	**Mean (SD)**	***P***	**Mean (SD)**	***P***	**Mean (SD)**	***P***	**Mean (SD)**	***P***
79.2 (12.2)		**3.0 (1.0)**		**1.0 (0.3)**		**1.9 (1.3)**		**4.8 (1.2)**	
80.7 (12.9)	**0.004**	3.0 (1.1)	0.254	0.9 (90.3)	**0.007**	2.1 (1.5)	**0.050**	4.9 (1.3)	0.600
81.5 (15.1)		3.2 (0.6)		0.8 (0.1)		2.3 (1.3)		5.0 (0.8)	
76.6 (10.6)		2.8 (1.0)		1.0 (0.4)		2.0 (1.2)		4.7 (1.1)	
78.7 (11.8)		3.0 (1.0)		1.0 (0.3)		1.7 (0.9)		4.8 (1.1)	
75.3 (11.3)	<**0.0001**	2.8 (0.9)	0.228	1.0 (0.4)	0.115	1.8 (1.0)	0.412	4.7 (1.1)	0.254
79.4 (12.3)		3.0 (1.0)		1.0 (0.3)		2.0 (1.5)		4.8 (1.2)	
80.2 (12.8)		3.0 (1.0)		0.9 (0.2)		2.0 (1.4)		4.9 (1.3)	
82.4 (10.4)		3.1 (1.1)		1.0 (0.3)		2.0 (1.3)		4.9 (1.2)	
79.6 (11.8)		3.0 (0.8)		1.0 (0.3)		1.6 (0.5)		4.7 (0.8)	
79.9 (12.2)	<**0.0001**	2.9 (1.0)	0.071	0.9 (0.3)	0.080	2.0 (1.3)	0.325	4.8 (1.1)	**0.046**
80.4 (11.8)		3.1 (1.0)		1.0 (0.3)		2.0 (1.4)		5.0 (1.2)	
75.8 (12.1)		2.9 (1.0)		1.0 (0.4)		1.8 (1.0)		4.7 (1.2)	
79.3 (11.9)	0.804	3.0 (1.0)	0.109	1.0 (0.3)	0.163	1.9 (1.3)	0.393	4.9 (1.1)	0.375
80.5 (13.2)		2.7 (0.8)		1.0 (0.4)		2.3 (2.7)		5.0 (1.6)	
77.9 (12.2)		2.7 (1.2)		0.9 (0.2)		2.1 (1.3)		4.6 (1.4)	
79.0 (13.7)		2.9 (1.0)		1.0 (0.4)		2.1 (1.0)		4.8 (1.1)	
79.1 (12.0)	0.844	3.0 (1.0)	0.358	1.0 (0.3)	0.106	1.9 (1.3)	0.296	4.8 (1.2)	0.105
78.7 (13.5)		3.0 (1.1)		1.1 (0.5)		2.2 (1.4)		5.0 (1.1)	
80.1 (13.9)		2.7 (0.9)		0.9 (0.2)		1.8 (0.8)		4.5 (0.9)	
79.2 (13.2)	0.932	3.1 (0.9)	0.112	0.9 (0.3)	0.051	1.8 (1.3)	0.193	4.9 (1.2)	0.383
79.2 (11.8)		2.9 (1.0)		1.0 (0.3)		2.0 (1.3)		4.8 (1.2)	
81.6 (12.6)	<**0.0001**	3.0 (0.9)	0.277	0.9 (0.3)	<**0.0001**	2.0 (1.4)	0.544	4.8 (1.2)	0.929
75.6 (10.5)		2.9 (1.1)		1.0 (0.3)		1.9 (1.2)		4.8 (1.2)	
79.2 (12.2)	0.974	3.0 (1.0)	0.363	1.0 (0.3)	0.386	1.9 (1.3)	0.886	4.8 (1.2)	0.699
79.1 (11.9)		2.6 (1.2)		0.9 (0.1)		2.0 (0.8)		4.7 (1.3)	
79.3 (12.2)	0.202	3.0 (1.0)	**0.048**	1.0 (0.3)	0.509	1.9 (1.3)	0.784	4.8 (1.2)	**0.042**
76.5 (11.4)		2.6 (90.9)		0.9 (0.5)		2.0 (0.7)		4.4 (1.1)	
79.3 (12.2)	0.136	3.0 (1.0)	0.191	1.0 (0.3)	**0.015**	1.9 (1.3)	0.589	4.8 (1.2)	0.459
75.1 (10.5)		2.7 (1.1)		1.2 (0.8)		1.8 (0.9)		4.6 (1.2)	
79.2 (12.2)	0.655	3.0 (1.0)	0.404	1.0 (0.3)	0.566	1.9 (1.3)	0.997	4.8 (1.2)	0.569
78.0 (9.6)		2.8 (1.1)		1.0 (0.7)		1.9 (1.2)		4.7 (1.1)	
79.4 (12.3)	**0.019**	3.0 (1.0)	0.146	1.0 (0.3)	**0.047**	1.9 (1.2)	0.148	4.8 (1.2)	0.107
73.2 (7.3)		2.6 (0.9)		0.8 (0.1)		2.4 (2.2)		4.4 (1.1)	
78.2 (11.4)	0.504	3.2 (1.2)	0.064	0.9 (0.2)	0.257	2.3 (1.4)	**0.040**	5.2 (1.3)	**0.009**
79.3 (12.3)		2.9 (1.0)		1.0 (0.3)		1.9 (1.3)		4.8 (1.2)	
80.1 (12.6)	<**0.0001**	3.0 (0.9)	**0.015**	1.0 (0.3)	0.433	1.7 (0.9)	<**0.0001**	4.7 (1.0)	**0.004**
77.1 (10.6)		2.9 (1.1)		1.0 (0.4)		2.3 (1.6)		4.9 (1.3)	
77.6 (12.6)		3.3 (1.0)		0.9 (0.2)		2.3 (2.0)		5.3 (1.4)	
90.8 (10.1)		3.5 (1.3)		0.8 (0.2)		1.9 (0.8)		5.1 (1.5)	
78.0 (14.5)	0.192	3.2 (1.0)	0.209	1.0 (0.3)	0.154	1.7 (1.4)	0.057	4.9 (1.1)	0.630
77.8 (10.6)		3.0 (1.0)		1.0 (0.3)		1.8 (1.0)		4.8 (1.1)	
79.7 (11.7)		2.9 (1.0)		1.0 (0.3)		1.9 (91.1)		4.7 (1.1)	
80.6 (12.8)		2.9 (1.0)		1.0 (0.4)		2.2 (1.7)		4.9 (1.3)	
80.2 (13.4)		3.1 (1.1)		0.9 (0.2)		2.1 (91.3)		4.9 (1.1)	
81.2 (13.8)	0.051	3.1 (0.8)	0.111	1.0 (0.3)	0.608	1.7 (0.8)	**0.035**	4.8 (0.9)	0.981
78.6 (11.7)		2.9 (1.0)		1.0 (90.3)		2.0 (1.4)		4.8 (1.2)	
76.3 (7.9)		2.3 (0.7)		0.8 (0.4)		2.1 (1.3)		4.9 (1.8)	
79.8 (12.2)	<**0.0001**	3.0 (1.0)	0.900	1.0 (0.3)	0.560	1.9 (1.3)	0.866	4.9 (1.2)	0.291
74.1 (10.7)		2.7 (0.9)		1.0 (0.3)		2.0 (1.4)		4.6 (1.2)	
69.0 (1.4)		2.6 (0.5)		0.8 (0.1)		2.0 (0.9)		4.4 (0.8)	

of antiplatelet agents corresponded to the prevalence of complications. Table 1 shows the sociodemographic characteristics of the patients according to biomarkers of disease. Table 2 shows the differences in clinical parameters and mean scores for the DDS-17, PHQ-9, WHOQOL-BREF, and MMAS-8 in the three health clinics. Figure 1 shows the proportion of patients according to the categories of DDS-17, PHQ-9, MMAS-8, and WHOQOL-BREF. DRD and DS showed a descending pattern of distribution, with most patients reported to have mild symptoms. With regard to MA, almost all patients reported low to medium adherence with their medication. In terms of HRQoL, the majority of patients experienced a medium level of quality of life (Figure 1).

In Pearson correlation analysis, the DDS-17 score correlated with systolic BP (r= −0.157, P<0.001), diastolic BP (r= −0.083, P<0.05), and HDL-C (r=0.105, P<0.05). The PD subscale score showed a significant correlation with triglycerides (r= −0.095, P<0.05) whereas the total DDS-17 score did not show any correlation. The PHQ-9 score correlated with CBG (r=0.087, P<0.05), LDL-C (r=0.115, P<0.001), HDL-C (r=0.118, P<0.001), and total cholesterol (r=0.134, P<0.001). The MMAS-8 score correlated with HbA_{1c} (r= −0.136, P<0.001), CBG (r= −0.088, P<0.05), diastolic BP (r= −0.130, P<0.001), LDL-C (r= −0.105, P<0.05), and total cholesterol (r= −0.136, P<0.001). Total WHOQOL-BREF score correlated with CBG (r= −0.111, P<0.001), HDL-C (r= −0.125, P<0.001), and total cholesterol (r= −0.084, P<0.05). Patient age showed a significant correlation with all disease control biomarkers except for CBG (Pearson r values ranged from −0.279 to 0.133). Diabetes duration (in years) correlated with HbA_{1c} (r=0.212, P<0.001), CBG (r=0.109, P<0.001), diastolic BP (r= −0.196, P<0.001), LDL-C (r= −0.106, P<0.05), and HDL-C (r=0.138, P<0.001).

Table 3 shows the adjusted effects of DDS-17 (and PD), PHQ-9, WHOQOL-BREF, and MMAS-8 on disease biomarkers. WHOQOL-BREF had significant effect on CBG (adjusted B= −0.06, P=0.024). Other associations that had near significant effects included MMAS-8 on HbA_{1c}, DDS-17 on systolic BP, PHQ-9 on LDL-C, PD on triglycerides, and WHOQOL-BREF and MMAS-8 on total cholesterol.

Table 2 Clinical variables according to the health clinics

	Health clinic, mean (SD) [valid n]				*F*	*P*-value
	Total	**Seri Kembangan**	**Dengkil**	**Salak**		
Age (years)	56.9 (10.18) [698]	58.8 (10.21) [222]	57.7 (11.08) [123]	55.5 (9.64) [353]	7.81	<0.0001
Diabetes duration (years)	6.5 (5.71) [677]	9.1 (7.05) [220]	6.3 (4.34) [123]	4.9 (4.43) [334]	39.94	<0.0001
HPT duration (years)	6.8 (5.80) [515]	8.4 (6.25) [171]	7.0 (4.59) [108]	5.6 (5.67) [236]	12.60	<0.0001
Dyslipidemia duration (years)	4.2 (3.01) [250]	4.9 (3.33) [124]	3.4 (2.28) [113]	5.1 (3.68) [13]	8.87	<0.0001
HbA_{1c} (%)	8.5 (2.14) [621]	8.5 (2.05) [190]	8.6 (2.21) [121]	8.4 (2.16) [310]	0.13	0.878
CBG (mmol/L)	9.4 (3.66) [687]	9.1 (3.12) [219]	9.3 (3.37) [123]	9.7 (4.05) [345]	2.00	0.137
SBP (mmHg)	136.9 (17.7) [695]	134.5 (15.1) [219]	131.1 (17.0) [123]	140.5 (18.6) [353]	16.71	<0.0001
DBP (mmHg)	79.2 (12.2) [695]	76.6 (11.0) [219]	76.4 (9.3) [123]	81.7 (13.2) [353]	16.57	<0.0001
LDL-C (mmol/L)	3.0 (1.00) [566]	3.0 (1.04) [201]	2.8 (1.11) [121]	3.0 (0.90) [244]	1.70	0.184
HDL-C in mmol/L	1.0 (0.32) [569]	1.2 (0.32) [202]	0.9 (0.32) [122]	0.9 (0.26) [245]	59.24	<0.0001
Triglycerides (mmol/L)	1.9 (1.39) [569]	1.8 (1.07) [201]	2.0 (1.01) [123]	2.0 (1.54) [245]	2.53	0.081
Total cholesterol (mmol/L)	4.8 (1.17) [619]	5.0 (1.09) [203]	4.7 (1.21) [123]	4.8 (1.20) [293]	2.51	0.082
DDS-17	37.1 (15.98) [663]	40.6 (17.34) [206]	40.3 (18.46) [118]	33.8 (13.35) [339]	14.93	<0.0001
Emotional burden	11.9 (5.33) [685]	11.9 (5.65) [219]	12.6 (6.03) [120]	11.6 (4.84) [346]	1.30	0.274
Physician distress	7.9 (4.67) [683]	9.6 (5.67) [216]	9.1 (4.68) [121]	6.4 (3.29) [346]	40.49	<0.0001
Regimen distress	11.3 (5.20) [690]	12.0 (5.36) [218]	12.2 (6.06) [121]	10.6 (4.65) [351]	7.88	<0.0001
Interpersonal distress	6.3 (3.65) [689]	7.2 (4.40) [217]	7.0 (3.95) [121]	5.6 (2.77) [351]	16.15	<0.0001
PHQ-9	4.6 (4.31) [684]	5.5 (4.91) [218]	4.2 (4.01) [121]	4.2 (3.90) [345]	7.69	<0.0001
MMAS-8	5.6 (1.42) [668]	5.6 (1.45) [216]	5.8 (1.31) [121]	5.6 (1.45) [331]	0.76	0.469
WHOQOL-BREF	55.5 (6.31) [694]	54.9 (6.66) [218]	55.0 (6.11) [123]	56.0 (6.12) [353]	2.70	0.068
Physical health	13.1 (1.70) [700]	12.8 (1.80) [224]	13.1 (1.65) [123]	13.3 (1.64) [353]	5.22	0.006
Psychological health	13.3 (1.88) [697]	13.0 (1.91) [221]	12.7 (2.03) [123]	13.6 (1.73) [353]	12.94	<0.0001
Social relationship	14.7 (2.40) [698]	14.7 (2.50) [222]	15.3 (2.45) [123]	14.5 (2.29) [353]	5.82	0.003
Environmental	14.4 (2.08) [697]	14.3 (2.47) [221]	13.9 (1.89) [123]	14.7 (1.83) [353]	8.19	<0.0001

Note: *P*-values are for the analysis of variance.

Abbreviations: DDS-17, Diabetes Distress Scale 17 items; PHQ-9, Patient Health Questionnaire 9 items; MMAS-8, 8-item Morisky Medication Adherence Scale; WHOQOL-BREF, World Health Organization Quality of Life-Brief 26 items; CBG, casual blood glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HPT, hypertension; SD, standard deviation; HbA_{1c}, glycated hemoglobin.

Table 3 Determinants of disease biomarkers

Model	Crude B (95.0% CI)	Adjusted B (95.0% CI)	Adjusted B (95.0% CI)	Significance	Adjusted R^2
HbA_{1c}		**n=441***	**n=441****		
Intercept	–	–	9.77 (8.488, 11.053)	<0.0001	0.308
MMAS-8	–0.21 (–0.329, –0.085)	–0.10 (–0.224, 0.018)	–0.11 (–0.224, 0.014)	0.082	
CBG		**n=613†**	**n=613††**		
Intercept	–	–	14.83 (11.526, 18.128)	<0.0001	0.110
PHQ-9	0.07 (0.010, 0.139)	0.01 (–0.067, 0.077)	0.01 (–0.068, 0.077)	0.900	
MMAS-8	–0.22 (–0.419, –0.029)	–0.11 (–0.311, 0.085)	–0.10 (–0.295, 0.100)	0.332	
WHOQoL-BREF	–0.06 (–0.107, –0.021)	–0.05 (–0.103, –0.005)	–0.06 (–0.105, –0.007)	0.024	
SBP		**n=623‡**	**n=623‡‡**		
Intercept	–	–	146.97 (136.544, 157.397)	<0.0001	0.166
DDS-17	–0.17 (–0.255, –0.089)	–0.09 (–0.174, –0.008)	–0.08 (–0.161, 0.005)	0.066	
LDL-C		**n=401§**	**n=401§§**		
Intercept	–	–	3.87 (3.018, 4.719)	<0.0001	0.052
PHQ-9	0.03 (0.007, 0.044)	0.02 (0.000, 0.044)	0.02 (–0.001, 0.043)	0.061	
MMAS-8	–0.07 (–0.133, –0.015)	–0.04 (–0.110, 0.030)	–0.03 (–0.103, 0.037)	0.356	
Triglycerides		**n=551‖**	**n=551‖‖**		
Intercept	–	–	2.74 (1.809, 3.660)	<0.0001	0.073
Physician distress	–0.03 (–0.049, –0.003)	–0.02 (–0.046, –0.001)	–0.02 (–0.046, 0.002)	0.072	
Total cholesterol		**n=569¶**	**n=569¶¶**		
Intercept	–	–	7.06 (5.816, 8.311)	<0.0001	0.082
PHQ-9	0.04 (0.014, 0.056)	0.02 (–0.006, 0.043)	0.01 (–0.011, 0.039)	0.265	
MMAS-8	–0.11 (–0.177, –0.046)	–0.07 (–0.139, 0.001)	–0.06 (–0.131, 0.009)	0.086	
WHOQoL-BREF	–0.02 (–0.030, –0.001)	–0.02 (–0.033, 0.001)	–0.02 (–0.032, 0.001)	0.070	

Notes: Variables in the model include: *age, diabetes duration, HPT duration, retinopathy, OHA, insulin; †diabetes duration, HPT, insulin, AHA agents; ‡age, ethnic, HPT, dyslipidemia, OHA, AHA agents §age, diabetes duration, HPT duration, ischemic heart disease, insulin; ‖age, gender, employment, OHA, insulin, LLA; ¶age, OHA, insulin, exercise, ischemic heart disease; **, ††, ‡‡, §§, ‖‖ and ¶¶In these models, health clinic is added.

Abbreviations: DDS-17, 17-item Diabetes Distress Scale; PHQ-9, 9-item Patient Health Questionnaire; MMAS-8, 8-item Morisky Medication Adherence Scale; WHOQoL-BREF, World Health Organization Quality of Life-Brief 26 items; HPT, hypertension; OHA, oral hypoglycemic agent; AHA, antihypertensive agent; LLA, lipid-lowering agent; APA, anti-platelet agent; CI, confidence interval; HbA_{1c}, glycated hemoglobin.

Discussion

This study examined the associations of DRD, DS, HRQoL, and MA with glycemia, BP, and lipid biomarkers in adults with T2D. There have been very few studies that have investigated these four patient self-reported outcomes in adults with T2D and a multicultural Asian background or their associations with the three important disease status variables (HbA_{1c}, BP, and lipids) in a single setting.

Sociodemographic characteristics, including age, gender, and ethnicity and their associations with disease control were similar to those in previous reports.[35–37] In contrast with other cross-sectional data from India,[38] Japan,[39] and the USA,[10,13] we did not observe any association between DRD or DS and HbA_{1c}. Similarly, the associations of age, gender, ethnicity, diabetes duration, and medication use with glycemia, BP, and lipid control were not in parallel with earlier registry-based studies.[21,35–37,40] This could be due to small differences in subgroups of these variables in this study or expanded power in the registry-based studies due to their very large sample size. The lack of an association between DRD and glucose biomarkers might indicate the relatively small effects of DRD, which were further diluted after adjusting for other sociodemographic variables. It is possible that DRD was a psychological state of coping (similar to the effects of DDS-17 on systolic BP, and the PD subscale on triglycerides, see below) and not related to failure of self-management that could affect HbA_{1c}. Further studies are needed to look into the role of DRD in self-management of diabetes in patients with different sociocultural backgrounds, relationship to illness perception, coping, MA, and HRQoL.[41]

The most intriguing results in this study were the higher DRD and the lower systolic BP, higher PD, and lower triglycerides. This consistent trend of DRD with disease biomarkers was marked, with the PD subscale showing the highest (among the DDS-17, PHQ-9, and MMAS-8) and most consistent negative correlation with HbA_{1c}, systolic and diastolic BP, and triglycerides. A plausible explanation for these observations is that DRD might indicate a state of psychological reaction or active coping by patients, resulting in heightened self-management. It is not uncommon for doctors in health clinics to become impatient with patients who do not adhere to advice, talk less even when patients

ask for more explanation, and display indifference to patients during busy clinic days.[42,43] In these situations, health conscious and capable patients might become distressed, which in turn motivates themselves towards self-care. This indirect and apparent effect of DRD on systolic BP, which is a form of psychological distress related to diabetes management, needs further investigation. Earlier studies reported that DRD was associated with poor diabetes self-care,[44–46] and to our best knowledge, none of these studies had made a similar association between DRD and systolic BP. Further research is needed to confirm this hypothesis, and should include measures that assess self-care activity, self-efficacy, coping, and physician behaviors at the same time.

Compared with the DDS-17, which assesses diabetes-specific emotional distress, the PHQ-9 which measures DS and thus implies higher severity of an emotional distress,[7] had shown more associations with the disease biomarkers. The presence of stronger associations between the PHQ-9, LDL-C, and total cholesterol suggests that DS affects lipid control more than DRD. A similar finding was reported in the USA, ie, after multivariable analysis, DRD was associated only with HbA_{1c} and not with BP or LDL-C.[47] However, in a study from Lithuania, significant correlations were found between scores for emotional state (tension-anxiety, depression-dejection, and confusion-bewilderment) and lipid levels (total cholesterol, triglycerides, and low-density lipoprotein cholesterol) in patients with T2D, especially women.[48] It is less clear whether there is any physiological link between DRD or DS and lipid metabolism compared to that is known between these emotional distress with glucose and BP.[12,49] Hence, DRD or DS might influence disease control through changed self-care activity[50] and health behavior, such as dietary choices, physical exercise, and adherence with therapy.[51] It was possible that factors related to the local health clinics themselves, such as accessibility, comfort, health care system, attitudes of health care providers, and availability of drugs[52] could affect disease control, as shown by a further reduction in effect size (>10%) after controlling for the health clinic variable.

The results for MA and disease control was consistent with those of previous studies showing a prevalent association and positive effects of MA on disease control biomarkers.[53,54] Higher MA was consistently shown to be associated with HbA_{1c}, CBG, LDL-C, and total cholesterol. The direct and potent effects of medications on these biomarkers would be expected. However, loss of MA's effects after controlling for covariates would suggest that disease control is multifactorial.[54] Indirectly, the results of this study show that other outcome measures or confounders should also be considered for DRD and DS in achieving disease control, such as diabetes self-care activity, HRQoL, and diabetes-specific quality of life.[55,56] In other words, holistic diabetes care that considers both appropriate use of medications and supporting the psychological states/behaviors of patients would constitute effective diabetes care.

HRQoL as measured by WHOQOL-BREF was the only variable that had a significant effect on CBG after controlling for the other covariates. The other near significant effect of HRQoL was on total cholesterol. It is not unexpected that better HRQoL contributes to better glycemic and lipid control. Previous studies have reported a prevalent association of poor HRQoL with high HbA_{1c}, BP, and lipids.[57–59] In addition to the probable mechanisms mentioned above, it is possible that HRQoL itself could have salutogenic effects on disease control.[60] This means that patients with better HRQoL would be more capable in terms of self-management, emotional well-being, and social engagement. These attributes would further translate into better health literacy and adherence to therapy, and lead to better disease control. However, the selective effect of HRQoL on CBG is hard to explain in this study. We hypothesize that patients with higher HRQoL adopt selective self-management measures depending on their perceived needs. They might implement glucose control measures more strongly in days leading up to a medical visit at the health clinic but be less stringent at other times. This possibility is suggested by the negative correlation between WHOQOL-BREF score and other disease control biomarkers. However, the small effect sizes of these observations in spite of the relatively large sample size in this study casts doubt regarding the presence of any real or clinically significant relationship between HRQoL and disease control in relatively healthy adult patients with T2D attending these public health clinics.

Limitations and strengths

There are some limitations to this study. The strict inclusion criteria might have led to selection of a study population that was healthier, more adherent, and had better disease control, given that patients who do not turn up regularly for their appointments or have recent blood investigations might consist of those with poorer psychological well being and disease control. In addition, missing data could have been occurred in differential ways across the different category of outcomes, and as such, complete case analyses strategy as adopted in this study might affect the results and conclusions.

However, we believe these biases are minimal, given that the distributions (distributions) of DRD, DS, HRQoL, and MA were all normal, and the distributions of disease control biomarkers were also normally distributed, indicating inclusion of a spectrum of disease biomarkers in the study population. The DDS-17, used in this study to measure DRD, may have inadequacies similar to those found with many standardized measures of diabetes distress,[14] including lack of comprehensiveness with regard to assessment of sources of diabetes distress; for example, distress attributable to starting insulin, emergence of a new complication, or the accumulated demands and burdens of self-care. This problem might have constrained the scope of T2D's impacts on the patients.

The strength of this study includes its real-world setting, high response rate, and good sample size. A further strength is that the study population is representative of the wider T2D patient population in this country, which enables generalization of the current findings.[61]

Conclusion

This study has shown associations of DRD, DS, HRQoL, and MA with glycemia, BP, and lipid biomarkers in adults with T2D at the primary care level. DS, MA, and HRQoL showed the expected associations with many disease biomarkers, except between DRD and BP. Efforts to increase MA may improve disease control more effectively than psychological interventions for DRD and DS. Therefore, the effects of DRD, DS, and HRQoL on MA are worthy of further study. DRD and DS had different effects on disease control, and might need different professional support. Lastly, the possible beneficial and therapeutic effects of DRD on BP require further study to determine the possible mechanisms underpinning this relationship.

Acknowledgments

This study was funded by the Research University Grants Scheme 2 (RUGS/04-02-2105RU). The authors acknowledge the Sepang and Petaling district health offices and officers for their support of this study and the Director-General of Health for giving permission to publish this research. They also acknowledge the World Health Organization and Harith Khalid Al-Qazaz for use of WHOQOL-BREF and the MMAS-8 Malay version, respectively. We thank Rimke Vos of the Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, the Netherlands, for her input into the initial draft of this manuscript. They would like to record their appreciation of Firdaus Mukhtar, Nor-Kasmawati Jamaludin, and Fuziah Paimin for their input during the planning of the study and assistance with data collection. Finally, they thank the staff at all the clinics for facilitating the data collection.

Disclosure

The authors report no competing interests in this work. The study sponsor had no role in the design or conduct of the study, the writing of this report, or the decision to submit it for publication.

References

1. Stuckey HL, Mullan-Jensen CB, Reach G, et al. Personal accounts of the negative and adaptive psychosocial experiences of people with diabetes in the second Diabetes Attitudes, Wishes and Needs (DAWN2) Study. *Diabetes Care*. 2014;37:2466–2474.
2. Das-Munshi J, Stewart R, Ismail K, Bebbington PE, Jenkins R, Prince MJ. Diabetes, common mental disorders, and disability: findings from the UK National Psychiatric Morbidity Survey. *Psychosom Med.* 2007;69:543–550.
3. Fisher L, Skaff MM, Mullan JT, Arean P, Glasgow R, Masharani U. A longitudinal study of affective and anxiety disorders, depressive affect and diabetes distress in adults with type 2 diabetes. *Diabet Med*. 2008; 25:1096–1101.
4. Lee S, Chiu A, Tsang A, Chow CC, Chan WB. Treatment-related stresses and anxiety-depressive symptoms among Chinese outpatients with type 2 diabetes mellitus in Hong Kong. *Diabetes Res Clin Pract*. 2006;74:282–288.
5. West C, McDowell J. The distress experienced by people with type 2 diabetes. *Br J Community Nurs.* 2002;7:606–613.
6. Li C, Ford ES, Zhao G, Balluz LS, Berry JT, Mokdad AH. Undertreatment of mental health problems in adults with diagnosed diabetes and serious psychological distress: the behavioral risk factor surveillance system, 2007. *Diabetes Care.* 2010;33:1061–1064.
7. Fisher L, Gonzalez JS, Polonsky WH. The confusing tale of depression and distress in patients with diabetes: a call for greater clarity and precision. *Diabet Med*. 2014;31:764–772.
8. Polonsky WH, Fisher L, Earles J, et al. Assessing psychosocial distress in diabetes: development of the Diabetes Distress Scale. *Diabetes Care*. 2005;28:626–631.
9. Fisher L, Skaff MM, Mullan JT, et al. Clinical depression versus distress among patients with type 2 diabetes: not just a question of semantics. *Diabetes Care*. 2007;30:542–548.
10. Fisher L, Mullan JT, Arean P, Glasgow RE, Hessler D, Masharani U. Diabetes distress but not clinical depression or depressive symptoms is associated with glycemic control in both cross-sectional and longitudinal analyses. *Diabetes Care*. 2010;33:23–28.
11. Skinner TC, Carey ME, Cradock S, et al. Depressive symptoms in the first year from diagnosis of type 2 diabetes: results from the DESMOND trial. *Diabet Med.* 2010;27:965–967.
12. Holt RI, de Groot M, Lucki I, Hunter CM, Sartorius N, Golden SH. NIDDK International Conference Report on Diabetes and Depression: current understanding and future directions. *Diabetes Care*. 2014;37:2067–2077.
13. Aikens JE. Prospective associations between emotional distress and poor outcomes in type 2 diabetes. *Diabetes Care*. 2012;35:2471–2478.
14. Polonsky WH, Anderson BJ, Lohrer PA, et al. Assessment of diabetes-related distress. *Diabetes Care*. 1995;18:754–760.
15. Berry E, Lockhart S, Davies M, Lindsay JR, Dempster M. Diabetes distress: understanding the hidden struggles of living with diabetes and exploring intervention strategies. *Postgrad Med J*. Epub 2015 Mar 31.
16. Nozaki T, Morita C, Matsubayashi S, et al. Relation between psychosocial variables and the glycemic control of patients with type 2 diabetes: a cross-sectional and prospective study. *Biopsychosoc Med*. 2009;3:4.

17. Gallo JJ, Bogner HR, Morales KH, Post EP, Ten Have T, Bruce ML. Depression, cardiovascular disease, diabetes, and two-year mortality among older, primary-care patients. *Am J Geriatr Psychiatry*. 2005;13:748–755.
18. Whiting DR, Guariguata L, Weil C, Shaw J. IDF Diabetes Atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract*. 2011;94:311–321.
19. Mastura I, Chew BH, Lee PY, et al. Control and treatment profiles of 70,889 adult type 2 diabetes mellitus patients in Malaysia. *Int J Collab Res Intern Med Public Health.* 2011;3:98–113.
20. Chew BH, Cheong AT, Mastura I, Rahman SASA. Diabetic hypertensive control and treatment: a descriptive report from the Audit Diabetes Control And Management (ADCM) registry. *Malays Fam Physician*. 2010; 5:134–138.
21. Chew BH, Mastura I, Lee PY, et al. Determinants of uncontrolled dyslipidaemia among adult type 2 diabetes in Malaysia: the Malaysian Diabetes Registry 2009. *Diabetes Res Clin Pract.* 2012;96:339–347.
22. Ibrahim WN, Aljunid S, Ismail A. Cost of type 2 diabetes mellitus in selected developing countries. *Malaysian Journal of Public Health Medicine*. 2010;10:68–71.
23. Currie CJ, Morgan CL, Dixon S, et al. The financial costs of hospital care for people with diabetes who have single and multiple macrovascular complications. *Diabetes Res Clin Pract*. 2005;67:144–151.
24. World Health Organization. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Report no. 99.2. 2013-08-22 17:19:23. Geneva, Switzerland: World Health Organization; 1999. Available from: http://apps.who.int/iris/handle/10665/66040. Accessed April 6, 2015.
25. Ministry of Health Malaysia. Management of type 2 diabetes mellitus. Putrajaya, Malaysia: Technology, Health Section, Assessment Division, Medical Development; 2009. Available from: http://www.moh.gov.my/attachments/3878.pdf. Accessed April 7, 2015.
26. American Diabetes Association. Standards of medical care in diabetes – 2015. *Diabetes Care*. 2015;38:S1–S93.
27. Fisher L, Hessler DM, Polonsky WH, Mullan J. When is diabetes distress clinically meaningful? Establishing cut points for the Diabetes Distress Scale. *Diabetes Care*. 2012;35:259–264.
28. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16:606–613.
29. Sherina MS, Arroll B, Goodyear-Smith F. Criterion validity of the PHQ-9 (Malay version) in a primary care clinic in Malaysia. *Med J Malaysia*. 2012;67:309–315.
30. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. *J Clin Hypertens*. 2008;10:348–354.
31. Al-Qazaz HK, Hassali MA, Shafie AA, Sulaiman SA, Sundram S, Morisky DE. The eight-item Morisky Medication Adherence Scale MMAS: translation and validation of the Malaysian version. *Diabetes Res Clin Pract.* 2010;90:216–221.
32. Skevington SM, Lotfy M, O'Connell KA. The World Health Organization's WHOQOL-BREF quality of life assessment: psychometric properties and results of the international field trial. A report from the WHOQOL group. *Qual Life Res*. 2004;13:299–310.
33. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods*. 2007;39:175–191.
34. van Bastelaar KM, Pouwer F, Geelhoed-Duijvestijn PH, et al. Diabetes-specific emotional distress mediates the association between depressive symptoms and glycaemic control in type 1 and type 2 diabetes. *Diabet Med*. 2010;27:798–803.
35. Chew BH, Shariff-Ghazali S, Mastura I, Haniff J, Bujang MA. Age ≥60 years was an independent risk factor for diabetes-related complications despite good control of cardiovascular risk factors in patients with type 2 diabetes mellitus. *Exp Gerontol.* 2013;48:485–491.
36. Lee PY, Cheong AT, Zaiton A, et al. Does ethnicity contribute to the control of cardiovascular risk factors among patients with type 2 diabetes? *Asia Pac J Public Health.* 2013;25:316–325.
37. Chew BH, Cheong AT, Ahmad Z, Mastura I. Men suffer more complications from diabetes than women despite similar glycaemic control and a better cardiovascular risk profile: the ADCM study 2008. *J Mens Health*. 2012;9:190–197.
38. Mathew CS, Dominic M, Isaac R, Jacob JJ. Prevalence of depression in consecutive patients with type 2 diabetes mellitus of 5-year duration and its impact on glycemic control. *Indian J Endocrinol Metab*. 2012; 16:764–768.
39. Tsujii S, Hayashino Y, Ishii H. Diabetes distress, but not depressive symptoms, is associated with glycaemic control among Japanese patients with type 2 diabetes: Diabetes Distress and Care Registry at Tenri (DDCRT 1). *Diabet Med*. 2012;29:1451–1455.
40. Chew BH, Mastura I, Shariff-Ghazali S, et al. Determinants of uncontrolled hypertension in adult type 2 diabetes mellitus: an analysis of the Malaysian Diabetes Registry 2009. *Cardiovasc Diabetol*. 2012;11:54.
41. McSharry J, Moss-Morris R, Kendrick T. Illness perceptions and glycaemic control in diabetes: a systematic review with meta-analysis. *Diabet Med*. 2011;28:1300–1310.
42. Tsiga E, Panagopoulou E, Sevdalis N, Montgomery A, Benos A. The influence of time pressure on adherence to guidelines in primary care: an experimental study. *BMJ Open*. 2013;3:pii e002700.
43. Hajos TR, Polonsky WH, Twisk JW, Dain MP, Snoek FJ. Do physicians understand type 2 diabetes patients' perceptions of seriousness; the emotional impact and needs for care improvement? A cross-national survey. *Patient Educ Couns*. 2011;85:258–263.
44. Ogbera A, Adeyemi-Doro A. Emotional distress is associated with poor self care in type 2 diabetes mellitus. *J Diabetes*. 2011;3: 348–352.
45. Zulman DM, Rosland AM, Choi H, Langa KM, Heisler M. The influence of diabetes psychosocial attributes and self-management practices on change in diabetes status. *Patient Educ Couns*. 2012;87: 74–80.
46. Thoolen BJ, de Ridder DT, Bensing JM, Gorter KJ, Rutten GE. Psychological outcomes of patients with screen-detected type 2 diabetes: the influence of time since diagnosis and treatment intensity. *Diabetes Care*. 2006;29:2257–2262.
47. Pandit AU, Bailey SC, Curtis LM, et al. Disease-related distress, self-care and clinical outcomes among low-income patients with diabetes. *J Epidemiol Community Health*. 2014;68:557–564.
48. Lasaite L, Lasiene J, Kazanavicius G, Gostautas A. Associations of emotional state and quality of life with lipid concentration, duration of the disease, and the way of treating the disease in persons with type 2 diabetes mellitus. *Medicina (Kaunas).* 2009;45:85–94. Lithuanian.
49. Lloyd C, Smith J, Weinger K. Stress and diabetes: a review of the links. *Diabetes Spectrum*. 2005;18:121–127.
50. Beverly EA, Ganda OP, Ritholz MD, et al. Look who's (not) talking: diabetic patients' willingness to discuss self-care with physicians. *Diabetes Care.* 2012;35:1466–1472.
51. Golden SH, Lazo M, Carnethon M, et al. Examining a bidirectional association between depressive symptoms and diabetes. *JAMA*. 2008;299: 2751–2759.
52. Ahola AJ, Groop PH. Barriers to self-management of diabetes. *Diabet Med*. 2013;30:413–420.
53. Bailey CJ, Kodack M. Patient adherence to medication requirements for therapy of type 2 diabetes. *Int J Clin Pract*. 2011;65:314–322.
54. Asche C, LaFleur J, Conner C. A review of diabetes treatment adherence and the association with clinical and economic outcomes. *Clin Ther*. 2011;33:74–109.
55. Tan MY, Magarey J. Self-care practices of Malaysian adults with diabetes and sub-optimal glycaemic control. *Patient Educ Couns*. 2008;72: 252–267.
56. Carper MM, Traeger L, Gonzalez JS, Wexler DJ, Psaros C, Safren SA. The differential associations of depression and diabetes distress with quality of life domains in type 2 diabetes. *J Behav Med*. 2014;37: 501–510.

57. Kiadaliri AA, Najafi B, Mirmalek-Sani M. Quality of life in people with diabetes: a systematic review of studies in Iran. *J Diabetes Metab Disord*. 2013;12:54.
58. Wandell PE. Quality of life of patients with diabetes mellitus. An overview of research in primary health care in the Nordic countries. *Scand J Prim Health Care*. 2005;23:68–74.
59. Papadopoulos AA, Kontodimopoulos N, Frydas A, Ikonomakis E, Niakas D. Predictors of health-related quality of life in type II diabetic patients in Greece. *BMC Public Health.* 2007;7:186.
60. Ventegodt S, Omar HA, Merrick J. Quality of life as medicine: interventions that induce salutogenesis. A review of the literature. *Soc Indic Res*. 2011;100:415–433.
61. Non-Communicable Disease Section, Disease Control Division, Department of Public Health. National Diabetes Registry Report, Volume 1: 2009-20122013. Available from: file:///C:/Users/susan/Downloads/National_Diabetes_Registry_Report_Vol_1_2009_2012.pdf. Accessed April 7, 2015.