Quality of life in Asians with type-2 diabetes mellitus: Development and validation of ethnic and language specific questionnaires, a cross-sectional study in Malaysia.

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PART A: General Declaration

Monash University

Declaration for thesis based or partially based on conjointly published or unpublished work
General Declaration

In accordance with Monash University Doctorate Regulation 17.2 Doctor of Philosophy and Research Master's regulations the following declarations are made:

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes [1] original papers published in peer reviewed journals and [3] unpublished publications. The core theme of the thesis is [Quality of Life in a multi-ethnic population]. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the candidate, working within the [School of Medicine and Health Sciences] under the supervision of [Prof. Dr.Rusli Bin Nordin and Prof. Dr. Khalid A. Kadir].

[The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.]

In the case of [Chapter 5] my contribution to the work involved the following:
Active involvement in designing the study and coordination, data collection, data analysis and writeup of the manuscript.

Thesis chapter	Publication title	Publication status*	Nature and extent of candidate's contribution
2	Review: evolution of diabetes management in the 21st century: the contribution of quality of life measurement in Asians.	In press	Extensive literature review and manuscript write-up.
3	Development and validation of the Asian Diabetes Quality of Life questionnaire (AsianDQOL)	Published	Conception of idea, designing the study, data gathering, data analysis and manuscript write-up.

4	Diabetes Quality of Life perception in a multi-ethnic population.	Published	Conception of idea, designing the study, data gathering, data analysis and manuscript write-up.
5	Sexual dysfunction in men with diabetes with or without cardiovascular disease.	Revision	Designing the study, data gathering, data analysis and manuscript write-up.

[* For example, 'published'/ 'in press'/ 'accepted'/ 'returned for revision']

I have renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Signed: 

Date: **……12 June 2015……**

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Giap Kah Goh

STATEMENT

This thesis contains no material, which has been accepted for any award or any other degree or diploma in any university.

To the best of my knowledge, this thesis does not contain any work published previously nor written by another person except where due reference is made in the text.

This thesis contains original work done by myself except for the contributions by my collaborators, which I have acknowledged.

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ABBREVIATIONS

In addition to chemical symbols, abbreviations for S.I units, and journal abbreviations as in Indexus Medicus, the following abbreviations have been used; -

DM	Diabetes mellitus
UKPDS	United Kingdom Prospective Diabetes Study
DCCT	Diabetes Control and Complications Trial
QOL	Quality of Life
T2DM	Type 2 diabetes mellitus
GLP	Glucagon like peptide
LADA	Latent autoimmune diabetes in adults
GAD	Glutamic acid decarboxylase
MODY	Maturity onset diabetes of the young
HNF-1α	Hepatic nuclear factor one alpha
NHMS	National health and morbidity survey
ACCORD	Action to control cardiovascular risk in diabetes
HbA1c	Glycated hemoglobin
IFG	Impaired fasting glucose
WHO	World Health Organization
DSM-IV	Diagnostic and statistical manual of mental disorders

SD	Sexual dysfunction
ED	Erectile dysfunction
PE	Premature ejaculation
ADS	Appraisal of diabetes survey
ADDQOL	Audit of Diabetes Dependent Quality of Life
DHP	Diabetes Health Profile
DIMS	Diabetes Impact Measurement Scale
DQOL	Diabetes Quality of Life Measure
D39	Diabetes 39
DSQOL	Diabetes specific quality of life
QSD-R	Revised Questionnaire on stress in patient with diabetes
WED	Well being enquiry for diabetics
SF-36	Medical outcome study short form 36
WHOQOL-BREF	World Health Organization quality of life brief questionnaire
EQ5D	European Quality of Life Questionnaire
IQOLA	International Quality of Life Assessment
DQLCTQ-R	Revised Diabetes Quality of Life clinical trial questionnaire
EFA	Exploratory factor analysis
RA	Reliability analysis

CFA	Confirmatory factor analysis
SEM	Structural equation modeling
CMIN	Chi-squared test
GFI	Goodness of fit
RMSEA	Root mean square error of approximation
CFI	Comparative fit index
KMO	Kaiser Meyer Olkin
SADMEN	Sexual function assessment in diabetic men
CVD	Cardiovascular disease
OR	Odds ratio
95 CI	95% confidence interval

SUMMARY

Diabetes mellitus (DM) is a complex and chronic disease with multiple complications leading to increased mortality and poor quality of life. Current studies have shown that lowering glycosylated hemoglobin (HbA1c) confers protection against microvascular complications. However, evidence showed that with more intensive glucose control to achieve HbA1c of less than 6.5%, there is a significant increased risk of mortality and cardiovascular events. The current recommendation worldwide is for "tailoring" of DM management to risk and also quality of Life (QOL) which is a crucial component in determining the success or failure of DM management. In Asia, DM has become a health crisis but there is a lack of QOL assessment tool that is specific for Asians with wide spectrum of ethnicity, languages, religions and socio-economic differences. The primary aim of this study is to construct a type-2 diabetes mellitus specific quality of life (QOL) tool for Asian populations that is valid and reliable across different ethnicities, languages, and socio-economic backgrounds. The secondary aim is to study the perception of diabetes quality of life in a multi-ethnic Malaysian population with type- 2 diabetes and to determine the factors contributing to QOL in our study population. The tertiary aim is to determine whether cardiac disease will worsen sexual dysfunction (SD) in diabetes, and determine the factors causing SD in a multi-ethnic population.

Methods: A focus group determined the domains affecting QOL in consultation with an expert group. A pilot study was conducted to validate the Asian Diabetes QOL (AsianDQOL) in English, Malay/Indonesian and Chinese- Mandarin. The World Health Organization Brief Quality of Life Questionnaire (WHOQOL-BREF) was used for comparison. Exploratory factor analysis (EFA), reliability analysis (RA) using Cronbach's alpha and test-retest reliability, and confirmatory factor analysis (CFA) using structural equation modelling (SEM) was undertaken using the statistical software IBM SPSS Statistics version 20. In

order to study the impact of westernization on the perception of QOL, a population based cross-sectional and longitudinal study were carried out in 3 different states in Malaysia. The Asian Diabetes Quality of Life (AsianDQOL) tool specific for Type 2 diabetes is the primary outcome tool for data gathering at 2 points of time. The subjects were tested 3 months apart. Stepwise multiple linear regression models were used for analysis. The Sexual Function Assessment in Diabetic Men (SAD-Men) tool specific for sexual dysfunction in men with diabetes is the primary outcome tool for data gathering. Chi-Squared test for independence was applied to evaluate for any significant differences in the three groups of participants. Stepwise multiple linear regression models were used for analysis.

Results EFA with eigen values (≥1) and factor loadings ≥ 0.3 for English and Malay language demonstrated 21 items and 5 components. CFA (English version) confirmed the model fit (CMIN 201.08, p-value 0.071, GFI 0.88, RMSEA 0.036, CFI 0.978). CFA (Malay version) confirmed the 5-factor model (CMIN 189.39, p-value 0.085, GFI 0.937, RMSEA 0.025, CFI 0.987). The corresponding Cronbach's alpha scores (English version) were 0.917, 0.818, 0.816, 0.749 and 0.719, respectively. The Malay/Indonesian version scored 0.833, 0.819, 0.816, 0.775, 0.673, respectively whilst the Chinese/Mandarin version scored 0.890, 0.719, 0.826, 0.862 and 0.759, respectively. Test-retest reliability showed Spearman's correlation of 0.664 (English version), 0.736 (Malay/Indonesian version) and 0.553(Chinese-Mandarin version). A scoring system was generated based on the 25^{th}, 50^{th} and 75^{th} centiles for all the three languages. A total of 664 subjects of different ethnicity were recruited. Analysis shown the main contributors of QOL for English language group of different ethnicities were sexual dysfunction(-4.5), having visual problems (-3.7), female (-2.8) glycaemic control (-1.6). Sexual dysfunction was negatively correlated with QOL in Malay, Chinese and Indian ethnic groups. The predictors of QOL were different in the westernized group compared to the traditional group. As for the study of sexual dysfunction among men

with diabetes and cardiovascular disease, a total of 424 subjects of different ethnicity were recruited. A total of 221 have diabetes only, 98 with cardiovascular disease without diabetes and 105 with diabetes and cardiovascular disease. The prevalence of SD in all subjects assessed using the SADMEN tool was 82%. The prevalence of SD in DM only group, CVD only group and DM plus CVD group was 80%, 78% and 91%, respectively. Those with DM and CVD experienced more severe SD compared to the other two groups. Regression model generated for SD score shows negative correlation of age (-0.4), duration of DM (-2.5), neuropathy (-3.5), retinopathy (-4.1), ischemic heart disease (-5.1) and depression symptoms (-6.3).

Conclusion The AsianDQOL is a valid, reliable and stable tool for assessing QOL in multi-ethnic and multi-lingual T2DM Asian populations. The perception of QOL is different across the ethnic groups and language. Significant differences in the English-speaking group and the traditional Non-English speaking group were detected within the same ethnicity. Sexual dysfunction severely impact QOL in a multi-ethnic Asian population and remained an important determinant regardless of ethnicity and language. The predictors of sexual dysfunction and its components were different. There is a high prevalence of SD among men with diabetes in a multi-ethnic Malaysian population. Men with diabetes and CVD are at higher risk of developing moderate to severe sexual dysfunction compared to men with diabetes alone.

CHAPTER ONE: INTRODUCTION

1.1 Background: The Evolution of Diabetes

Diabetes mellitus (DM) is defined as a metabolic disorder of multiple causes characterized by chronic hyperglycemia due to defects in insulin secretion, action or both. It is a chronic condition with insidious onset of organ damage even before the diagnosis is made. Multiple studies have shown the presence of retinopathy, neuropathy, microalbuminuria, myocardial infarction, ischemic heart disease and peripheral arterial disease at the point of diagnosis [Spijkerman 2003; Spijkerman 2004].

The UK Prospective Diabetes Study (UKPDS) started in 1977 for more than 10 years showed that intensive blood sugar lowering decreased the risk of microvascular complications by 25% [UKPDS, 1998] and for every 1% reduction of mean HbA1c, there is a corresponding 14% reduction of myocardial infarction risk and 37% reduction of microvascular complications [Stratton 2000]. Similar studies done in Japan and on Type 1 diabetes by the Diabetes Control and Complications Trial (DCCT) supports the strong correlation between improving glycemic control and reduction of DM complications.

Post UKPDS and DCCT study of another 10 years found that the reduction of risk of complications remained low in the intensively treated group despite similar HbA1c levels to the controls [DCCT/EDICT, 1993]. This finding of legacy effect or glucose memory swerved the management of DM towards intensive blood sugar lowering to prevent the onset of complications. However, in 2008 strong evidence showed that lowering the HbA1c level to less than 6.5% significantly increased the mortality and cardiovascular events in type 2 diabetics [ACCORD 2008; Ismail-Belgi et al., 2010; ADVANCE 2008; Duckworth W et al., 2009]. Thus, current guidelines support early diagnosis and treatment of DM with tailoring of treatment modalities to target glycemic control. DM management tailoring is a broad concept

involving multiple factors such as duration of disease, symptoms, presence of complications, age, glycemic control, treatment satisfaction, socio-economic background and etc. How do we judge if the management modality is suitable or is the best for the patient? Besides "chasing" after the HbA1c levels, it is important to consider the wellbeing of the patient reflected by the quality of life (QOL).

QOL is an expansive ranging concept that can be affected by the individual's physical health, psychological state, level of independence, social relationships, personal beliefs and relationship to salient features of his/her environment [WHO 1997]. People living with DM often endure great stress, both physically in terms of therapy and psychosocially, which can affect the self-care behavior, glycemic control and QOL [Fisher EB Jr et al., 1996; Glasgow R et al., 1992]. The evolution of DM management to a more holistic approach has made QOL an important outcome measure for interventions and disease management making its accurate measurement crucial. The challenge lies in accurately reflecting subjective perception of QOL into objective scores for assessment. In order to do this, the tool must be sensitive and relevant to the local population as different languages, races, cultures, socio-economic progress and religious beliefs within the population can have a significant direct or indirect effect on the QOL.

The dynamics of DM epidemic has shifted from the West to Asia. Asia has become the epicenter of DM due to the rapid economic development, urbanization and transition in nutritional status in the recent decades [Chan J et al., 2009]. The challenge for Asia is the vast difference in ethnicities, cultures, languages and socio-economic development. Compared to the Western population, Asians are more diabetogenic and tends to develop DM younger and at a lower body mass index with lesser weight gain [Zhang P et al., 2010; Ramachandran A et al., 2010]. There is also a stronger genetic link between type- 2 DM in the Asian population rather than sporadic autoimmune contribution in the Western population. [Mohan V et al.,

1985; Ng MCY et al., 2001]. Another contributing factor is the shift in lifestyle and dietary habits consistent with the rapid economic development experienced by many developing nations in Asia. A more sedentary lifestyle coupled with high consumption of refined carbohydrates lead to higher tendency of abdominal obesity and insulin resistance [Yoon KH et al., 2006; Hu FB 2011].

In Asia, there is a lack of a QOL instrument specifically focused on the diverse ethnic, language, culture, education level, religion and structures of medical care. In view of this complexity, many researchers in Asia chose to translate and adapt instruments developed in Western countries rather than developing a new tool [Cheung YB et al., 2006]. The question lies in the ability of these translated or adapted tools in accurately reflecting the QOL in the complex Asian population. In the recent years, there is increasing apprehension on the quality of the translation process in the adaption of QOL instruments. The concern is mainly focused on the loss of cultural differences during translation and the assumption that perception of QOL remains unchanged across different population [Hunt SM 1993].

A population-based study was conducted in Singapore and found that ethnicity remained an important factor influencing QOL in a multi-ethnic sample of Asians with diabetes independent of age, gender and education [Wee HL et al., 2006]. The question raised is whether there are any differences across ethnicity and preferred languages with respect to QOL. Malaysia's population is similar to Singapore in terms of the different ethnic group composition. The education system in Malaysia practices multi-lingual concept resulting in a majority of Malaysians who are proficient in more than one language for example Malay language and English or Malay language and Mandarin regardless of ethnicity. Their lingua franca is mainly influenced by the medium of education and influence of family and social network [Gaudart H 1987; Ozóg CK 1993]. There is limited data on the impact of westernization on the perception of QOL in a multi-ethnic population. The lingua franca of

the subject reflecting his or her upbringing may determine the impact of westernization. Those who preferred English language tend to be English educated locally or overseas and have a higher exposure to western culture and lifestyle compared to the more traditional group who are still following local customs, lifestyles and beliefs.

In the global epidemic of DM, Asian countries will bear 60% of the world's DM population [Chan J et al., 2009]. However, there is a lack of a reliable QOL assessment tool that is constructed based on Asians of different ethnicities, languages, and socio-economic background. There is also limited data on the differences between the different ethnic groups in Asian countries. Very little is known about the perception of QOL among the different ethnic groups and their lingua franca. All these data is crucial to the management of DM in order to achieve the highest standard of care.

1.2: Research Question

i. Is there a difference in perception of QOL between and within the different ethnic groups in Malaysia?

ii. What are the main factors determining QOL in the Malaysian population?

iii. Will changes in diabetes control affect QOL?

iv. Will presence of diabetes complication affect the QOL?

1.3:Objectives

i. To develop and validate a T2DM specific QOL tool that is reliable and sensitive across the diverse culture, religion, language, ethnicity and socio-economic background in Asia.

ii. To analyze the factors contributing to QOL in a population with diverse ethnicity, religious beliefs, and languages but sharing the same socio-demographic background.

iii. To investigate the role of glycemic control (HbA1c) in determining QOL and changes in QOL.

1.4 Research hypothesis

i. The perception of QOL will be different among the different major ethnic groups sharing the same socio-economic background in Malaysia.
ii. The perception of QOL will be different within the same ethnic group (Malay ethnicity) with different lingua franca English speaking and Malay speaking.
iii. The presence of DM complications will affect QOL score.
iv. Changes in glycemic control over a period of 3 months will change the QOL score.

CHAPTER 2

LITERATURE REVIEW

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CHAPTER 2: LITERATURE REVIEW

2.1 Definition of diabetes mellitus

Diabetes mellitus (DM) is defined as a metabolic disorder of multiple causes characterized by chronic hyperglycemia due to defects in insulin secretion, action or both. There is an also associated disturbance of carbohydrate, fat and protein metabolism. The chronic hyperglycemia is associated with damage and failure of various organs especially eyes, kidneys, nerves, heart and blood vessels [WHO, 1999, American Diabetes Association, 2004].

2.2 Glucose homeostasis

Blood glucose levels are regulated closely and maintained at the range of 3.5-8.0 mmol/L (63-144mg/dL) despite food intake, exercise, activities or fasting. The liver maintains glucose homeostasis by absorbing and storing glucose as glycogen post meals and breaking down the glycogen into the circulation between meals. Insulin is the principal hormone involved in storage and release of glucose from food. Insulin is produced in the beta cells of the pancreas. It is synthesized as 86 amino acid precursor polypeptide, preproinsulin and subsequent proteolytic processing by removal of amino-terminal signal peptide formed proinsulin. Cleavage of internal 31 residue fragment of proinsulin generates C-peptide and insulin molecule. The mature insulin and C-peptide are stored together and co-secreted making C-peptide a useful marker for insulin secretion.

When food is ingested, glucose stimulates insulin synthesis and release from the pancreas into the portal venous system, where 50% is degraded by the liver. The unextracted insulin binds to receptors in target sites and stimulates translocation of facilitative glucose transporter to the cell surface leading to increase glucose uptake by skeletal muscles and fat. Activation

of other pathways leads to glycogen synthesis, protein synthesis and lipogenesis. Incretins such as glucagon-like peptide 1 (GLP-1) is released from L cells of gastrointestinal tract following food ingestion and stimulates insulin secretion only when blood glucose is above fasting level.

In the fasting state, the liver combines 3 carbon molecules from breakdown of fats, muscle glycogen (lactate) and protein into glucose by the process of gluconeogenesis in response to the low insulin levels. This process is also stimulated by glucagon, a hormone secreted by pancreatic alpha cells in response to low glucose and insulin levels.

2.3 Types of Diabetes

2.3.1 Type 1 diabetes mellitus (T1DM)

This form of immune mediated diabetes accounts for only 5-10% of those with diabetes. The aetiology is due to cellular-mediated autoimmune destruction of the beta cells of pancreas. The rate of destruction is variable in different individuals, with a majority presenting in the childhood or adolescent years. However, the slowly progressive form may occur in adulthood and is referred as the latent autoimmune diabetes in adults (LADA)[Zimmet et al.,1994]. Autoantibodies such as islet cell autoantibodies, autoantibodies to insulin, autoantibodies to glutamic acid decarboxylase (GAD) and antibodies to tyrosine phosphatase are present in 85-90% of individuals leading to little or no insulin secretion [Willis et al., 1996]. There is a group of Type 1 diabetes with no know aetiology. Most are of African and Asian descendant and they present will need permanent insulin replacement therapy [American Diabetes Association, 2004].

2.32 Type 2 diabetes mellitus (T2DM)

This form of diabetes accounts for 90-95% of those with diabetes and is mainly due to insulin resistance with relative insulin deficiency. Most patients in this group have central obesity and this leads to insulin resistance [Campbell et al.,1993; Kissebah et al., 1982]. Insulin secretion is also suboptimal in this form of diabetes and insufficient to overcome the insulin resistance. It is often associated with a strong genetic predisposition. The hyperglycemia develops gradually and patients are often diagnosed late. This group of patients is also at higher risk of developing macrovascular and microvascular complications of diabetes. The risk of developing T2DM increases with age, obesity, lack of physical activity, in individuals with hypertension or hyperlipidemia and in women with previous history of gestational diabetes.

2.3.3 Other types of DM

Several forms of diabetes are associated with monogenic defects in beta cell function presenting at an early age (generally before age of 25) with elevated blood sugar. They are referred to as maturity onset diabetes of the young (MODY) and is inherited in an autosomal dominant pattern. They have impaired insulin secretion with minimal or no defect in insulin action [Byrne et al., 1996]. The most common form is mutation on chromosome 12 in hepatic nuclear transcription factor referred to as HNF-1α [Yamagata et al., 1996]. There are also some uncommon causes of diabetes which result from genetically determined abnormalities of insulin action. It is associated with mutations of the insulin receptor and some individuals have acanthosis nigricans and women may have virilization and enlarged cystic ovaries [Kahn et al.,1976].Diffuse injury to the pancreas can cause diabetes and acquired process include as pancreatitis, trauma, infection and pancreatic carcinoma [Gullo et al.,1994; Larsen et al.,1987]. Cystic fibrosis, hemochromatosis and Wilson's disease can also lead to

damaged beta cells and impaired insulin secretion [Moran et al., 1994; Phelps et al., 1989]. Certain hormones produced by our body antagonize the action of insulin such as growth hormone, cortisol, glucagon and epinephrine. Disease associated with excess secretion of these hormones such as Acromegaly, Cushing's syndrome, Glucagonoma and Phaechromocytoma can cause diabetes which is reversible when the excess hormone is removed. Coxsackie B, rubella, cytomegalovirus, adenovirus and mumps virus infection have been implicated with beta cell destruction leading to type 1 diabetes [Forrest et al.,1971; King et al.,1983; Karjalainen et al., 1988; Pak et al.,1988]. Many genetic syndromes are also linked to diabetes mellitus such as Down's syndrome, Klinefelters syndrome and Turner's syndrome.

2.4 Prevalence of diabetes

Diabetes mellitus is a growing worldwide epidemic with a prevalence of 171 million in year 2000 and is estimated to increase to 366 million by year 2030 [Wild S et al.,2004]. A more recent projection in 2010 estimated a 20% increment to 439 million in 2030[Shaw et al., 2010]

The 54% increase in the number of diabetes from year 2004 to 2030 is contributed by population growth, ageing population and the effect of urbanization with a more sedentary lifestyle [Shaw et al., 2010]. Asia being the world's most populous region will bear 60% of the world diabetic population resulting in increased healthcare expenditure [Chan J et al., 2009]. The greatest increase will be contributed by West Asia, India and China [Wild S et al., 2004]. Asia faces a big challenge to curb the tremendous rise of diabetes due to the vast difference in ethnicity, cultures and socio-economic development, which can affect the clinical presentation, management, prevention of DM and perception of QOL [Chan J et al., 2009]. Malaysia is a multi-ethnic, multi-cultural and multi-religious country in the South-east

Asia region that is struggling against the rise of the diabetic epidemic. The first National Health and Morbidity Survey (NHMS I), conducted in 1986 showed the prevalence of diabetes to be 6.3%. Ten years later, this figure had increased to 8.3% and in 2006, an alarming rise to 11.6% [Letchuman GR et al., 2010]. In a more recent cross sectional study done in 2010, the prevalence of diabetes in Malaysia was 22.6%, an increase of twofold in merely four years [Wan Nazaimoon et al., 2013]. There are a few points in Asia that are of major concern, firstly is due to the rapid rate of increase in DM especially in the younger aged group (between 30-50 years) in developing countries[Cockram et al.,2000; Kim et al.,2006; Lu FH et al.,1998; Cockram et al.,1993; Takahashi Y et al.,2000]. Secondly, there is also a high number of T2DM in children and adolescents compared to the Western counterparts. Another contributing factor is the shift in lifestyle and dietary habits consistent with the rapid economic development experienced by many developing nations in Asia [Hu FB, 2011]. The many different religions in Asia need to be considered when designing a tool for assessing QOL for Asians as spirituality, religion and personal beliefs is highly correlated to psychological and social domains of QOL [WHOQOL SPRB Group, 2006]. Special attention to ethnicity and language is particularly important in the assessment of QOL not only due to the subjectivity but also the cultural framework essential to the construct [Guarnaccia PJ, 1996].

2.5 Diabetes in Asia

Asia is divided into 5 regions. Central Asia consists of Kazakhstan, Kyrgyzstan, Tajikstan, Uzbekistan, Turkmenistan and Xinjiang of western China. The main religions are Islam and Buddhism. East Asia consists of China, Taiwan, Hong Kong, Japan, South Korea and North Korea. The main religions are Confucianism, Buddhism and Christianity. North Asia is made up of Russia and Mongolia with most of the ethnic groups being composed of nomads. South

Asia consists of Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan and Sri Lanka. The main religions are Hinduism, Buddhism, Jainism, Sikhism, Islam and Christianity. South East Asia consists of Burma, Thailand, Laos, Cambodia, Vietnam, Indonesia, Malaysia, Singapore, East Timor, Brunei and the Philippines. The main religions are Islam, Buddhism, Christianity, and Hinduism. South East Asia also has a lot of Western influence due to the legacy of colonialism. West Asia consists of Middle Eastern countries from to Yemen. The predominant religion is Islam.

DM, previously a disease of the West, has now rapidly become a health crisis in Asian countries. The chronicity and complications of the disease threaten the economic growth of developing countries as the global healthcare expenditure for DM is expected to hit USD490 billion in 2030 [Chan et al, 2009]. A big challenge for Asia is the vast difference in ethnicity, cultures and socio-economic development within Asia, which can affect the clinical presentation, management and prevention of DM. The Asian population is more diabetogenic compared to the European population. Asians tend to develop DM at a younger age, at lower body mass index and with lesser weight gain [Zhang P et al., 2010; Ramachandran et.al, 2010]. The Asian population is genetically and phenotypically different with stronger genetic link between type 2 DM rather than sporadic autoimmune contribution. [Mohan V et.al,1985, Ng MCY et.al, 2001]. Asians have a greater tendency for abdominal obesity resulting in increased insulin resistance [Yoon KH et al, 2006]. Another contributing factor is the shift in lifestyle and dietary habits consistent with the rapid economic development experienced by many developing nations in Asia. A more sedentary lifestyle coupled with high consumption of refined carbohydrates is driving the DM epidemic [Hu FB, 2011].

2.6 Impact of westernization in Asia

In Asia especially South East Asia, there is a strong element of Western culture influence or westernization likely due to the history of colonialism. Westernization represents a lifestyle or behavioral approach to health in epidemiology [Salant T et al, 2003]. DM is considered to be one of the diseases associated with westernization [Fujimoto WY, 1992]. In an extensive review by Fujimoto in 1992, there is a higher prevalence of DM among migrant Asians than in their homeland. This review summarized many of the prevalence studies of DM in migrant Asian populations as well as in their countries of origin [Fujimoto WY, 1992]. This strengthens the point that as Asia become more westernized; insulin resistance and glucose intolerance will become more common. Westernization is linked to globalization and with globalization and economic growth there is a nutrition shift to high consumption of processed food, increased calories and a more sedentary lifestyle [Hu FB, 2011]. The combination of excessive calorie intake and reduced energy output leads to increased obesity and insulin resistance [Hu FB, 2011].

2.7 ***Complications of diabetes***

The complications of DM are divided into macrovascular and microvascular. Microvascular complications of diabetes comprises of nephropathy, neuropathy and retinopathy. Diabetic nephropathy is the leading cause of kidney failure and World Health Organization (WHO) estimates that 10-20% of people with diabetes will die of kidney failure. [(19)] Strict glycemic and blood pressure control has been highlighted in multiple well-established studies to improve survival rate by delaying the progression of nephropathy and retinopathy [UKPDS 38, 1998; Bruno G et al., 2003; Margolis et al., 2008]. Macrovascular complications include coronary heart disease, peripheral arterial disease and cerebrovascular disease. Over the years there have been multiple international studies linking diabetes to depression, cognitive

impairment and dementia [Goldney et al., 2004; Gonzalez et al., 2008; Lustman et al., 2000; Cukierman et al., 2005] A meta-analysis review of literature found that depression was associated with hyperglycemia [Lustman et al., 2000] and people with diabetes are at a greater risk of cognitive decline at a more rapid rate as compared with people without diabetes [Cukierman et al., 2005]. The risk of complications increases with duration and degree of hyperglycemia.

2.8 Relationship between glycemic control and complications of DM

The UK Prospective Diabetes Study (UKPDS) started in 1997 to determine if intensive blood glucose control will reduce the complications in type 2 diabetes. After 10 years of follow up, the intensive treatment group showed a substantial reduction of 25% risk of microvascular complications [UKPDS 33, 1998]. The UKPDS also found that for every 1% reduction in mean HbA1c, there is a corresponding 21% reduction in DM complications, 21% reduction of deaths related to DM, 14% reduction of myocardial infarction and 37% reduction of microvascular complications [UKPDS 35, 2000]. The Kumamoto study was designed to compare intensive insulin therapy using multiple insulin injections versus conventional insulin therapy to evaluate the development and progress of microvascular complications in Type 2 diabetes. They were followed up for 6 years and the intensive group achieved mean Glycated hemoglobin (HbA1c) of 7.1% versus 9.4% in the conventional group. The risk of retinopathy is reduced by 69% and the risk of nephropathy is reduced by 70% in the intensive group [Ohkubo et al., 1995]. In the Diabetes Control and Complications Trial (DCCT) conducted in Type 1 diabetics for 6 years, a reduction of HbA1c of 2% between the intensively treated to conventionally treated group showed a significant reduction in risk of diabetes complications of about 60%[DCCT,1993]. Post UKPDS follow-up study of 10 years found that the reduction of risk in developing complications remained lower in the intensively treated group despite similar HbA1c levels to the controls [Holman et al., 2008].

Similarly, the EDIC study that followed up Type 1 diabetics post DCCT trial concluded long-term reduction of cardiovascular risk in the intensively treated group despite worsening of the glycemic control comparable to controls [DCCT, 2005]. This is due to the "legacy effect" or "metabolic memory" supporting early aggressive treatment of diabetes to reduce the risk of complications. Contradicting the amazing risk reduction results, the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study found that lowering the HbA1c level to less than 6.5% significantly increased the mortality and cardiovascular events in type 2 diabetics [ACCORD,2008; Ismail-Belgi et al., 2010]. Similar studies to intensively lower HbA1c have yet to show any beneficial effect of lowering the HbA1c level below 6.5% [ADVANCE, 2008; Duckworth et al., 2009].

2.9 Diagnostic criteria for DM

The World Health Organization (WHO)/ International Diabetes Federation (IDF) criteria for diagnosis of diabetes on any of the following;

- Fasting plasma glucose (FGP) ≥7.0mmol/l(126 mg/dl) or,
- 75g oral glucose tolerance test (OGTT) with FPG≥ 7.0mmol/l (126 mg/dl) and/or 2 hour plasma glucose ≥ 11.1 mmol/l (200mg/dl) or
- Glycated hemoglobin (HbA1c) ≥6.5%/48mmol/mol, or
- Random plasma glucose ≥11.1mmol/l(200mg/dl) in the presence of classical diabetes symptoms.

Impaired fasting glucose (IFG) is defined as fasting plasma glucose between 6.1mmol to 6.9mmol/l (110mg/dl to 125 mg/dl). Impaired glucose tolerance (IGT) is fasting plasma glucose of 7.0mmol/l (126mg/dl) and 2 hour plasma glucose of ≥7.8mmol/l and, 11.1mmol/l (140mg/dl and 200md/dl).

2.10 Glycated hemoglobin (HbA1c)

Glycohemoglobin is formed by the non-enzymatic attachment of glucose to hemoglobin (Hb). HbA1c is a minor component of Hb variant separated by charge that is composed mainly of glycohemoglobin [Peterson et al., 1998]. The most precise method to measure glycosylated hemoglobin is the chromatographic technique. This involved the use of cation exchange resin and is the most widely applied method. Other methods are electrophoretic technique and calorimetric method.

2.12 Diabetes and quality of life

The UKPDS study group elaborately explained the impact of diabetes on QOL. They performed two cross-sectional studies of patients enrolled in randomized controlled trials of intensive blood glucose control versus conventional control group and tight blood pressure control versus less tight control group. QOL was affected by DM complication but not by the treatment regime [UKPDS, 1999]. Medical survey done in United States found that QOL decreased in relation to the number of complications. Male gender, longer duration of DM and patients on insulin regime tend to have a poorer QOL [Glasgow et al., 1997]. The American findings were supported by a study in Netherlands suggesting that insulin therapy, obesity and complications of diabetes were associated with poorer QOL regardless of age and gender [Redekop et al., 2002]. In both studies a general QOL tool was used which could lead to reduced sensitivity and data loss. A diabetes specific tool will provide a better reflection of QOL. The findings are overwhelming but it is crucial to note that QOL is subjective and is perceived differently by different population. The tool used to measure QOL is also important to ensure accurate data capture.

2.12 What is Quality of Life?

Quality of life (QOL) is defined by the Constitution of the World Health Organization (WHO) as "an individual's perception of his/her position in life in the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards and concerns". QOL is an expansive ranging concept that can be affected by the individual's physical health, psychological state, level of independence, social relationships, personal beliefs and relationship to salient features of his/her environment [WHO, 1997]. The current shift of diabetes care from the traditional "glycemic oriented" to a more "holistic patient care" has made QOL an important outcome measure for interventions, making its accurate measurement crucial. Measurement of QOL also provides a mean for measuring the cost impact of medical interventions from the health economic point of view [Read JL, 1993]. DM being a chronic disease, can significantly impact the QOL due to its many complications and to date is still a major cause of mortality, morbidity and high health care expenses [Lloyd A et al., 2001; Brown GC et al., 2000]. People living with DM often endure great stress, both physically in terms of therapy and psychosocially, which can affect the self-care behavior, glycemic control and QOL [Fisher EBJ et al., 1996; Glasgow R et al., 1992].

2.13 Impact of westernization on perception of QOL

There is limited data on the impact of westernization on the perception of QOL in a multi-ethnic population. The preferred language of the subject reflecting his or her upbringing may determine the impact of westernization. Those who preferred English language tend to be English educated locally or overseas and have a higher exposure to western culture and lifestyle compared to the more traditional group who are still following local customs, lifestyles and beliefs. Malaysia's population is similar to Singapore in terms of the different ethnic group composition. The education system in Malaysia practices bilingual concept

resulting in a majority of Malaysians who are proficient in more than one language. Their preferred language is mainly influenced by the medium education and influence of family and social network [Gaudart H, 1987; Ozóg CK, 1993]. Whorf in 1956 explained that language guides our cognition and shaped our conceptual knowledge and subsequently there is strong evidence supporting the theory that language directs thoughts and behavior in human beings [Whorf BL, Ervin-Tripp S, 1967].

2.14 Sexual dysfunction and diabetes

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) classified sexual dysfunction (SD) as a disorder in one or more of the four stages of the sexual response cycle: desire, excitement, orgasm and resolution [DSSM IV, 2000]. Male SD is also categorized into erectile dysfunction (ED), ejaculatory/ orgasmic disorders (premature ejaculation) and sexual interest disorders [Isidro ML, 2012]. SD has major health consequences on the individual, both physically and psychologically. This effect in turn aggravates the SD, creating a vicious cycle [Isidro ML, 2012].

Diabetes (DM) is a highly prevalent condition in Asia and has been commonly associated with SD, especially ED and premature ejaculation (PE). Worldwide, the prevalence of ED among diabetic population ranges from 39% to 71% [Berardis GD et al., 2002; Giuliano FA et al., 2004; Eardley I et al., 2007]. A Chinese based cross-sectional study showed ED prevalence rate of 75% among the diabetic patients [Yang G et al., 2010]. On the other hand, prevalence of PE in diabetes has been quoted to be around 40%-56%, with a higher prevalence among men with DM [Burke JP et al., 2007, El-Sakka AI et al., 2003; Malavige LS et al., 2008; Owiredu WK et al., 2011]. Worsening this dilemma is the concomitant presence of PE and ED with DM [Malavige LS et al., 2008]. In terms of other forms of

orgasmic disorders and sexual interest disorders, very little information was found among the diabetic population.

The topic of sex and sexuality is considered a taboo in Asia and is not comfortably discussed in public. A study on sexual behavior and dysfunction and help-seeking patterns in the urban population of Asians was carried out in China, Taiwan, South Korea, Japan, Thailand, Singapore, Malaysia, Indonesia and the Philippines found that although sexual dysfunction is prevalent in the middle age group, socio-cultural factors seem to prevent the afflicted individuals from seeking treatment [Nicolosi A et al., 2005]. Self-reported questionnaire is the best way to capture such delicate data from the Asian population [Hisasue S et al., 2005; Nicolosi A et al., 2005]. It is vital that this component be included in the QOL measurement tool to accurately reflect the impact of sexual dysfunction on QOL. The score obtained from the self-reported QOL tool could also help the doctor or health care personnel to detect problems of sexual dysfunction for further action without causing any embarrassment or discomfort to the patient.

2.15 *Review paper: Evolution of diabetes management in the 21st century; contribution of quality of life in Asians.*

Abstract: Diabetes mellitus (DM) is a complex and chronic disease with multiple complications leading to increased mortality and poor quality of life. Current studies have shown that lowering glycosylated hemoglobin (HbA1c) confers protection against microvascular complications. However, with more intensive glucose control to achieve HbA1c of less than 6.5%, there seems to be a significant increased risk of mortality and cardiovascular events. The current recommendation worldwide is for "tailoring" of DM management to risk and also quality of Life (QOL) which is a crucial component in determining the success or failure of DM management. In Asia, DM has become a health crisis but there is a lack of QOL assessment tool that is specific for Asians with wide spectrum of ethnicity, languages, religions and socio-economic differences. In this review, we discuss the evolution of DM management over the decade and the issues pertaining to QOL among people with diabetes in Asia.

Introduction

Diabetes mellitus (DM) is a chronic condition associated with multiple complications even at the point of diagnosis. In 2003, the Hoorn Screening Study in the Netherlands reported the following at the point of diagnosis: retinopathy (7.6%), impaired foot sensitivity (48.1%), microalbuminuria (17.2%), myocardial infarction (13.3%), ischemic heart disease (39.5%) and peripheral arterial disease (10.6%) [Spijkerman AMW et al., 2003; Spijkerman AMW et al., 2004]. This clearly indicates the insidious onset of organ damage even before diagnosis of DM. Since 1986, glycosylated hemoglobin (HbA1c) has become the standard for assessment of control of DM and by 2006, the gold standard for diagnosis of DM [WHO, 2006]. However, guidelines recommendation for target HbA1c level still varies across the globe [American Diabetes Association, 2012; Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, 2008; Colagiuri et al., 2009; NICE, 2009]. The UK Prospective Diabetes Study (UKPDS) started in 1977 showed that over 10 years, a difference of HbA1c of 0.9% between the intensively treated versus the conventionally treated group decreased the risk of microvascular complications by 25%; however, no difference was observed for macrovascular complications [UKPDS, 1998]. The UKPDS also found that for every 1% reduction in mean HbA1c, there is a corresponding 21% reduction in DM complications, 21% reduction of deaths related to DM, 14% reduction of myocardial infarction and 37% reduction of microvascular complications [Stratton IM et al., 2000]. The Kumamoto study in Type-2 Japanese diabetics on insulin therapy found that with intensive treatment achieving a mean HbA1c of 7% delayed the onset and progression of microvascular complications [Ohkubo Y et al., 1995]. In the Diabetes Control and Complications Trial (DCCT) conducted in Type 1 diabetics for 6 years, a reduction of HbA1c of 2% between the intensively treated to conventionally treated group showed a significant reduction in risk of diabetes complications of about 60% [DCCT, 1993]. These studies

indicated a strong correlation between improvements of glycemic control as assessed by HbA1c to reduction of diabetes complications.

Post UKPDS follow-up study of 10 years found that the reduction of risk in developing complications remained lower in the intensively treated group despite similar HbA1c levels to the controls [DCCT/EDIC group, 2005]. Similarly, the EDIC study that followed up Type 1 diabetics post DCCT trial concluded long-term reduction of cardiovascular risk in the intensively treated group despite worsening of the glycemic control comparable to controls [DCCT/EDIC group, 2005]. This "legacy effect" or "metabolic memory" threw the diabetes management into a glycemic frenzy stage to reduce HbA1c to lower than 6.5% in order to reduce complications and cardiovascular events. Contradicting the risk reduction results, the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study found that lowering the HbA1c level to less than 6.5% significantly increased the mortality and cardiovascular events in type 2 diabetics [The Action to Control Cardiovascular Risk in Diabetes group,2008; Ismail-Beigi F et al., 2010]. Similar studies to intensively lower HbA1c have yet to show any beneficial effect of lowering the HbA1c level below 6.5% [The ADVANCE Collaborative group, 2008; Duckworth W et al.,2009]. Thus, current guidelines support early diagnosis and treatment of DM with 'tailoring' of treatment modalities to target glycemic control. DM management "tailoring" is a broad concept involving multiple factors such as duration of disease, symptoms, presence of complications, age, glycemic control, treatment satisfaction, socio-economic background and etc. How do we judge if the management modality is suitable or is the best for the patient? Besides "chasing" after the HbA1c levels, it is important to consider the well being of the patient reflected by the quality of life (QOL).

The impact of diabetes on QOL was elaborately explained by the UKPDS study group between 1977 and 1991 when they performed two cross-sectional studies of patients enrolled

in randomized controlled trials of intensive blood glucose control versus conventional control group and tight blood pressure control versus less tight control group. QOL was affected by DM complication but not by the treatment regime [UKPDS, 1999]. In the United States, a medical survey done found that QOL decreased in relation to the number of complications. Male gender, longer duration of DM and patients on insulin regime tend to have a poorer QOL [Glasgow RE et al., 1997]. The American findings were supported by a study in Netherlands suggesting that insulin therapy, obesity and complications of diabetes were associated with poorer QOL regardless of age and gender [Redekop W et al., 2002]. The findings are overwhelming but it is crucial to note that QOL is subjective and is perceived differently by different population. In both studies a general QOL tool was used which could lead to reduced sensitivity and data loss. A diabetes specific tool will provide a better reflection of QOL. The tool used to measure QOL is also important to ensure accurate data capture. We will discuss QOL in the Asian context addressing the perception, similarities, differences and the gap in detailed.

Diabetes in Asia

Asia is divided into 5 regions. Central Asia consists of Kazakhstan, Kyrgyzstan, Tajikstan, Uzbekistan, Turkmenistan and Xinjiang of western China. The main religions are Islam and Buddhism. East Asia consists of China, Taiwan, Hong Kong, Japan, South Korea and North Korea. The main religions are Confucianism, Buddhism and Christianity. North Asia is made up of Russia and Mongolia with most of the ethnic groups being composed of nomads. South Asia consists of Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan and Sri Lanka.The main religions are Hinduism, Buddhism, Jainism, Sikhism, Islam and Christianity. South East Asia consists of Burma, Thailand, Laos, Cambodia, Vietnam, Indonesia,

Malaysia, Singapore, East Timor, Brunei and the Philippines. The main religions are Islam, Buddhism, Christianity, and Hinduism. South East Asia also has a lot of Western influence due to the legacy of colonialism. West Asia consists of Middle Eastern countries from to Yemen. The predominant religion is Islam [United Nations, 2012].

DM, previously a disease of the West, has now rapidly become a health crisis in Asian countries. The International Diabetes Federation predicted that the number of individuals with DM will increase from 366 million in 2011 to 552 million in 2030[Whiting DR et al.,2011]. The greatest increase will be contributed by West Asia, India and China [Wild S et al.,2004] The chronicity and complications of the disease threaten the economic growth of developing countries as the global healthcare expenditure for DM is expected to hit USD490 billion in 2030 [Chan J et al.,2009]. A big challenge for Asia is the vast differences in ethnicity, cultures and socio-economic development within Asia, which can affect the clinical presentation, management, prevention of DM and perception of QOL. The Asian population is more diabetogenic compared to the European population. Asians tend to develop DM at a younger age, at lower body mass index and with lesser weight gain [Zhang P et al., 2010; Ramachandran A et al., 2010]. The Asian population is genetically and phenotypically different with stronger genetic link between type 2 DM rather than sporadic autoimmune contribution. [Mohan V et al., 1985; Ng MCY et al., 2001]. Asians have a greater tendency for abdominal obesity resulting in increased insulin resistance [Yoon KH et al., 2006]. Another contributing factor is the shift in lifestyle and dietary habits consistent with the rapid economic development experienced by many developing nations in Asia [Hu FB et al., 2011]. The many different religions in Asia need to be considered when designing a tool for assessing QOL for Asians as spirituality, religion and personal beliefs is highly correlated to psychological and social domains of QOL [WHOQOL SPRB Group, 2006]. Special attention

to ethnicity and language is particularly important in the assessment of QOL not only due to the subjectivity but also the cultural framework essential to the construct [Guarnaccia, 1996]

What is Quality of Life?

Quality of life (QOL) is defined by the Constitution of the World Health Organization (WHO) as "an individual's perception of his/her position in life in the context of the culture and value systems in which he/she lives and in relation to his/her goals, expectations, standards and concerns". QOL is an expansive ranging concept that can be affected by the individual's physical health, psychological state, level of independence, social relationships, personal beliefs and relationship to salient features of his/her environment [WHO,1997]. The current shift of diabetes care from the traditional "glycemic oriented" to a more "holistic patient care" has made QOL an important outcome measure for interventions, making its accurate measurement crucial. Measurement of QOL also provides a mean for measuring the cost impact of medical interventions from the health economic point of view [Read JL, 1993]. DM being a chronic disease, can significantly impact the QOL due to its many complications and to date is still a major cause of mortality, morbidity and high health care expenses [Lloyd A et al., 2001; Brown GC et al., 2000]. People living with DM often endure great stress, both physically in terms of therapy and psychosocially, which can affect the self-care behavior, glycemic control and QOL [Glasgow RE, 1997; Glasgow R et al., 1992].

Impact of westernization in Asia

In Asia especially South East Asia, there is a strong element of Western culture influence or westernization likely due to the history of colonialism. Westernization represents a lifestyle

or behavioral approach to health in epidemiology [Salant T et al., 2003]. DM is considered to be one of the diseases associated with westernization [Fujimoto WY, 1992]. In an extensive review by Fujimoto in 1992, there is a higher prevalence of DM among migrant Asians than in their homeland. This review summarized many of the prevalence studies of DM in migrant Asian populations as well as in their countries of origin [Fujimoto WY, 1992]. This strengthens the point that as Asia become more westernized; insulin resistance and glucose intolerance will become more common. Westernization is linked to globalization and with globalization and economic growth there is a nutrition shift to high consumption of processed food, increased calories and a more sedentary lifestyle [Hu FB, 2011]. The combination of excessive calorie intake and reduced energy output leads to increased obesity and insulin resistance [Hu FB, 2011].

Quality of Life: the Asian Perspective

The developments of QOL assessment instruments were not prominent until the late 70's in North America and Western Europe. Since then, the evolution of QOL measuring instrument development has produced countless well-established and internationally recognized tools. In Asia however, there is a lack of a QOL instrument specifically focused on the diverse ethnic, language, culture, education level, religion and structures of medical care. In view of this complexity, many researchers in Asia chose to translate and adapt instruments developed in Western countries rather than developing a new tool [Cheung YB et al., 2006]. The question lies in the ability of these translated or adapted tools in accurately reflecting the QOL in the complex Asian population. These well recognized tools including the Appraisal of Diabetes (ADS) [Carey MP et al., 1991], Audit of Diabetes Dependent Quality of Life (ADDQoL) [Bradley C et al., 1999], Diabetes Health Profile (DHP) [Meadows et al., 1996], Diabetes

Impact Measurement Scale (DIMS) [Hammond GS et al., 1992], Diabetes Quality of Life Measure (DQOL) [DCCT Research Group, 1988], Diabetes-39 (D-39)[Boyer JG et.al, 1997], Diabetes Specific Quality of Life (DSQOLS) [Bott Uwe et al., 1998], Questionnaire on Stress in Patients with Diabetes Revised (QSD-R)[Herschbach P et al., 1997], the Well-being Enquiry for Diabetics (WED) [Mannucci E et al., 1996], Medical Outcome Study Short Form 36 (SF-36) [Ware Je et al., 1992], and the World Health Organization Quality of Life Brief Questionnaire (WHOQOL-BREF) [Skevington SM et al.,2004] were all developed based on the American or European population. Most of the development process involves focus group discussions to analyze the domains of QOL perceived as important in that population or group of individuals [Garratt Am et al., 2002]. In the recent years, there is increasing apprehension on the quality of the translation process in the adaption of QOL instruments. The concern is mainly focused on the loss of cultural differences during translation and the assumption that perception of QOL remains unchanged across different population [Hunt SM et al., 1993]. A critical systemic review of the translation and adaption process of generic QOL measures in Africa, Asia, Middle East, Eastern Europe and South America indicated that among the QOL tools studied including WHOQOL [Skevington SM et al., 2004], SF-36 [Ware JE et al., 1992], and Euro QOL (EQ5D) [The Euroqol Group, 1990], only 24.2% of these tools measured local conceptions of QOL. Majority of these tools are eager to accept confirmation of validity and reliability as proof of suitability for use in target population without consideration of item equivalent and cultural applicability [Bowden A et al., 2003]. Alice Cheng et al. in 1999 have provided an excellent example in developing and adapting the Diabetes Quality of Life (DQOL) measure in Chinese population with DM [Cheng AY et al., 1999]. In this study, a focus group interview of ten elderly Chinese with Type 2 DM was undertaken to gain their insight of the DQOL measure. Amendments were made based on the discussion to make the DQOL more culturally appropriate. The first adjustment was the

addition of 2 questions on food and eating habits that was deemed important by the focus group. The second was the deletion of two questions on sex life that was considered a taboo subject by the focus group. This new tool is good but there are still a few points that needed highlighting. Firstly, the focus group was mainly formed by elderly Chinese patients and perhaps because of the age factor, sexual relationships may not be an important factor in determining QOL. This cannot be applied across the different age groups with DM who are sexually active and should be considered before removing this component on sexual relationships. Secondly, it has been well-established that diet and food is a major component for Asians especially Chinese [Cheung YB et al., 2006; Cheng AY et al., 1999; Wee HL et al., 2006; Lau A et al., 1998] and the addition of 2 questions on food and eating was a brilliant move by the group albeit not sufficiently reflecting the impact on life satisfaction and QOL. In view of the high weightage placed on diet and food, more in-depth questions should be allocated.

The best solution to overcome the issue of cultural difference lost in translation is by performing equivalence studies in countries with a significant proportion of residents who are proficient in English and their mother tongues. Countries such as Malaysia, Singapore, Indonesia, Brunei, Hong Kong and Philippines are the most suited as both versions of the measurement (English and Asian) can be compared within the same social environment and population. A cross-over trial involving these bilingual subjects can further strengthen the psychometric properties of the instrument including construct validity [Cheung YB et al., 2006; Cheng AY et al., 1999; Thumboo J et al., 2002]. Cross-over trial would mean that the same subject who is proficient in English and the translated language is given both sets of questionnaires to answer and this will show if there are any discrepancies between the two languages. A population-based study was previously conducted in Singapore and found that ethnicity remained an important factor influencing QOL in a multi-ethnic sample of Asians

with diabetes independent of age, gender and education [Wee HL et al., 2006]. However, in this study, the Indian ethnic group was over represented with 47% versus 27% Chinese and 24% Malay. The research question is whether there are any differences across ethnicity and preferred languages with respect to QOL. More studies on multi-lingual Asian populations and perception of QOL are needed. It is undeniable that the Western and Asian population do share commonalities in the domains of physical health, social relationships and life satisfaction. However, the differences in preferences and ranking (i.e. which component of the QOL is more important than others) of certain domains such as social relationships, economic well-being and eating habits must be taken into consideration when adapting or developing a new tool for the different populations in Asia. [Lau A et al., 1998].

Review of Existing QOL Measures

A good example of a valid and reliable generic QOL measurement tool would be the World Health Organization's WHOQOL-BREF questionnaire. This is an abbreviated 26-item version of the WHOQOL-100, which analyzes domains of physical, psychological, social and environment [Skevington SM et al., 2004]. This tool was developed in 2003 using a cross-sectional design across 23 countries. The questions were very basic and choices of answer on a 5 point Likert scale were clear making this tool widely applicable on any disease. However, due to its simplicity, detailed information could not be gathered using this tool. The Medical Outcome Study Short Form with 36 items (SF-36) is a renowned measure of general health and has been validated and broadly used in many eminent studies worldwide [Ware JE et al., 1992, Glasziou P et al., 2007; Boonen A et al., 2007; Brazier J et al., 2004]. This generic tool was developed in 1991 as part of the International Quality of Life Assessment (IQOLA) project. This self-administered questionnaire summarizes health states into eight dimensions

involving physical functioning, role limitations due to physical problems, role limitations due to emotional problems, social functioning, mental health, energy, bodily pain and general health perception [Brazier J et al., 2004].

The EQ-5D questionnaire is a generic measure of QOL developed by the EuroQol group, an international research team from the Netherlands, Sweden and the United Kingdom. This tool defines health in five dimensions— mobility, self care, daily activities, pain and anxiety. The validity and reliability of EQ-5D have been proven and the instrument has been widely used in multiple large-scale studies [The Euroqol Group, 1990; Ellis JJ et al., 2005; Dolan P, 1997; Kind P et al., 1998 ; Barton G et al., 2008]. Nonetheless, the drawback of this popular questionnaire is in the nature of it being less sensitive at the two extremes of health states.

The Diabetes Quality of Life (DQOL) measure was an innovative instrument developed for use in the Diabetes Control and Complication Trial (DCCT) in the early 1980's. The DQOL questionnaire contains 46 items and four dimensions (treatment satisfaction, treatment impact, worry about complications and social issues) which the subjects ranked on a 5-point Likert scale [DCCT Research Group, 1988]. However, this questionnaire was specifically designed for type 1 diabetics with insulin treatment and though it has been tested and validated in Type 2 diabetics, it is still lacking in certain areas for the assessment of non-insulin dependent subjects. Furthermore, having been designed for a much younger population, many of the items in this questionnaire were deemed not appropriate for the elderly population with Type 2 DM [Jacobson AM et al., 1994].

The Revised Diabetes Quality of Life Clinical Trial Questionnaire (DQLCTQ-R) was developed for use in both Type 1 and Type 2 DM [Shen W et al., 1999]. This questionnaire is a result of focus group and expert discussions across Canada, France, USA and Germany.

The strong point of this study is that the validation process is done using the data from clinical trials. This longitudinal data collection appropriately addressed the issue of responsiveness to change that has been understudied in the past due to the cross-sectional method of data collection. The revised version of the questionnaire contains a total of 57 questions addressing 8 domains such as physical function, energy, health distress, mental health, satisfaction, treatment flexibility, treatment satisfaction and frequency of symptoms. It is extremely challenging to develop a QOL assessment tool that can be used accurately and satisfactorily in both type I and type II DM due to the differences between the two. The DQLCTQ-R is a valid and reliable tool that can be used in both types of DM but in our assessment, the questionnaire may not be suitable in the diverse Asian population with different degrees of westernization and food habits. Some of the questions are worded in a way that is not commonly used in the local context of various Asian countries and region and hence may be confusing to the subjects. Some choices of answers were based on a Likert scale of 1-6 with choices such as ‘all of the time’, ‘most of the time’, ‘a good bit of the time’, ‘some of the time’, ‘a little of the time’ and ‘none of the time’ were misleading and difficult to differentiate.

The Diabetes-Specific Quality of-Life Scale (DSQOLS) comprising 64 items on individual goals, satisfaction and perceived burden of DM was originally developed in Germany. The DSQOLS was affirmed to be a valid and reliable tool as it was able to distinguish between patients with different treatment and detect social inequities [Hammond GS et al., 1992]. The questionnaire was validated based on patients with type I DM; hence, this instrument may not be suitable for type 2 diabetics.

Asians and Their Eating Habits

Why is food and eating habits so important to Asians? In Asia, food and eating have complex meanings and implications for different population but in general the activity of eating is viewed in the context of social bonding and interaction, good health, valued leisure activity often involving close friends and family members [Lawton J et al., 2008]. This culture is not only practiced in Asian countries but also strongly rooted in Asian populations living all over the world [Lau A et al., 1998; Wahlqvist ML, 2002]. This preoccupation with food and eating has led to formation of a strong bond between the ability to eat freely, freedom to participate in such social rituals and life satisfaction. The importance of food is reflected in some Asian culture for example in Chinese, Taiwanese, Malaysia, Singapore, Indonesia [Lawton J et al., 2008] that when they meet they would usually greet each other with "Have you eaten?" instead of the Western way of "How do you do?" or "How are you?" It is thus crucial to include this component when assessing the QOL of Asians. There are differences in the diet of various Asian region and population versus the Western diet. Asian consumes a much higher portion of carbohydrates that are high in glycemic index such as white rice, noodles and white bread compared to non-Asian populations [Hu FB, 2011]. This has detrimental effect on diabetes prevalence and diabetes control as Asians tend to store more fat and are at a higher risk of insulin resistance at a lower body mass index [Hu FB, 2011]. Reviewing the literature, there is a lack of questions assessing diet and eating habits. The diabetes-specific QOL (DSQOL) instrument did ask about diet satisfaction and burden of giving up tasty food but such questions were lacking in other QOL assessment tool that was designed for type 2 diabetics. The DQLCTQ-R focused more on the amount and flexibility of making choices in meals rather than the satisfaction issue [Shen W et al., 1999]. A more in-depth study to look at the impact of food and eating habits on QOL in Asian diabetics is warranted.

Economic Well-being

Economic well-being is strongly linked to good living and life satisfaction and is ranked highly as an important factor in QOL [Lau A et al., 1998]. Out of pocket payment are the principal means of financing healthcare in most part of Asia [Van Doorslaer E et al., 2007]. Van Doorslaer et al. in 2006 estimated the magnitude and distribution of out-of-pocket expenses for health care in 14 countries, amounting to 81% of Asian population found heavy reliance on out-of-pocket financing of health care in Asia [Van Doorslaer E et al., 2007]. The burden of medical cost is often borne by the state government or by the patients themselves. This is especially important for DM because of the chronicity of the disease and the potential to develop multiple arrays of complications incurring exorbitant medical costs in terms of drugs, procedures and disease monitoring. Assessment of financial burden is important and this is especially true with inflation of medical cost leading to high financial burden and affecting QOL. The WHO-QOL used the most simple and general question by asking subjects if they have "enough money to meet their end", whereas in SF-36 there were no mention of financial component assessment [Ware JE et al., 1992; Garratt AM et al., 2002]. This is not sufficient to explore the economic stability of the subject and issues of financial constraints of medical costs, worries on future medical costs should be included to accurately reflect the QOL domain.

Physical Health Assessment

Assessment of physical function remains a very important basic component of all QOL tools available as the ability to go through daily activities independently and freely is considered a major determinant of QOL. This statement is supported by many studies worldwide and one of the study on diabetic neuropathy found that patients with chronic symptomatic diabetic

peripheral neuropathy has impaired QOL especially in the domains of physical mobility, emotion, energy and sleep [Benbow SJ et al., 1998]. These questions: “To what extent do you feel that physical pain prevents you from doing what you need to do?,” “How well are you able to get around?,” and “How satisfied are you with your ability to perform your daily living activities?” were developed by the WHO in the WHOQOL-BREF questionnaire to assess the physical mobility of subjects and satisfaction of the ability [Skevington SM et al., 2004].

However, some of the questions were rather confusing; for example, in item 4 “How much do you need any medical treatment to function in your daily life?”, item 9 “How healthy is your physical environment?” and item 13 “How available to you is the information that you need in your day to day life?”, hence making this questionnaire less suitable to be widely used in our Asian population as the patients may not be able to understand the actual meaning of the question. In SF-36, the questions asked were more detailed about certain limitation to specific activities of daily living that the author deemed important such as running, lifting groceries, climbing stairs, bending, kneeling or stooping. The DSQOLS, a disease-specific QOL tool also incorporated physical function assessment and physical activity satisfaction as part of their domain but being designed for type 1 diabetics, majority of the questions were aimed at the younger age group and those on insulin treatment [Bott UWE et al., 1998]. The DQLCTQ-R assessed the physical functions by asking detailed questions about limitation to perform certain daily activities in the last 4 weeks. However, though more detailed, the questions were more confusing in terms of the different modes of answer choices. Accurate assessment of physical function or limitation is utmost important in determining QOL and hence the questions must be simple yet relevant to the local lifestyles.

Psychosocial Assessment

Depression, being one of the most important patient-related co-morbidity of any chronic disease (DM in the context of this study), could significantly affect the patient's QOL. A much higher prevalence of depression in diabetics (24%), compared to non-diabetics (17%) was reported [Goldney RD et al., 2004]. A study conducted by the Harvard Medical School in 2008 demonstrated a strong relationship between depression and poor diabetes care [Gonzalez JS et al., 2008]. Nonetheless, this study also showed only small to medium range of effect of depression on medication concordance [Gonzalez JS et al., 2008]. Over the years, there are numerous studies eliciting a correlation between depression and poor glycemic control, leading to functional disability in diabetics, highlighting the importance of early detection and proper management of depression in order to maintain the highest possible standards of life in diabetics [Egede LE, 2004]. Psychosocial and emotional stability of diabetic patients has been identified by studies worldwide as an important domain as it can affect the QOL, compliance, control and outcome of treatment. Most of the QOL assessment tools are aimed at detecting early symptoms of depression or emotional instability. However, the accuracy of such assessment is still questionable as in order to diagnose depression, detailed questions are unavoidable and hence will make the tool too tedious. The SF-36 uses questions such as Item 9A, "Did you feel full of prep in the last 4 weeks?" and item 9F "Have you felt downhearted and blue for the past 4 weeks?" The structure of the sentences and the vocabulary used made these sentences rather difficult for our Asian population to comprehend. Similar questions were also noted in the DQLCTQ-R. In WHOQOL-BREF, only one question was noted asking if subjects have experienced any negative feelings such as "blue mood, despair, anxiety and depression." In many developing countries in South East Asia, stigmatization against people with psychiatric disorder or mental illness is still very widespread compared to the Western world [Lauber C et al., 2007]. Accurately assessing

symptoms of depression becomes extremely challenging, as the subjects are not willing to divulge honest answers due to fear of stigmatization.

Sexual Dysfunction in Asians

The topic of sex and sexuality is considered a taboo in Asia and is not comfortably discussed in public. However, the prevalence of sexual dysfunction in both genders is significantly higher in Asian population with DM— 63.6% reported erectile dysfunction and 23.3% in women [Siu SC et al., 2001; Nicolosi A et al., 2005]. A study on sexual behavior and dysfunction and help-seeking patterns in the urban population of Asians was carried out in China, Taiwan, South Korea, Japan, Thailand, Singapore, Malaysia, Indonesia and the Philippines found that although sexual dysfunction is prevalent in the middle age group, socio-cultural factors seem to prevent the afflicted individuals from seeking treatment [Nicolosi A et al., 2005]. Self-reported questionnaire is the best way to capture such delicate data from the Asian population [Hisasue S et al., 2005; Nicolosi A et al., 2005]. It is vital that this component be included in the QOL measurement tool to accurately reflect the impact of sexual dysfunction on QOL. The score obtained from the self-reported QOL tool could also help the doctor or health care personnel to detect problems of sexual dysfunction for further action without causing any embarrassment or discomfort to the patient.

Conclusion

There is a global shift of diabetes care from "gluco centric" to holistic approach. The diverse culture, language, religion and complexity of socio-economic differences between Asia possess a big challenge for diabetes prevention, management, education and counseling. There is an increase of diabetes prevalence in Asia but still a lack of QOL assessment tool built specifically for Asians. Most of the available QOL assessment tool are adapted or translation from the American or European. Being constructed for the Western population, the problem of item equivalence and cultural relevant exists and must be addressed in order to get a true reflection of QOL in the Asian population. Different regions of Asia have different population group and it is recommended that for every population, a focus group consisting of an acceptable number of individuals from different age, culture, religion and socio-economic background is established to assessed the perception of QOL in that particular population of Asian. This important in capturing the essence of QOL domains that is important for Asians. In order to overcome translation problems it is recommended that an equivalence study be conducted in bilingual respondents. With such a specific QOL assessment tool constructed based on the multi-lingual Asian population that is stable across the different cultures, ethnicities, languages, religion and socio-economy within Asia, the physician will be at a better advantage to "tailor" the management of DM in Asians.

CHAPTER THREE: DEVELOPMENT AND VALIDATION OF THE ASIAN DIABETES QUALITY OF LIFE QUESTIONNAIRE (ASIANDQOL)

Presented in part as poster presentation at the International Diabetes Federation World Diabetes Congress December 2013 in Melbourne Australia (Appendix 2)

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CHAPTER 3: Development and validation of the Asian Diabetes Quality of Life questionnaire (AsianDQOL)

The following paper describe the development and validation process of the AsianDQOL in English, Malay language and Chinese-Mandarin.

3.1 Abstract:

Aim: The aim is to construct a type-2 diabetes mellitus specific quality of life (QOL) tool for Asian populations that is valid and reliable across different ethnicities, languages, and socio-economic backgrounds. **Methods:** A focus group determined the domains affecting QOL in consultation with an expert group. A pilot study was conducted to validate the Asian Diabetes QOL (AsianDQOL) in English, Malay and Chinese- Mandarin. The World Health Organization Brief Quality of Life Questionnaire (WHOQOL-BREF) was used for comparison. Exploratory factor analysis (EFA), reliability analysis (RA) using Cronbach's alpha and test-retest reliability, and confirmatory factor analysis (CFA) using structural equation modelling (SEM) was undertaken using the statistical software IBM SPSS Statistics version 20. **Results** EFA with eigen values ($\geq$1) and factor loadings $\geq$ 0.3 for English and Malay language demonstrated 21 items and 5 components. CFA (English version) confirmed the model fit (CMIN 201.08, p-value 0.071, GFI 0.88, RMSEA 0.036, CFI 0.978). CFA (Malay version) confirmed the 5-factor model(CMIN 189.39, p-value 0.085, GFI 0.937, RMSEA 0.025, CFI 0.987). The corresponding Cronbach's alpha scores (English version) were 0.917, 0.818, 0.816, 0.749 and 0.719, respectively. The Malay version scored 0.833, 0.819, 0.816, 0.775, 0.673, respectively whilst the Chinese/Mandarin version scored 0.890, 0.719, 0.826, 0.862 and 0.759, respectively. Test-retest reliability showed Spearman's correlation of 0.664 (English version), 0.736 (Malay version) and 0.553(Chinese-Mandarin version). A scoring system was generated based on the 25th, 50th and 75th centiles for all the

three languages. **Conclusion** The AsianDQOL is a valid, reliable and stable tool for assessing QOL in multi-ethnic and multi-lingual T2DM Asian populations.

3.2 Introduction

Diabetes mellitus (DM) is a growing worldwide epidemic and Asia will bear 60% of the world diabetic population [Chan J et al., 2009]. Malaysia is a multi-ethnic, multi-cultural and multi-religious country in South-east Asia experiencing the diabetic epidemic. The first National Health and Morbidity Survey (NHMS I) in 1986 showed the prevalence of DM to be 6.3% that has increased to 8.3% in 2006 [Letchuman GR et al., 2010], and escalated to 22.6% by 2010[Wan Nazaimoon WM et al., 2013].

Quality of Life (QOL) is defined by the World Health Organization (WHO) as "an individual's perception of his/her position in life in the context of the culture and value systems" [Saxena S et al., 1997]. Generic tools cover a range of QOL dimensions in a single questionnaire while disease specific tools measure only relevant dimensions pertaining to the specific illness [Jacobson AM et al., 1994; Jacobson AM et al., 1996].

DM has profound effects on the social, psychological and physical well being of a person making the management of DM a complex and tedious process for both the patient and the health care professionals. Before the development of QOL tools, biochemical or clinical assessment were the only indicators of disease outcome. These measures do not reflect the psychological and social state of the patient. Psychosocial impact of DM is one of the five strongest predictors of mortality in diabetic patients, surpassing the importance of clinical and physiological variables [Hanestad BR et al., 1991]. However, QOL measurement remains elusive with many contributing factors that are dependent on the individual's perception. The challenge lies in accurately reflecting subjective perception of QOL into objective scores for assessment. In order to do this, the tool must be sensitive and relevant to the local population

as different languages, races, cultures, socio-economic progress and religious beliefs within the population can have a significant direct or indirect effect on the QOL.

Ethnic disparities are important in determining the prevalence, care, treatment outcomes and QOL of diabetics as shown by many international studies including the San Antonio Heart Study (SAHS)[Hong CY et al., 2004; Cowie CC et al., 1989; Abate N et al., 2004; Mitchell BD et al.,1990]. A population-based study in Singapore reported that ethnicity is an important factor influencing QOL [Wee H-L et al., 2006]. This study was conducted across a multiethnic sample sharing the same sociocultural background similar to Malaysia. The Medical Outcome Study Short form 36 (SF-36) were used [Ware JE et al., 1992; Brazier J et al., 2002]. The SF-36 English and Mandarin versions were previously validated for use in Hong Kong and Singapore [Thumboo J et al., 2001; Lam CLK et al., 1999]. The SF-36 Mandarin version is a direct translation of the English version [Lam CLK et al., 1999]. The constructs of the questionnaire were mainly based on these Western populations and may not be accurate in the Asian population. A focus group to review the construct of SF-36 as part of the local QOL conceptual measurement will strengthen the usage of this tool [Bowden A et al., 2003]. Both questionnaires used in the study were not disease-specific. The Chinese population answering the SF-36 in Chinese was thus not assessed for their cultural differences.

In Malaysia, the population is almost similar but there are 65% Malays, 25% Chinese and 10% Indian and others. Many Malaysians, irrespective of their ethnicities, are educated in English and are highly westernized. However, there are also Chinese who are educated in Mandarin and retain their values similar to the Indians who were brought up in Tamil schools. The preferred language usually reflects their cultural values. The early education medium will influence the perception, cognition, behavior and lifestyle of the individual regardless of ethnicity. Having this in mind, we decided to develop a new diabetes QOL tool

in English so as to be able to incorporate the different ethnic groups (Malay, Chinese and Indian) to gain their input in the construction of this tool.

We choose the Malaysian population because it gives a fair representation of the diverse composition of different ethnic groups similar to many countries in Asia.

The primary aim is to construct a DM-specific QOL tool built specifically for the Asian population, which is valid, sensitive and reliable across different ethnicities, languages, and socio-economic backgrounds.

3.3 Methods/Design

Ethnics clearance was granted by the Monash University Human Research Ethics Committee (MUHREC), approval no CF2630 – 2011001537(Appendix 3). Written informed consent was obtained from all participants (Appendix 4).

3.3.1 Construction of the questionnaire

The questionnaires were constructed based on focus group discussions. Focus groups are a form of group interview that relies on communication between researcher and participants to generate data [Kitzinger J, 1995]. The number of participants will depend on the aims and the available resources [Kitzinger J, 1995]. The English language focus group consisted of 30 subjects with T2DM. Ten subjects were of Malay ethnicity, 10 Chinese and 10 Indians. They were of different gender, age groups, duration of DM and socio-economic background with English as their common mode of communication. Individual interviews were conducted to assess factors that they felt would affect their QOL in terms of priority. The Malay language focus group consisted of 10 individuals (6 Malays, 2 Chinese and 2 Indians). The same interview process as for the English language was conducted. The Chinese-Mandarin focus

group comprised of 10 Chinese participants. They were mainly Chinese-educated and preferred Mandarin as their main language of communication. The English focus group members were different from the other two languages. The expert group consisting of two endocrinologists, general practitioners, a public health expert and a diabetic nurse were sought on the factors that could affect a patient's QOL. The primary role of the expert group is to edit and supervise the development process. The content of the new QOL tool focused on the important measures of QOL in East Asia population. Existing QOL questionnaires such as the Diabetes Quality of Life Clinical Trial Questionnaire Revised (DQLCTQ-R), Diabetes Specific Quality of Life (DSQOL), Audit of Diabetes Dependent Quality of Life (ADDQoL), SF-36 and World Health Organization Quality of Life Brief (WHOQOL-BREF) were used as references [Ware JE et al., 1992; Carey MP et al., 1991;Bradley C et al., 1999; Meadows K et al.,1996; Hammond GS et al., 1992; DCCT Research group, 1988; Boyer JG et al., 1997; Bott UWE et al., 1998; Herschbach P et al., 1997; Mannucci E et al., 1996; Shen W et al., 1999; Skevington SM et al., 1999]. An initial questionnaire in English and Malay language was drafted based on findings of the focus group discussion. This initial draft comprised of 30 questions. The choices of answers were in a 5- point rating scale ranging from "very dissatisfied" to "very satisfied". Each answer was given a score. As part of the face validation, the expert group panel commented on the structure of the questions, the choices of answers provided and the relevance of question to our local population. Multiple revisions were made based on the feedbacks and the final draft of the English and Malay language consisted of 21 questions altogether. The initial Chinese-Mandarin version had 25 items in total and 7 items were later removed due to repetition, vague structure and being less important. Subjects participated in the focus group were excluded from participation in the pilot study for validation purpose.

3.3.2 Validation of the Asian Diabetes Quality of Life (AsianDQOL) questionnaire in English

A pilot study was conducted and the WHOQOL-BREF edition 2004 in English (Appendix5) was co-administered for comparison [Yao G et al., 2002]. WHOQOL-BREF is a generic tool that was proven to be valid and reliable in chronic diseases such as DM [Yao G et al., 2002; Hsiung PC et al., 2005]. It is also available in English, Mandarin and Malay language [Eren I et al., 2008; Hasanah CI et al., 2003]. Permission was obtained from the WHOQOL group. A total of 136 subjects were recruited. Inclusion criteria were patients with T2DM with or without pharmacological treatment, above 18 year's old have, completed at least primary education and is able to give written consents. Exclusion criteria were subjects with concurrent Parkinson's disease, Alzheimer's disease, dementia or severe visual impairment, or with mental illness and unable to give valid consents.

Subjects recruited were English-educated of different races, gender, religion and socio-economic background residing in Malaysia. Basic demographics data collected are shown in Table 1. Medical history taken covers concomitant medical illness, years of having DM, drug and surgical history. Physical examination was done to assess blood pressure, height, weight and signs of diabetic complications. Subjects were given both questionnaires to fill in an area provided to respect their privacy. The questionnaires were given randomly with no specific order of presentation to avoid order effect. The same sets of questionnaires were given to them in lesser than six weeks interval.

3.3.3 Validation of the AsianDQOL (Malay) language and AsianDQOL Chinese (Mandarin) language.

A total of 250 patients with T2DM of different ethnic groups were recruited for validation of the Malay language version. Inclusion and exclusion criteria remained the same as for the

validation in the English language version. Medical history and physical examination was done as previous. Subjects then completed the AsianDQOL (Malay) and the same cohort of patients retested on the same questionnaire in less than 6 weeks apart.

The validation of the AsianDQOL Chinese language in Mandarin involved 62 subjects. They were retested in less than 6 weeks apart. The statistical analysis as done before to validate the English version was applied to the Malay and Chinese Mandarin versions as well. Subjects recruited for validation of the English version were different from those in the Malay and Chinese Mandarin group.

3.3.4 Statistical analysis

Data gathered were analyzed using the statistical software IBM SPSS version 20 for validation of the questionnaires. The American Psychological Association in 1985 states that in order to develop a new scale, the measure should demonstrate content validity, criterion-related validity, construct validity, and internal consistency [Hinkin TR, 1995]. Content validity refers to the adequacy of the measure to assess the domain of interest. Criterion-related validity refers to the relationship between the measure and another independent measure. Construct validity is the relationship of the measure to the underlying attributes it is attempting to assess and internal consistency refers to the homogeneity of the items [Hinkin TR, 1995].Factor analysis to uncover the underlying structure of a large set of variables was done. Factor analysis is a multivariate statistical procedure to reduce a large number of variables into a smaller set of variables. It is also used to establish underlying dimensions between measured variables and latent constructs and to provide construct validity evidence of self-reporting scales [Williams B et al., 2012]. There are two classes of factor analysis: Exploratory factor analysis (EFA) and Confirmatory factor analysis (CFA). EFA allows the researcher to explore the main dimensions to generate a theory or model from a large set of

latent constructs without any expectations of the number of variables [Swisher LL et al., 2004; Williams B et al., 2012]. CFA is used to test a proposed theory and has fixed assumptions and expectations based on prior theories regarding number of factors [Swisher LL et al., 2004; Williams B et al., 2012].

3.3.4.1 Exploratory factor analysis

There are five steps involved in EFA. The first step is to ensure adequate sample size. Search of literature resulted in varying opinions and lack of agreement on sample size recommendation for EFA[Hogarty K et al., 2005]. However, in order to assess the suitability of the respondent data for factor analysis, several tests should be done. The Kaiser-Meyer-Olkin (KMO) Measure of Sampling Adequacy and Bartlett's Test of Sphericity is recommended [Williams B et al., 2012; Bartlett MS, 1950]. The KMO index of 0.50 is considered suitable for factor analysis and the Bartlett's Test of Sphericity should be significant ($p<0.05$). The second step is to determine how will the factors be extracted. There are numerous ways to extract factors such as principal component analysis (PCA), principal axis factoring, image factoring, maximum likelihood, alpha factoring and canonical [Williams B et al., 2012]. PCA is the most commonly used and is also recommended when no prior theory or model exists [Williams B et al., 2012]. The third step is to determine the criteria that will assist in determining factor extraction. Thompson B et al in 1996 suggested the use of multiple decision rules rather than single criteria [Thompson B et al., 1996]. Among the many extraction rules and approaches are Kaiser's criteria (eigenvalue> 1 rule), the Scree test, the cumulative percent of variance extracted, and parallel analysis. The fourth step is to determine the rotational method. Rotation maximizes high item loadings and minimizes low item loadings producing a more simplified solution [Williams B et al., 2012].

The main objective of rotation is to provide easier interpretation of results and produce a more parsimonious solution [Kieffer KM, 1999]. The available rotation techniques and option are the orthogonal Varimax or orthogonal quartimax and oblique olbimin or oblique promax. The most common rotational technique used in factor analysis is orthogonal Varimax, which produce uncorrelated factor structures [Costello et al., 2005]. The result of rotation will allow the researcher to examined items that did not load or were unable to be assigned to any factors and decide if the items should be discarded. The final step involves interpretation of results whereby the examiner will determine which variables are attributable to a factor and giving a name or theme to that factor. It is recommended that at least two or three variables must load on a factor to be meaningful [Henson RK et al., 2006]. It is important to ensure that the labels or contructs reflect the theoretical and conceptual intent [Williams B et al., 2012].

3.3.4.2 Confirmatory factor analysis

CFA is a theory driven confirmatory technique. The planning of the analysis is drive by the theoretical relationships among the observed and unobserved variables. Observed variables are designated graphically by a square or rectangle. Unobserved variables or latent factors are depicted graphically with circles or ovals. In reference to model fit, researchers use numerous goodness-of-fit indicators to assess a model [Schreiber JB et al., 2006]. Some of the common fir indexes are the Normed Fit Index (NFI), Non-Normed Fit Index (NNFI), Incremental Fit Index (IFI), Comparative Fit Index (CFI), and Root mean square error of approximation (RMSEA). Hu and Bentler in 1999 suggested that for continuous data, RMSEA<0.06, TLI>0.95, CFI>0.95 [Hu LT et al., 1999]. The fit indexes cutoff levels for determining model fit are illustrated in a chart. (Table 1)

Table 1 Cutoff Criterion for Several Fit Indexes

Indexes	Shorthand	General rule for acceptable fit if data are continuous	Categorical
Absolute/predictive fit			
Chi-square	X^2	Ratio of X^2 to *df* ≤ 2 or 3, useful for nested models/model	
Akaike information criterion	AIC	Smaller the better; good for model comparison(nonnested) not a single model	
Browne-Cudeck criterion	BCC	Smaller the better; good for model comparison, not a single model	
Bayes information criterion	BIC	Smaller the better; good for model comparison(nonnested) not a single model	
Consistent AIC	CAIC	Smaller the better; good for model comparison(nonnested) not a single model	
Expected cross-validation index	ECVI	Smaller the better; good for model comparison(nonnested) not a single model	
Comparative fit		Comparison to a baseline(independence) or other model	
Normed fit index	NFI	≥ 0.95 for acceptance	
Incremental fit index	IFI	≥ 0.95 for acceptance	
Tucker-Lewis index	TLI	≥ 0.95 can be 0> TLI>1 for acceptance	0.96
Comparative fit index	CFI	≥ 0.95 for acceptance	0.95
Relative noncentrality fit index	RNI	≥ 0.95, similar to CFI but can be negative, therefor CFI better	
Parsimonious fit			
Parsimony-adjusted NFI	PNFI	Very sensitive to model size	
Parsimony-adjusted CFI	PCFI	Sensitive to model size	
Parsimony-adjusted GFI	PGFI	Closer to 1 the better, though typically lower than other indexes and sensitive to model size	
Other			
Goodness-of-fit index	GFI	≥ 0.95 Not generally recommended	
Adjusted GFI	AGFI	≥ 0.95 Performance poor in simulation study	
Hoelter 0.05 index		Critical N largest sample size for accepting that model is correct	
Hoelter o.o1 index		Hoelter suggestion, N=200, better for satisfactory fit	
Root mean square residual	RMR	Smaller, the better;0 indicates perfect fit	
Standardized RMR	SRMR	≤ 0.08	
Weighted root mean residual	WRMR	<0.90	<0.90
Root mean square error of approximation	RMSEA	<0.06 to 0.08 with confidence interval	<0.06

3.3.4.3 Reliability assessment

There are two components of reliability assessment; consistency of items within a measure and stability of the measure over time. The most commonly accepted measure is internal consistency reliability using Cronbach's Alpha score [Hinkin TR, 1995]. It is recommended that an alpha score of 0.70 be the minimum acceptable standard for demonstrating internal consistency [Hinkin TR, 1995]. However, some researcher may retain items with lower factor loadings due to conceptual importance. Stability of a measure is assessed by test-retest reliability. Concordant reliability was carried out by comparing the reliability coefficient of the new tool to WHO-QOL BREF.

3.4 Results

Demographic data of the 136 subjects recruited for the English version are depicted in Table 2. Eighty-seven subjects were men (64%) and 49 (36%) women. The mean age was 53 and duration of DM was 16 years (Table 2). Differences were detected for types of occupation ($p<0.05$) and mode of treatment ($p<0.05$). Some differences were present for hypertension ($p<0.05$), hyperlipidemia ($p<0.05$), cardiac disease ($p<0.05$), and erectile dysfunction ($p<0.05$). (Table 2)

Table 2 Demographic, co-morbidities and treatment characteristics of the English, Malay and Chinese -Mandarin groups

Characteristics	English No. (%)	Malay No. (%)	Chinese Mandarin No. (%)	Significance P<0.05
Gender				0.840
Men	87(64)	157(62)	36(58)	
Women	49(36)	96(38)	26(42)	
Marital status				0.003
Married	120(88)	226(89)	49(79)	
Single	16(12)	13(5)	8(13)	
Others	0(0)	14(6)	5(8)	
Mean age +SD(year)	53 ± 11	53 ±11	58 ±12	0.870
Education Level				0.740
Secondary school	54(40)	109(43)	24(39)	
Tertiary and above	82(60)	143(57)	37(60)	
Occupation				0.001
Working full-time	77(57)	134(53)	22(36)	
Working part-time	15(11)	14(6)	6(10)	
Unemployed/Not working	13(10)	40(16)	4(7)	
Retired	31(23)	65(26)	30(48)	
Duration of DM (year)	16	14	12	0.470
Co-morbidities				
Hypertension	73(54)	146(58)	47(76)	0.011
Hyperlipidemia	66(49)	115(46)	39(63)	0.048
Cardiac disease	36(27)	39(15)	13(21)	0.030
Visual problems	31(23)	79(31)	22(36)	0.11
Nerve problems	42(31)	75(30)	15(24)	0.62
Sexual dysfunction	35(26)	69(27)	10(16)	0.19
Peripheral vascular disease	0(0)	5(2)	3(5)	0.05
Renal problems	5(4)	8(3)	2(3)	0.96
Erectile dysfunction	40(46)	64(41)	7(19)	0.02
Vaginal problems	6(12)	18(19)	6(24)	0.42
Type of treatment for DM				0.02
Diet therapy alone	7(5)	22(9)	0(0)	
Oral pills only	87(65)	143(61)	46(74)	
Insulin only	8(6)	20(9)	1(1)	
Oral pills and insulin	29(22)	45(19)	11(18)	
Not on any treatment	2(2)	3(1)	3(5)	
Diet therapy and pills	0(0)	0(0)	1(2)	

KMO measure for sampling adequacy for English language was 0.761, Malay language 0.798 and Mandarin 0.653. The Bartlett's test of sphericity showed significant p-value for all the three languages indicating that the sample size was adequate for factor analysis. (Table 3)

Table 3 KMO and Bartlett's test

		English	Malay	Mandarin
Kaiser-Meyer-Olkin Measure of Sampling Adequacy		0.761	0.798	0.653
Bartlett's test of Sphericity	Sig.	0.000	0.000	0.000
Cumulative %		67	62	73

EFA of the English version showed 21 items and 5 components. (Table 4) CFA confirmed the model fit (Fig.1) (CMIN 201.08, p-value 0.071, GFI 0.88, RMSEA 0.036, CFI 0.978) (Table 5). Reliability analysis showed component on financial (5 items) scored 0.917, energy levels (3 items) scored 0.818, memory and cognition (4 items) scored 0.816, relationship (3 items) scored 0.749 while diet (6 items) scored 0.719 (Table 6). Analysis done on the total score (English) showed a non-normal distribution, the median score 81, the 25th centile score 74 and 75th centile 88. Based on this, it was decided that for the AsianDQOL (English), a score of 74 points and below is considered poor, 75-81 moderate, 82-88 good and above 88 points is excellent QOL. (Table 7)

Table 4 EFA for English language

	Component				
	1	2	3	4	5
Financial					
Future medical expenses	0.904				
Medical cost	0.897				
Financial burden family	0.843				
Medical Expenses difficulties	0.840				
Financial burden	0.799				
Diet					
Eating habits		0.756			
Satisfied diet		0.065			
Sad about diet		0.692			
Left out		0.675			
Enjoy diet		0.630			
Burden diet		0.500			
Memory and cognition					
Recent recall			0.873		
Old recall			0.773		
Memory			0.799		
Recognition			0.713		
Energy					
Quality of work				0.871	
Activities				0.871	
Weak tired				0.561	
Relationship					
Relationship with partner					0.876
Sexual problem					0.874
Sexual desire					0.669

Rotation: Varimax with Kaiser Normalization. Rotation converged in 6 iterations.

Table 5 Summary of goodness of fit for English and Malay language

	Recommended value	English	Malay
Model chi-square (p-value)	p>0.05	201 (p=0.07)	189 (p=0.09)
Degree of freedom		173	164
Root mean square error of approximation(RMSEA)	Less than 0.07	0.036	0.025
Goodness of fit (GFI)	Values greater than 0.95	0.88	0.94
Comparative fit index (CFI)	Values greater than 0.95	0.98	0.99

Figure1 CFA English language

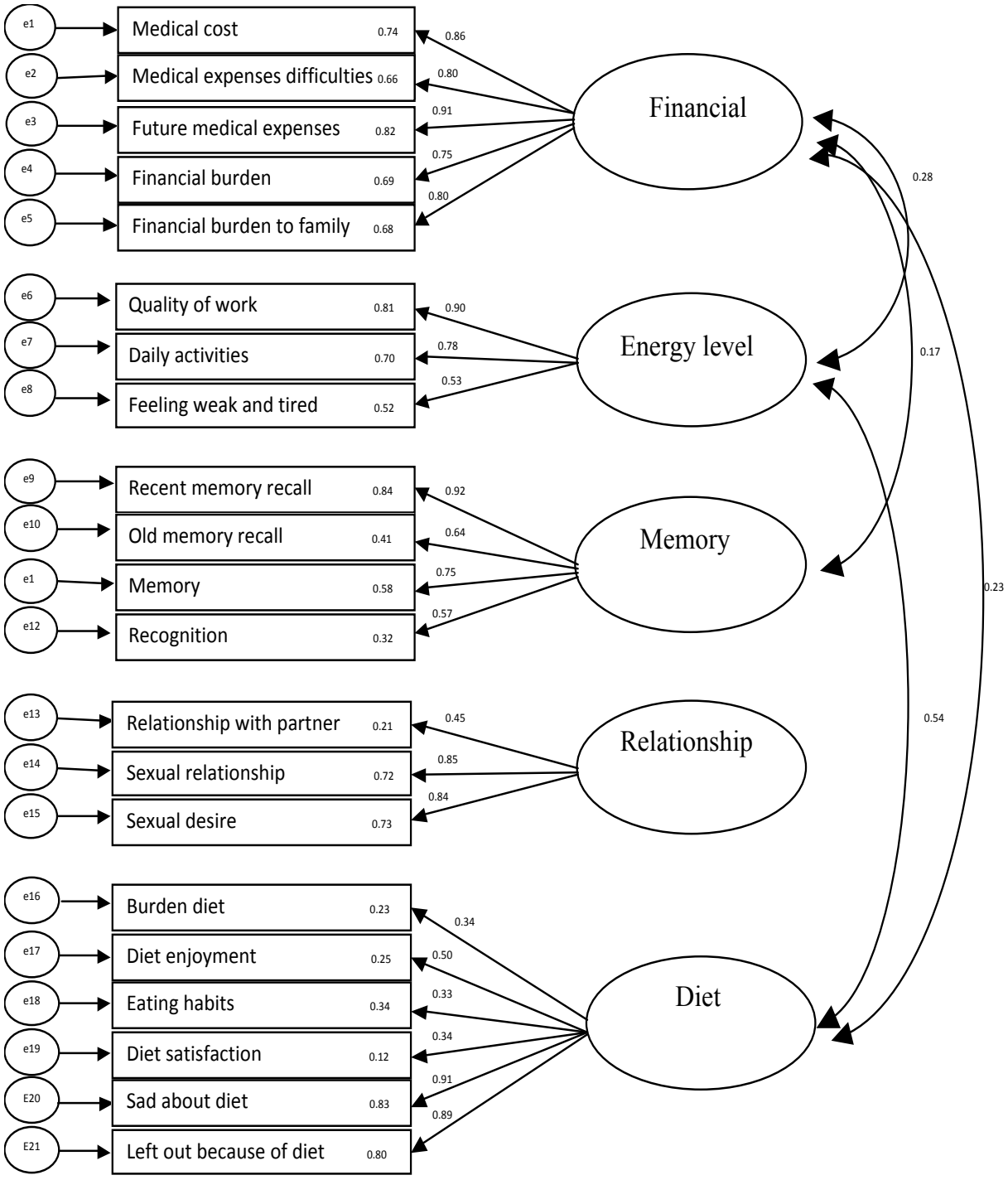


Table 6 Component analysis of the 3 languages

Component	Cronbach's Alpha score	No of items
English		
Financial aspects	0.92	5
Energy levels	0.82	3
Memory	0.82	4
Relationships	0.75	3
Diet	0.72	6
Malay/Indonesian		
Financial aspects	0.83	5
Energy levels	0.82	4
Memory and cognition	0.82	4
Relationships	0.78	4
Diet	0.67	4
Chinese-Mandarin		
Financial aspects	0.89	6
Relationships	0.86	3
Memory	0.83	2
Diet and activities	0.76	4
Energy levels	0.72	3

Table 7 AsianDQOL score

	Poor	Moderate	Good	Excellent
English	≤74	75-81	82-88	≥89
Malay/Indonesia	≤76	77-85	86-91	≥92
Chinese-Mandarin	≤64	65-70	71-79	≥80

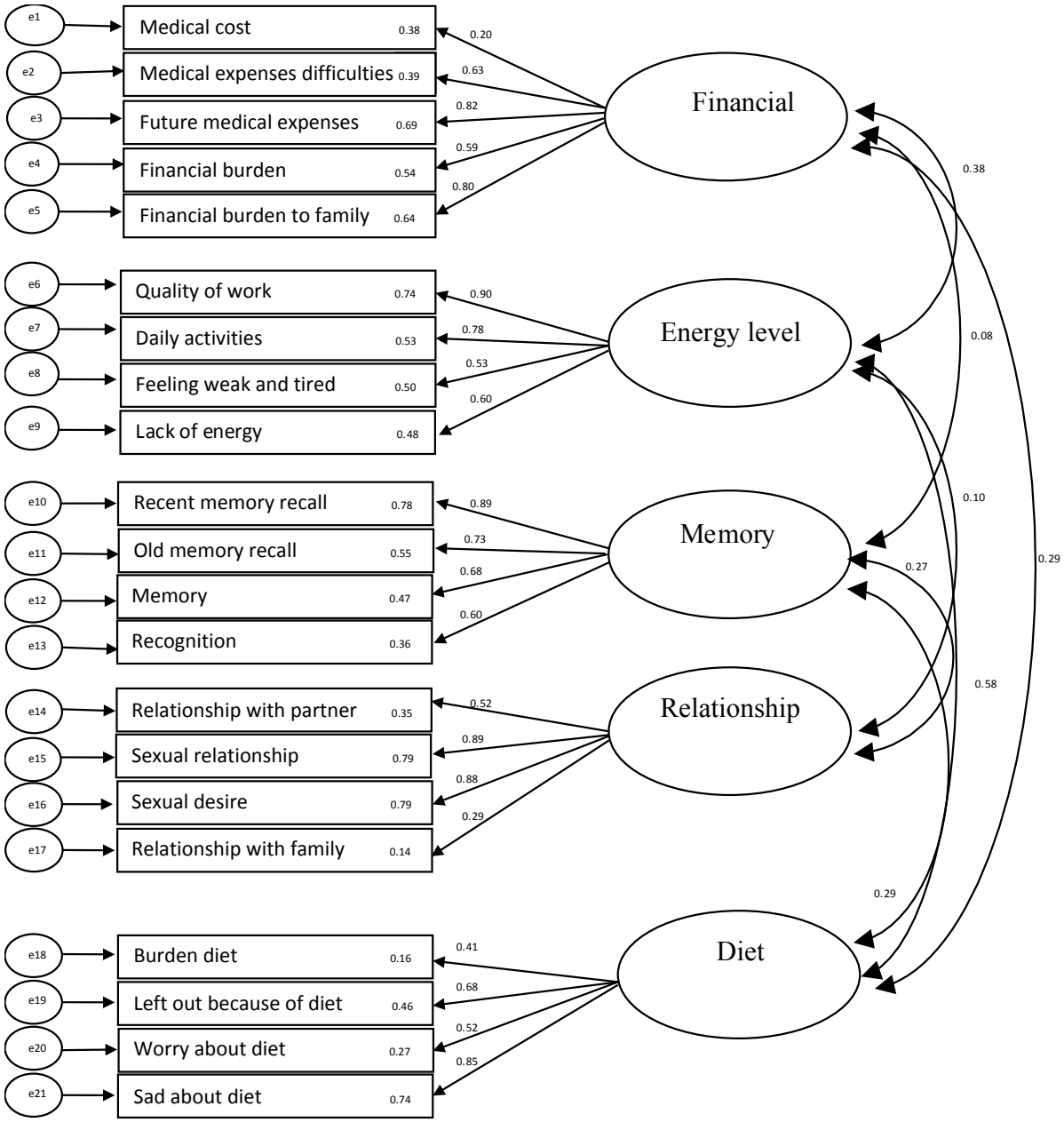
Subsequently, EFA for the Malay language demonstrated 21 items and 5 components (Table 8). CFA confirmed the 5-factor model (Fig.2) (CMIN 189.39, p-value 0.085, GFI 0.937, RMSEA 0.025, CFI 0.987)(Table 5). The component on financial scored 0.833, energy levels scored 0.819, memory and cognition scored 0.816, relationship scored 0.775 and diet scored 0.673 (Table 6). The scores from the Malay/Indonesian language were also non-normal with a median of 85, 25th centile of 76, and 75th centile 91 points. The AsianDQOL (Malay) scoring system of 76 points and below is considered poor, 77-85 moderate, 86-91good and above 91 points is excellent QOL, almost similar to that for the English AsianDQOL scoring system. (Table 7)

Table 8: EFA of Malay language

	1	2	3	4	5
Financial					
Future medical expenses	0.822				
Medical cost	0.660				
Financial burden family	0.814				
Medical Expenses difficulties	0.721				
Financial burden	0.747				
Diet					
Sad about diet		0.772			
Left out		0.757			
Worry about diet		0.518			
Burden diet		0.642			
Memory and cognition					
Recent recall			0.839		
Old recall			0.808		
Memory			0.771		
Recognition			0.695		
Energy					
Quality of work				0.810	
Activities				0.683	
Weak tired				0.805	
Lack of energy				0.713	
Relationship					
Relationship with partner					0.748
Sexual problem					0.875
Sexual desire					0.858
Relationship with family					0.520

Rotation: Varimax with Kaiser Normalization. Rotation converged in 6 iterations.

Figure 2: CFA of Malay language



EFA for the Chinese-Mandarin version showed 5 components with 18 items (Table 9). Component on financial concerns (6 items) scored 0.890. Component on relationship (3 items) scored 0.862, memory (2 items) scored 0.826, diet and activities (4 items) scored 0.759, the final component on energy levels (3 items) scored 0.719 (Table 6). CFA could not be performed due to small sample size. The scoring system of the AsianDQOL Chinese (Mandarin) was also non-normal with the median 71, 25^{th} centile 65, and 75^{th} centile 80. Scores below 65 points is poor, 65 to 70 moderate, 71 to 79 good and above 80 points is excellent QOL. This scoring system is very close to those for the Malay/Indonesian language. (Table 7)

Significant differences were seen in the Cronbach's Alpha score of the three languages. The component of diet and eating habits were significant in both the English language and Chinese-Mandarin versions but were not in the Malay language. Differences between the three languages in terms of loading of the questions were accounted for. (Table 6) Test-retest reliability with minimum of at least 6 weeks apart for all the three languages is 0.664, 0.736 and 0.553 respectively ($p<0.01$).

Concordant validity was performed with WHO-QOL (BREF). Domain 1 on physical health was compared to self-care domain of AsianDQOL and showed correlation coefficient of 0.493 while domain 2 of WHO-QOL (BREF) on psychological issues matched against emotional domain on AsianDQOL showed correlation coefficient of 0.520. Domain 3 of WHO-QOL(BREF) on social relations was compared to domain on relationships of AsianDQOL and showed correlation coefficient of 0.387. Overall correlation coefficient comparing the new AsianDQOL to the WHO-QOL (BREF) was 0.612. ($p< 0.01$)

Table 9: Principal Component Analysis (Mandarin language)					
	1	2	3	4	5
Financial					
Future medical expenses	0.807				
Medical cost	0.835				
Financial burden family	0.803				
Medical Expenses difficulties	0.799				
Financial burden	0.847				
Burden to family	0.588				
Diet and activities					
Sad about diet		0.586			
Left out		0.917			
Activities		0.699			
Burden diet		0.675			
Memory and cognition					
Recent recall			0.880		
Recognition			0.887		
Energy					
Quality of work				0.565	
Weak tired				0.782	
Lack of energy				0.796	
Relationship					
Relationship with partner					0.721
Sexual problem					0.929
Sexual desire					0.930

Rotation: Varimax with Kaiser Normalization. Rotation converged in 6 iterations.

3.5 Discussion

The present study describes the development of a new quality of life assessment tool for Asians in English, Malay and Chinese- Mandarin language (Appendix 6, 7, 8) based on the 3 ethnic groups in Malaysia. This resulted in 3 different questionnaires in English, Malay and Mandarin language and not one questionnaire translated into different language. The study design was unique because the core focus was on generating a new quality of life measurement tool that was constructed based on Asian population with English as their main language. The construct of the AsianDQOL was developed based on in-depth focus group discussions. The focus group consisted of T2DM subjects of different ethnicities, religion and socio-economic background with English as their lingua franca. The focus group for the Malay version comprised of T2DM of different ethnicities (Malay, Indian and Chinese) with Malay/ Indonesian as their preferred language. AsianDQOL takes into consideration the effects of different culture, religion and beliefs on QOL and will play a significant role in diabetes management in terms of reflecting a more accurate QOL.

In Asia, food and eating have complex meanings and implications for different population but in general the activity of eating is viewed in the context of social bonding and interaction, good health, valued leisure activity often involving close friends and family member [Hu FB, 2011]. The Asians consumes a much higher proportion of carbohydrates that are high in glycemic index such as white rice, noodles and white bread compared to non-Asian populations [Lawton J et al., 2008]. The items in our diet component were mainly referring to carbohydrate rich diet that is detrimental to sugar control. As such, people living with diabetes are frequently advised not to consume carbohydrate in their diet. However, for Asians, this has a significant impact on their daily living, life satisfaction and their perception of quality of life.

The topic of sex and sexuality is very sensitive to Asians and not comfortably discussed in public. A study on sexual behavior and dysfunction help seeking patterns across urban populations in China, Taiwan, South Korea, Japan, Thailand, Singapore, Malaysia, Indonesia and the Philippines found that although sexual dysfunction is prevalent, but socio-cultural factors seem to prevent the afflicted individuals from seeking treatment [Hisasue S et al., 2005; Nicolosi A et al., 2005]. Self-reported questionnaire is still the best way to capture such delicate information [Hisasue S et al., 2005].

All the five newly developed subscales (English) had high degree of internal consistency with 3 components showing coefficients of >0.8 while the other two components are >0.7. The high degree of factor analysis and internal consistency confirmed the uniform construct of the questionnaire. As for the Malay language version, only one subscale (Diet) scored 0.673, which indicates that this component although showing substantial importance in the other languages may not be the case among Malay speaking population. All the five subscales for the Mandarin version showed high internal consistency with 3 components showing coefficients > 0.8 while the other 2 components scored >0.7.

In our study, we found that the components of the three languages were different highlighting the differences in the perception on quality of life. The perception of quality of life was not only influenced by ethnicity but also the lingua franca. This finding is unique and could be contributed by westernization. In Asia especially South East Asia, there is a strong element of Western culture influence or westernization likely due to the history of colonialism. Westernization represents a lifestyle or behavioral approach to health in epidemiology [Salant T et al., 2003]. There is limited data on the impact of westernization on the perception of QOL in a multi-ethnic population. The preferred language of the subject reflecting his or her upbringing may determine the impact of westernization. Those who preferred English language tend to be English educated locally or overseas and have a higher

exposure to western culture and lifestyle compared to the more traditional group who are still following local customs, lifestyles and beliefs. Malaysia's population is of the different ethnic group composition. The education system in Malaysia practices multi-lingual concept resulting in a majority of Malaysians who are proficient in more than one language for example Malay language and English or Malay language and Mandarin. Their preferred language is mainly influenced by the medium education and influence of family and social network.

The total score for AsianDQOL is unique to the respective language. The total score is the summation of scores obtained from all the components. This will allow the clinician/ doctor to know which components contributed to the poor quality of life or vice versa. The total score can also be used to classify patient's global quality of life score ie. "Poor quality of life" or "good quality of life" for clinical assessment purposes. However, this scoring system was based on a small sample and a cross-sectional study with larger sample size is currently in progress to verify the scores.

The AsianDQOL is more suitable for use in Malaysian population compared to DQOL, DQLCTQ-R and DSQOLS because it is disease specific and was constructed based on the Malaysian population. We also recruited subjects of different ethnicities and this is a better representative sample of our local population.

We found acceptable correlations between AsianDQOL and WHO-QOL (BREF) domains of physical health, psychological aspects and social relations. The QOL score for each language were determined based on the 25^{th}, 50^{th} and 75^{th} centile. The score varied stressing that there are differences between the three languages even though the subjects were from the same country. However, this scoring system will need to be confirmed in larger studies. A population based, cross-sectional study is currently ongoing in 3 different states in Malaysia.

The study demonstrated that across different ethnicities and languages, there are significant differences in factors determining QOL. In the English and Chinese (Mandarin) group, the components of diet and eating habits were shown to have a significant impact on QOL whereas in the Malay language group this component did not achieve a significant impact. We also found that there were differences in the number of items across the 3 languages. This support our theory that subjects of the same ethnic group but of different language group think differently and this was reflected in their perception of QOL. The Chinese-Mandarin language group was smaller in number and this could have effect on the outcome. MacCallum et.al, 1999 concluded that aspect of sampling (small size) that has detrimental effect receives a low weight if the communalities are high (above 0.6)[MacCallum RC et al., 1999]. Results from the analysis showed that the communalities for the Chinese-Mandarin group were all above 0.7 minimizing the effect of sample size. The KMO and Bartlett's test showed adequate sample size for factor analysis.

Factors such as financial issues, memory and cognition that were significant in all the three study groups were not discussed much in existing questionnaires. The strength of this study is the ability of AsianDQOL to resolve the limitations faced by other QOL tools in a multi-ethnic population credited to the availability in different languages and the core construct of the tool based on Asian population from different levels of socio-economic background. Our findings were based on Malaysian population of different ethnicities and cannot be applied to other Asian population until further studies are done to assess the suitability in the 3 languages.

In order to further improve the AsianDQOL and assess the suitability for use in Asians outside of Malaysia, studies are currently ongoing in Asian population living in Australia, Singapore and Indonesia using the 3 languages.

CHAPTER FOUR: DIABETES QUALITY OF LIFE PERCEPTION IN A MULTIETHNIC POPULATION

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Presented as an invited speaker at the Asia Diabetes Conference 2014 (Appendix 9)

Abstract

Aim: The aim of this study is to determine ethnic differences and predictors of the perception of quality of life (QOL) in a multi-ethnic Malaysian population with type-2 diabetes. **Methods:** A population based cross-sectional study was done in 3 different states in Malaysia. The Asian Diabetes Quality of Life (AsianDQOL) tool specific for Type 2 diabetes is the primary outcome tool. One-way analysis of covariance (ANCOVA) was undertaken to examine ethnic differences on the total and component AsianDQOL scores controlling for important covariates. Stepwise multiple linear regression models were used for selecting predictors for the AsianDQOL score with stratification for ethnicity and language. **Results** A total of 647 subjects (338 Malays, 160 Chinese and 149 Indians) were recruited. Chinese scored significantly lower (78.1±11.6) on the AsianDQOL (total) score compared to Malays (81.4±9.0) and Indians (81.5±9.2) ($F=3.060$, $p=0.049$, $\eta^2=0.02$). Likewise, Chinese scored significantly lower (21.0±4.3) on the AsianDQOL (diet) score compared to Malays (22.8±3.6) and Indians (22.5±3.7) ($F=4.96$, $p=0.008$, $\eta^2=0.04$). The main predictors of AsianDQOL (total) score for the English language group of different ethnicities were sexual dysfunction (-4.5), having visual problems (-3.7), female (-2.8) and glycaemic control (-1.6). Sexual dysfunction was negatively correlated with QOL in Malay, Chinese ethnic group and Indian ethnic groups. **Conclusion** The perception of AsianDQOL is different across ethnic groups and languages spoken. Significant differences in the English-speaking group and the non-English speaking group are detected within the same ethnicity. Sexual dysfunction severely impacts AsianDQOL in a multi-ethnic Asian population and remains an important determinant regardless of ethnicity and language.

Introduction

Quality of life (QOL) measurement apart from physical indices or glycemic control is becoming increasingly important with rapid progression in the field of medicine. QOL has become a crucial outcome measure for management of diabetes (DM). The current available QOL tools are divided into generic and disease specific. In Asia, most of the QOL tools were translated from those developed based on the Western population [Ware JE et al., 1992; Skevington SM et al., 2004]. The translated versions were then validated for use in the local Asian population [Cheng AY et al., 1999; Thumboo J et al., 2002]. A review of the translation and adaptation process of QOL tools in Asian countries show only 24% measured the local conception of QOL [Bowden A et al., 2003].

QOL is a broad concept and perception of QOL can be affected by different factors such as the socio-economic status, culture, population group and even ethnicity [Thumboo J et al., 2002; Lau A et al., 1998; Wee H-L et al., 2006]. Anna Lau et al., 1998 studied the self-perceived QOL of Chinese elderly people in Hong Kong and concluded that general commonalties of health, life satisfaction and social relationships with studies done in Western countries. However, differences in the characteristics and ranking of components are present and must be adjusted or modified for a better reflection of QOL [Lau A et al., 1998]. Several population-based studies in Singapore concluded that ethnicity and socio-economic status is important in determining QOL in a multi-ethnic Asian population [Thumboo J et al., 20024; Wee H-L et al., 2006]. There is limited data on the impact of westernization on the perception of QOL in a multi-ethnic population. The preferred language of the subject reflecting his or her upbringing may determine the impact of westernization on South East Asian countries Malaysia, Singapore, Brunei, Indonesia and the Philippines. Those who preferred English language tend to be English educated locally or overseas and have a higher exposure to

western culture and lifestyle compared to the more traditional group who are still following local customs, lifestyles and beliefs.

Malaysia's population is similar to Singapore in terms of the different ethnic group composition. The education system in Malaysia practices bilingual concept resulting in a majority of Malaysians who are proficient in more than one language. Their preferred language is mainly influenced by the medium of education and influence of family and social network [Gaudart H, 1987; Ozóg CK, 1993]. Whorf in 1956 explained that language guides our cognition and shaped our conceptual knowledge and subsequently there is strong evidence supporting the theory that language directs thoughts and behavior in human beings [Whorf BL et al.,1956; Ervin-Tripp S, 1967]. We hypothesized that a population of the same ethnicity but with different preferred language will not share the same perception of QOL. We also want to determine the factors influencing QOL and the impact of DM on QOL in our population with diverse ethnicities and languages.

Methods/Design

Study design

A population based cross-sectional study was conducted across the 3 most populous states in Peninsular Malaysia. The minimum sample size was calculated for multiple regression based on recommendations by Knofczynski GT et al. in 2007[Knofczynski GT et al., 2008]. The recommended minimum sample size of good prediction level with 5 predictor variables and medium population correlation coefficients of 0.50 were 65 subjects [Knofczynski GT et al., 2008]. The Malaysian statistics department states that of the 28 million population, 60% are Malays, 23% Chinese, 7% Indians and 10% others. The prevalence of diabetes in Malaysia in

2013 was highest in Indian ethnic group (38%) compared to Malays (24%) and Chinese (18%) [Wan Nazaimoon WM et al., 2013]. Recruitment sampling takes into consideration these two factors. Convenient sampling method was used but in order to reduce bias and to cater for the above variables, subjects were recruited from different levels of healthcare facilities across 3 states in Malaysia. The healthcare system in Malaysia is divided into the private sector and the government section. The government sector is free for all Malaysians while patients in the private sectors will have to bear their own expenses if they are not covered by insurance. According to the Malaysia Health System review by WHO Western Pacific Region in 2012, the government sector (Free or subsidized fee) covers 82% of inpatient and 35% of outpatient care while the private sector (self-paying or 3rd party paying) covers 18% of inpatient and 62% of outpatient care [World Health Organization, 2012]. The study sample gives a fair representative with 56% from government sector, 36% from private sector and 4% of both. Subjects were also recruited from clinic and hospital with consultants, internal medicine specialist and general practitioner clinics. This is to ensure comprehensive coverage of subjects from all different socio-economic background and levels of medical care. Subjects were of major ethnic groups residing in Malaysia (Malay, Chinese, Indian) with different preferred language e.g. English speaking group of Malay ethnicity. This will ensure a fair representative sample of the Malaysian population who has DM. Patients must have at least 6 years of formal education. The literacy rate in Malaysia (2008-2013) is 93% [UNICEF, 2013]. Our study population comprised of the working group and non-working group that consisted of retirees, housewives, students and unemployed. Subjects were from 3 most populous states in Malaysia (Selangor, Johor and Wilayah Persekutuan), which covered the urban and sub-urban group. The study population also included patients with long-standing DM (more than 5 years), the newly diagnosed and those who are diagnosed less than

5 years with or without DM complications, on different types of treatment and levels of glycemic control.

The inclusion criteria are subjects with Type 2 DM, with or without pharmacological treatment, above 18 years to 80 years old, completed at least 6 years education and able to give written consent. The exclusion criteria were concurrent Parkinson's disease, Alzheimer's disease, dementia, and severe visual impairment. The nature of the study was explained to the subjects and a copy of the information consent form. Subjects consenting to the study were given a copy of AsianDQOL in their preferred language to fill. Thorough medical history and physical examination was done by the researcher. Physical examination includes measurement of height, weight, blood pressure, waist circumference body mass index and other complications of diabetes. Anthropometric measurements were taken according to the World Health Organization (WHO) guidelines [World Health Organization, 1995]. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2). The waist circumference was taken as between the lowest rib margin and iliac crest. Blood sample for HbA1c levels were taken via venous sampling and analysis were done using the Arkray Adams HA-8160(Arkray, Inc.,Nakagyo-ku, Kyoto Japan) Diabetes Control and Complications Trial aligned cation-exchange chromatographer analyzer for HbA1c. Ethics clearance was granted by the Monash University Human Research Ethics Committee (MUHREC), approval no CF2630 – 2011001537. Written informed consent was obtained from all participants.

Primary outcome tool

In our previous study, we have developed and validated a QOL assessment tool specific for Type 2 DM in Asia. The tool (AsianDQOL) was constructed based on the diverse ethnicity, culture, language, religion and socio-demographic in Malaysian population. This tool shows good reliability and is available in English, Malay/Indonesian language and Chinese-Mandarin. The English and Malay language questionnaire had 5 components and 21 items while the Chinese-Mandarin language version had 5 components with 18 items. The questionnaires showed good reliability with Cronbach's alpha's score of >0.7. Among the domains assessed were diet and eating habits, emotion and self-care, memory and cognition, financial aspects and inter-personal relationships. The scoring system of this questionnaire is such that each component can be assessed individually or as total score. Based on the total score, the subjects can be classified as having 'excellent QOL', 'good QOL', 'moderate QOL', or 'poor QOL'.

Statistical analyses

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20. A one-way ANOVA was used to analyze mean differences across ethnic groups; chi square test was used to analyze categorical differences across ethnic groups. A one-way analysis of covariance (ANCOVA) was used to compare ethnic differences of the AsianDQOL (total) and component scores controlling for significant covariates. Stepwise multiple linear regressions were used to identify significant predictors of the AsianDQOL total score across ethnicities and languages. Statistical significance was set at $p<0.05$.

Results:

The total number of subjects recruited was 704, 57 (8%) subjects were removed due to incomplete data and the final number for analysis was 647. Table 10 depicts the demographic data, co-morbidities and treatment characteristics of the study population by the different ethnic groups. Chinese scored significantly lower (78.1±11.6) on the AsianDQOL (total) score compared to Malays (81.4±9.0) and Indians (81.5±9.2) (F=3.060, p=0.049, η^2=0.02). Likewise, Chinese scored significantly lower (21.0±4.3) on the AsianDQOL (diet) score compared to Malays (22.8±3.6) and Indians (22.5±3.7) (F=4.96, p=0.008, η^2=0.04)(Table 11). A preliminary one way between groups analysis of covariance was conducted to analyze the effect of ethnicity and different covariates such as age, gender, working status, duration of DM, education level, types of DM treatment, DM care centre and HbA1c on AsianDQOL score. Only HbA1c was significant (Table 11). ANCOVA was used to compare the effect of ethnicity on the perception of QOL. The independent variable was the ethnic groups (Malay, Chinese, Indian) and the dependent variable was the QOL score measured by AsianDQOL. Participant's HbA1c level was used as the only covariate in this analysis. Preliminary checks were conducted to ensure that there was no violation of the assumptions of normality, linearity, homogeneity of variances, regression slopes and reliable measurement of the covariate. Analysis showed significant differences between the ethnic groups on QOL (F=3.060, p=0.049, η^2=0.02). (Table 11).

Table 10 Demographic, co-morbidities and treatment characteristics of the Malay, Chinese and Indians with type 2 diabetes mellitus

Characteristics	Malay No. (%)	Chinese No. (%)	Indian No. (%)	χ^2	df	P
Age(mean ±SD)(year)	55.0±11.6	57.5±11.2	54.5±10.9			*0.24
Gender				2.90	2	0.41
Men	214(63.3)	103(64.4)	106(71.1)			
Women	124(36.7)	57(35.6)	43(28.9)			
Language				453.80	4	0.00
Malay	255(75.4)	5(3.1)	32(21.5)			
English	83(24.6)	82(51.2)	117(78.5)			
Mandarin	0(0.0)	73(45.6)	0(0.0)			
Marital status				4.69	2	0.20
Married	304(89.9)	133(83.1)	130(87.2)			
Not married	34(10.1)	27(16.9)	19(12.8)			
Education Level				14.40	2	0.03
Secondary school	137(40.7)	54(34.2)	44(29.5)			
Tertiary and above	200(59.3)	104(65.8)	105(70.5)			
Occupation				16.10	2	0.00
Working	191(56.5)	91(56.9)	111(74.5)			
Not working/Retired	147(43.5)	69(43.1)	38(25.5)			
Co-morbidities						
Hypertension	198(58.6)	97(60.6)	75(50.3)	4.00	2	0.26
Hyperlipidemia	167(49.4)	87(54.4)	70(47.0)	1.90	2	0.60
Cardiac disease	70(20.7)	28(17.5)	37(24.8)	2.60	2	0.46
Visual problems	96(28.4)	47(29.4)	44(29.5)	4.40	2	0.22
Nerve problems	101(29.9)	39(24.4)	48(32.2)	2.80	2	0.43
Sexual dysfunction	140(41.4)	58(36.3)	59(39.6)	2.00	2	0.58
Peripheral vascular disease	5(1.5)	4(2.5)	3 (2.0)	8.50	2	0.04
Renal problems	12(3.6)	7(4.4)	9 (6.0)	2.40	2	0.50
Type of treatment				19.90	8	0.34
Diet therapy alone	22(6.5)	3(1.9)	7(4.7)			
Oral pills only	205(60.7)	110(68.8)	92(61.7)			
Insulin only	28(8.3)	7(4.4)	13(8.7)			
Oral pills and insulin	53(15.7)	26(16.3)	24(16.1)			
Not on any treatment	6(1.8)	5(3.1)	3(2.0)			
Duration of diabetes				6.94	4	0.64
Less than 1 year	47(13.9)	18(11.2)	19(12.8)			
Between 1 to 5 years	98(29.1)	40(25.0)	45(30.2)			
> 5 to <10 years	80(23.8)	48(30.0)	31(20.8)			
More than 10 years	112(33.2)	54(33.8)	54(36.2)			
Centre for diabetes care				27.50	4	0.74
Government sector	195(60.2)	79(52.3)	86(59.7)			
Private sector	115(35.5)	64(42.4)	54(37.5)			
Government and private sector	14(4.3)	8(5.3)	4(2.8)			
HbA1c levels				14.30	6	0.11
Less than 6.5%	63(19.4)	29(19.8)	32(23.0)			
Between 6.5% to 7.5%	73(22.5)	48(32.9)	42(30.2)			
Between 7.6% to 8.5%	67(20.7)	26(17.8)	19(13.7)			
More than 8.5%	121(37.4)	43(29.5)	46(33.1)			

*One way analysis ANOVA used

Table 11 One-way analysis of covariance with AsianDQOL (total) score as dependent variable

Independent variable	Mean± SD	Tests of between-subject effects			Estimated marginal means		
		F	p	η^2	Mean	95% Confidence Interval	
						Lower	Upper
Ethnic group		3.06	0.049	0.02			
Malay (n=80)	81.4±9.0				81.50	79.34	83.65
Chinese (n=77)	78.1±11.6				78.17	75.98	80.37
Indian (n=114)	81.5±9.2				81.38	79.57	83.18
HbA1c status		8.32	0.004	0.03			

Dependent variable: AsianDQOL (total) score. Levene's Test of Equality of Error Variance: F=2.9(p=0.056)
Gender (F=0.19,p=0.667), Age (F=0.31,p=0.577), Working status (F=1.80,p=0.182), Duration of DM (F=2.15,p=0.143), Education level (F=0.01,p=0.931), Types of treatment (F=0.00,p=0.992), DM care centre (F=0.01,p=0.920)

When we analyzed the different components' score as dependent variable, only the diet component showed significant differences between the ethnic groups. This indicates that the perception on diet were different between the ethnic groups (Table 12). The other components such as relationship, memory, energy level and financial was not significant (Table 12).

Table 12 One-way analysis of covariance with component score as dependent variable

Independent variable	Mean± SD	Tests of between-subject effects			Estimated marginal means		
		F	p	η^2	Mean	95% Confidence Interval	
						Lower	Upper
Diet component							
Ethnic group		4.96	0.008	0.04			
Malay (n=80)	22.8±3.6				22.88	22.06	23.69
Chinese (n=77)	21.0±4.3				21.08	20.25	21.91
Indian (n=114)	22.5±3.7				22.39	21.71	23.08
HbA1c status		20.90	0.000	0.07			
Relationship component							
Ethnic group		1.97	0.141	0.02			
Malay (n=80)	8.1±3.2				8.07	7.33	8.81
Chinese (n=77)	8.4±3.7				8.41	7.66	9.16
Indian (n=114)	9.0±3.2				9.01	8.39	9.63
HbA1c status		1.19	0.276	0.00			
Memory component							
Ethnic group		2.37	0.096	0.02			
Malay (n=80)	16.6±2.1				16.59	16.08	17.10
Chinese (n=77)	16.1±2.4				16.13	15.61	16.65
Indian (n=114)	16.9±2.4				16.88	16.45	17.30
HbA1c status		0.03	0.865	0.00			
Energy level component							
Ethnic group		2.20	0.113	0.02			
Malay (n=80)	12.5±2.1				12.55	11.94	13.16
Chinese (n=77)	11.7±3.0				11.75	11.12	12.37
Indian (n=114)	11.8±3.0				11.80	11.29	12.31
HbA1c status		0.56	0.456	0.02			
Financial component							
Ethnic group		0.52	0.593	0.00			
Malay (n=80)	21.4±3.6				21.42	20.54	22.30
Chinese (n=77)	20.8±4.5				20.81	19.91	21.70
Indian (n=114)	21.4±4.0				21.30	11.29	22.04
HbA1c status		9.69	0.002	0.04			

Levene's Test of Equality of Error Variances: Diet component:(F=1.60,p=0.200), Relationship component: (F=1.60, P=0.200), Memory component: (F=1.27, p=0.282), Energy level component: (F=3.95, p=0.200), Financial Component: (F=1.01, p=0.370).

Stepwise multiple linear regressions on the 647 subjects to analyze the possible contributors to QOL score were done. Linear regression done on 292 Malay language speaking subjects of different ethnicities (255 Malays, 32 Indians, and 5 Chinese) showed longer duration of DM and sexual dysfunction is negatively associated with QOL score (Table 13). The equation generated, QOL=90 (Constant) -1.8(Duration of DM)-5.9(Sexual dysfunction). For example, for a subject with diabetes for 10 years with complication of sexual dysfunction would obtain a score of 66. Excluded variables were age, gender, education level, glycemic control (HbA1c), BMI, ethnicity, comorbidities such as heart disease, hyperlipidemia, hypertension, visual problems and nerve problems (Table 13).

Analysis of the 282 English language cohort entailing 83 subjects of Malay ethnicity, 82 Chinese, 117 Indian showed the following equation (Table 13): QOL=91(Constant) -1.6(HbA1c) -2.8(Female)-3.7(Visual problems)-4.5(Sexual dysfunction). For example, a male subject with HbA1c score of 10 with sexual dysfunction will score 70.5. This result demonstrates that having poorer glycemic control, presence of visual problems and sexual dysfunction predicts a poorer QOL score. When compared to Malay language group, the duration of DM is no longer a determinant of QOL score. Excluded variables were glycemic control (HbA1c), education level, ethnicity, BMI, duration of DM and comorbidities such as hyperlipidemia, heart disease and kidney disease.

Analysis of the 73 Mandarin language group of Chinese ethnicity showed glycemic control and sexual dysfunction is negatively associated with QOL score while hyperlipidemia is associated with better QOL score (Table 13). QOL=71(Constant) +4.6(Hyperlipidemia)-1.9(HbA1c)-5.9(Sexual dysfunction). For example, a subject with HbA1c of 10 and associated hyperlipidemia and sexual dysfunction will score 50.7. Excluded variables were

education level, duration of DM, and comorbidities such as hypertension, heart disease, visual problems, nerve and kidney problem.

Table 13 Predictors of AsianDQOL (total) score stratified by language: Stepwise multiple linear regression

Predictor variable	βCoefficient		95% Confidence Interval		p
	Unstandardized	Standardized	Lower	Upper	
Malay/Indonesian (*n=292, R-squared=0.11*)					
Constant	90.30		86.90	93.71	0.000
Duration of diabetes	- 1.82	-0.18	-2.98	-0.66	0.002
Sexual dysfunction	-5.87	-0.26	-8.41	-3.33	0.000
English (n=282, R-squared=0.11)					
Constant	90.95		86.24	95.65	0.000
HbA1c	-1.56	-0.18	-2.59	-0.54	0.000
Gender	-2.77	-0.13	-5.35	-0.18	0.036
Visual problems	-3.65	-0.16	-6.40	-0.90	0.010
Sexual dysfunction	-4.49	-0.18	-6.95	-2.03	0.000
Mandarin (n=73, R-squared=0.22)					
Constant	71.45		65.94	76.96	0.000
Hyperlipidemia	4.56	0.27	0.47	8.65	0.029
HbA1c	-1.85	-0.26	-3.55	-0.15	0.034
Sexual dysfunction	-5.87	-0.33	-10.10	-1.65	0.007

Analysis of 255 more traditional Malay language speaking of Malay ethnicity cohort generated an equation of 98(Constant)-2.3(Duration of DM) -6.0 (Sexual dysfunction). Sexual dysfunction and duration of DM negatively predicts QOL in this group. The R-squared value was 0.14 indicating the model explained 14% of total QOL score (Table 14). Analysis of the 83 subjects of the English speaking of Malay ethnicity group showed diabetes renal problems was associated with worse QOL score (Table 5). QOL= 82(Constant)-22(Renal problems). The R-squared value was 0.13 indicating the model explained 13% of the total QOL score. For example, a man of Malay ethnicity with Malay language as his lingua franca and has diabetes for 10 years with chronic kidney disease will obtain a score of

75 while a man of Malay ethnicity with English language as his lingua franca and has diabetes for 10 years with chronic kidney disease will obtain a score of 60.

Analysis of the English speaking group of Chinese ethnicity revealed negative association of sexual dysfunction and female gender to QOL scores (Table 14). Equation generated: QOL=90(Constant)-5.9(Female gender)-10.0(Sexual dysfunction). The R-squared value was 0.15 explaining 15% of the total QOL score. The traditional Mandarin speaking group of Chinese ethnicity group demonstrated positive association of hyperlipidemia and negative association of glycemic control and sexual dysfunction with QOL. The equation, QOL=71(Constant) +4.6(Hyperlipidemia)-1.9(Glycemic control)-5.9(Sexual dysfunction). The R-squared value was 0.21 explaining 21 % of the total QOL score. For example a male of Chinese ethnicity with English language as his lingua franca, has HbA1c of 10% and complications of hyperlipidemia and sexual dysfunction will score 80 points while a male of Chinese ethnicity with Mandarin language as his lingua franca, has HbA1c of 10% and complications of hyperlipidemia and sexual dysfunction will score 56.6 points.

The 117 subjects from the English speaking Indian ethnicity group show strong negative association of experiencing nerve problems and sexual dysfunction to QOL scores (Table 14). The equation formed: QOL=85(Constant) -3.8(Sexual dysfunction)-5.7(Nerve problems). The R-squared value was 0.11 explaining 11 % of the total QOL score. The equation generated from analysis of the Malay speaking Indian ethnicity group shows 113(Constant) -8.3(Mode of treatment)-8.5(Working status). This shows that patient on lesser type of treatment (i.e. oral versus combination of oral and insulin) and those who are working has a higher QOL score. The R-squared value was 0.45 explaining 45% of the total QOL score.

Table 14 Predictors of AsianDQOL (total) score stratified by ethnicity and language: Stepwise multiple linear regression

Predictor variable	βCoefficient		95% Confidence Interval		p
	Unstandardized	Standardized	Lower	Upper	
Malay ethnicity Malay language (*n*=255, R-square:0.14)					
Constant	97.98		88.44	95.53	0.000
Duration of diabetes	- 2.28	-0.23	-3.49	-1.07	0.000
Sexual dysfunction	-6.01	-0.27	-8.68	-3.34	0.000
Malay ethnicity English Language (*n*=83, R-square:0.13)					
Constant	81.79		79.81	83.76	0.000
Renal problems	-21.79	-0.37	-34.24	-9.26	0.001
Chinese ethnicity Mandarin language (*n*=73, R-square:0.21)					
Constant	71.45		65.94	76.96	0.000
Hyperlipidemia	4.56	0.27	0.47	8.65	0.029
HbA1c	-1.85	-0.26	-3.55	-0.15	0.034
Sexual dysfunction	-5.87	-0.33	-10.10	-1.65	0.007
Chinese ethnicity English Language (*n*=82, R-square:0.15)					
Constant	90.47		81.47	99.48	0.000
Gender	-5.87	-0.24	-11.60	-0.13	0.045
Sexual dysfunction	-9.99	-0.42	-15.49	-4.49	0.001
Indian ethnicity English language (*n*=117, R-square:0.11)					
Constant	84.77		82.42	87.12	0.000
Sexual dysfunction	-3.79	-0.20	-7.27	-0.30	0.033
Nerve problems	-5.70	-0.28	-9.38	-2.02	0.003
Indian ethnicity Malay language (*n*=32, R-square:0.45)					
Constant	113.27		98.85	127.69	0.000
Treatment	-8.26	-0.66	-11.83	-4.68	0.000
Working status	-8.53	-0.35	-15.56	-1.48	0.019

Discussion

The most significant new finding of the study is the perception of QOL is different across ethnicity and the lingua franca in a population sharing the same basic socio-economic background. This has not been demonstrated before. Analysis of this study demonstrated significant differences between the ethnic groups (Malay, Chinese and Indian) on perception of QOL. In depth analysis of the components of QOL showed significance differences between the ethnic group's perceptions on diet component. This demonstrates that ethnic differences do exist in a population sharing similar socio-cultural contexts. This finding is similar to Singapore where a population based study by Wee H-L et al. in 2005 showed ethnicity as an important factor influencing QOL in people with diabetes [Wee H-L et al., 2006]. However, a generic tool was used to measure QOL and this could limit the sensitivity in participants with DM. Only English language tools were used in that study limiting the study population to only those proficient in English. When we compared the different ethnic groups in Malaysia, the predictors of QOL were different in the Malay ethnic group compared to the Chinese and Indian. Within the Malay ethnic group, marked differences were detected with the more English language speaking group (ELS) versus the more traditional Malay language speaking group (MLS). The (ELS) group was primarily concerned about presence of renal impairment while the (MLS) group was affected by the duration of DM and sexual dysfunction. This could be that the ELS group is associated with higher education level (25% have at least secondary education and 75% have above secondary education) compared to the MLS group (54% have at least secondary education and above). Higher education level is associated with better economic security and job prospects. Glasgow et al. in 1997 found that lower education level and lesser income were associated with a lower QOL score [Glasgow RE et al., 1997]. The presence of DM complications was linked to lower QOL score especially for co-existent of microvascular and macrovascular

complications [Glasgow RE et al., 1997; UK Prospective Diabetes Study Group, 1999; Coffey JT et al., 2002]. The presence of chronic kidney disease further worsens the QOL especially in end-stage renal failure and with initiation of dialysis [Perlman RL et al., 2005; Merkus MP et al., 1997]. This is consistent with ELS group with strong negative association of renal impairment on QOL score.

The Chinese ethnic group also showed significant differences between the ELS group versus the traditional Mandarin speaking group. The main determinant of QOL in the ELS group is sexual dysfunction versus HbA1c, hyperlipidemia and sexual dysfunction in the Mandarin-speaking group. The ELS group being more westernized in their behavior and lifestyle could have an impact on their perception compared to the more traditional Mandarin-speaking group. The presence of hyperlipidemia as a determinant of QOL scores in the Mandarin speaking Chinese group is unique. This finding highlights the importance of the eating culture and health among the more traditional Chinese population. A population based study in Hong Kong Chinese population found that the activity of eating was viewed as an important activity signifying good health, social bonding with family and friends[Lau A et.al, 1998]. This led to formation of a strong bond between the ability to eat freely, freedom to participate in such social rituals and life satisfaction affecting QOL [Glasgow RE et al., 1997; UK Prospective Diabetes Study Group, 1999; Coffey JT et al., 2002]. The Chinese ethnic group regardless of the preferred language is severely affected by presence of sexual dysfunction.

The predictors of QOL in the ELS Indian ethnic group were different from the Malay speaking Indians. In the Malay language-speaking group of Indian ethnicity, the mode of treatment and working statues explains 45% of the total QOL score. In this group, having a permanent job is associated with better financial stability and better QOL. Poorer QOL were associated with insulin usage perhaps due to the complications of insulin. This is consistent

with findings of Glasgow E et al. in 1996 linking insulin use to poorer QOL [Glasgow RE et al., 1997].

Our study highlights that perception of QOL is not only different across the ethnic groups but also among the more English-speaking and native language-speaking group within the same ethnicity. This indicates that perception of QOL is very much influenced by exposure to westernization that can be assessed by their lingua franca. Current study to look at the effect of westernization on perception of QOL among Asian population living in Australia will shed more light into this area.

In our study we did not find any differences of QOL between subjects from private (self-paying, higher income) or government healthcare sector (free, lower income group). The mode of treatment did not affect QOL in our study group. This is consistent with the findings of the UKPDS group via two cross-sectional studies of patients in randomized controlled trials of intensive blood glucose control versus conventional control and tight blood pressure control versus less tight control, stating that the therapeutic policies had no effect on QOL [UK Prospective Diabetes Study Group, 1999]. Other studies done post UKPDS also found that insulin therapy in poorly controlled type 2 DM had no adverse events on QOL [de Grauw WJ et al., 2001] or even higher QOL score in the initiation of insulin phase due to relief of hyperglycemic symptoms [Davies M et al., 2006]. However, there are several studies that detected a lower QOL score in subjects on insulin compared to those on oral medications [Glasgow RE et al., 1997; Jacobson AM et al., 1994].

Complications of diabetes are associated with detrimental impact on QOL [Glasgow RE et al., 1997; Stewart AL et al., 1989; UK Prospective Diabetes Study Group, 1999; Merkus MP et al., 1997]. Our study shows that among the complications, sexual dysfunction, retinopathy and nephropathy severely reduced QOL. Sexual dysfunction is also strongly

negatively correlated with QOL in all the three major ethnic groups. Sexual dysfunction in this study was taken as having experienced erectile dysfunction (ED), having poor libido, premature ejaculation, vaginal dryness, dyspareunia and anorgasmia. This is consistent with findings globally that found a strong link between DM, ED and worse QOL [Person DF et al., 2003; De Berardis G et al., 2002]. A comprehensive study done by De Berardis et.al.2002, across 114 DM outpatient clinics and 112 general practitioners found that ED affects 1/3 of patients with diabetes and they have higher depressive symptoms and poorer QOL [De Berardis G et al., 2002]. However, this study takes into account self-reported symptoms with no clinical diagnosis and QOL was assessed using a general assessment tool (SF-36). A year later, Person DF et al. in year 2003 compared impotent men with DM to those without and found more severe dysfunction and worse QOL in the group with DM [Person DF et al., 2003]. Although the sample size for DM group was relatively small (n=20) but a disease specific tool was used increasing the sensitivity. In women, sexual dysfunction is frequent in patients with DM and is associated with reduction in overall QOL with 77% having lack of libido and 38% with vaginal dryness [Enzlin P et al., 2002; Erol B et al., 2002]. We conclude that in a multi-ethnic Asian population sexual dysfunction is highly associated with DM and in view of the detrimental effect on QOL, it is important for early detection and proper management to maintain good QOL.

However, there are limitations that need to be considered. First, using a self-assessment technique by questionnaire for recruitment, only subjects who have basic education are included in the study. In view of the high literacy rate in Malaysia, our study did capture a good sample of the population [UNICEF 2013]. Secondly, the number of Chinese-Mandarin language individuals is smaller compared to Malay/Indonesia and English group. This is mainly due to the lack of Chinese-Mandarin competent subjects in the

recruitment area. Our findings are based on Malaysian population and may not be applicable to other populations in Asia.

CHAPTER FIVE: PREDICTORS OF SEXUAL DYSFUNCTION IN MEN WITH DIABETES WITH OR WITHOUT CARDIOVASCULAR DISEASE.

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CHAPTER FIVE: PREDICTORS OF SEXUAL DYSFUNCTION IN MEN WITH DIABETES WITH OR WITHOUT CARDIOVASCULAR DISEASE.

Abstract

The primary aim is to determine the predictors of the different components of sexual dysfunction among men with diabetes with or without cardiovascular disease in a multi ethnic Asian population. The secondary aim is to determine the prevalence SD. **Methods**: A population based cross-sectional study was carried out in 3 different states in Malaysia. The Sexual Function Assessment in Diabetic Men (SAD-Men) tool specific for sexual dysfunction in men with diabetes is the primary outcome tool for data gathering. Chi-Squared test for independence was applied to evaluate for any significant differences in the three groups of participants. Stepwise multiple linear regression models were used for analysis. **Results:** A total of 424 subjects of different ethnicities were recruited. A total of 221 have diabetes only, 98 with cardiovascular disease without diabetes and 105 with diabetes and cardiovascular disease. Regression model generated for total SD score shows negative correlation of age (-0.3), hypertension (-3.4), retinopathy (-4.4), and neuropathy (-5.1). The predictors for erectile dysfunction score, libido score and premature ejaculation score were different. The prevalence of SD in DM only group, CVD only group and DM plus CVD group was 80%, 78% and 91%, respectively. Those with DM and CVD experienced more severe SD compared to the other two groups. **Conclusion:** The predictors of total SD score were different from the predictors of the ED score, libido score and premature ejaculation score. The predictors of the different groups were also different for the ED score, libido score and premature ejaculation score.

Introduction

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) classified sexual dysfunction (SD) as a disorder in one or more of the four stages of the sexual response cycle: desire, excitement, orgasm and resolution [American Psychiatric Association, 2000]. Male SD is also categorized into erectile dysfunction (ED), ejaculatory/ orgasmic disorders (premature ejaculation) and sexual interest disorders [Isidro ML, 2012]. SD has major health consequences on the individual, both physically and psychologically. This effect in turn aggravates the SD, creating a vicious cycle [Isidro ML, 2012].

Diabetes (DM) is a highly prevalent condition in Asia and has been commonly associated with SD, especially ED and premature ejaculation (PE). Worldwide, the prevalence of ED among diabetic population ranges from 39% to 71% [Berardis GD et al., 2002; Giuliano FA et al., 2004; Eardley I et al., 2007]. A Chinese based cross-sectional study showed ED prevalence rate of 75% among the patients with DM [Yang G et al., 2010]. In Malaysia, the overall prevalence rate of ED in general population was 70.1% with 32.8% experiencing mild ED, 17.7% mild to moderate ED, 5.1% moderate ED, and14.5% severe ED [Khoo EM et al.,2008]. Only 20% of the study population has DM. On the other hand, prevalence of PE in diabetes was estimated to be 40%-56%, with a higher prevalence among men with DM [Khoo EM et al., 2008; Burke JP et al., 2007; El-Sakka AI et al., 2003; Malavige LS et al., 2008; Owiredu WK et al., 2011]. Worsening this dilemma is the concomitant presence of PE and ED with DM [Malavige LS et al., 2008]. In terms of other forms of orgasmic disorders and sexual interest disorders, very little information is known.

Khoo et al, (2008) performed cross-sectional community based study in Malaysia and concluded that ED, depression and androgen deficiency symptoms were common in urban aging men. The study also suggested that the increasing prevalence of CVD and DM might

lead to increasing prevalence of ED [Khoo EM et al., 2008]. However, the focus of this study was limited to ED alone and not the other components of SD. Moreover, structured interviews were carried out to obtain data on ED, which could lead to courtesy bias and dishonesty due to embarrassment. Corona et al, (2006) suggested that self-administered questionnaire is the best way to address such sensitive issue to avoid embarrassment [Corona G et al., 2006].

Another common condition among the Asian community is cardiovascular disease (CVD), which has been correlated with ED. The association between CVD and ED has been widely studied, with more emphasis made on ED as a risk predictor for cardiovascular disease [Batty GD et al., 2010; Montorsi P et al., 2008; Sasayama S et al., 2003]. Two studies showed that the prevalence of ED in angiographically diagnosed coronary artery disease patients range from 46-49% [Foroutan SK et al., 2007; Montorsi F et al., 2003]. However, there are very limited or no data associating orgasmic disorders or sexual interest disorders with CVD.

ED in patients with diabetes and CVD may be due to neuropathy, vasculopathy or psychosocial disorders [Montorsi F et al., 2003; De Angelis L et al., 2001; Nehra A et al., 2001]. In addition, most of the patients with diabetes or CVD are older, suggesting a contribution of age to ED. Previous studies found androgen deficiency to be prevalent in men with diabetes and CVD implying that low testosterone may be involved in the development of ED in these groups of men [Biswas M et al., 2012; Mulligan T et al., 2006; Fukui M et al., 2007; Grossmann M et al., 2008; Corona G et al., 2011]. Hence, it cannot be presumed that ED in men with diabetes and CVD are solely due to neuropathy and vasculopathy. Multiple factors contribute to the development of ED. Very little is known about other sexual disorders such as PE and libido disorders.

CVD is the principal cause of mortality and morbidity worldwide accounting for 20.3% of medically certified deaths in 1995[Ministry of Health Malaysia, 1995]. However, little is known about the prevalence of SD in men with CVD. DM and CVD are rapidly increasing in Malaysia and these conditions often exist simultaneously increasing the complexity of disease management. Furthermore, there is limited data on the predictors of SD and its components in a multi-ethnic population. The objective of this study is to determine the predictors of SD and its components among urban Malaysian men with DM, with or without CVD. The secondary objective is to determine the prevalence of SD.

Methodology:

This was a cross-sectional community based study of urban Malaysian men. Subjects were recruited from two medical research centers, one private hospital, one public hospital and one public community clinic across 3 most populous states in Malaysia (Kuala Lumpur, Selangor and Johor). Clustered sampling method was adapted in this study where participants were categorized into three groups, those with DM only, CVD only and with both DM and CVD. As there were no prevalence data for the overall SD in patients with diabetes, CVD and both, the prevalence of ED was used to calculate the sample size for this study. A 10% margin of uncertainty for prevalence of ED among diabetic patients (50-60%) could be achieved with a sample size of 92 (with 20% attrition rate= 110). A 10% margin of uncertainty for prevalence of ED among cardiovascular disease (CVD) patients (39-49%) could be achieved with a sample size of 96 (with 20% attrition rate= 115).

As there were no prevalence data for ED among patients with both, diabetes and CVD, we used 115 to represent all of the 3 groups, as it was the largest sample size. Hence, the overall sample size aimed was 350. The sample size was calculated using Epi Info version 6.

The inclusion criteria were men above 18 years of age and able to give valid consent. Subjects with type-2 DM with or without CVD were recruited. The exclusion criteria were subjects with history of spinal cord injury, pelvic radiotherapy, radical pelvic surgery, multiple sclerosis and unable to give a valid consent. Ethics approval was obtained from the Monash University Human Research Ethics Committee. Patients visiting the above clinics and hospitals for their medical care were invited to participate in this study. The nature of the study was explained to these men by the researcher. Written informed consent was obtained from individual subjects.

Primary outcome measurement tool

There were a number of questionnaires previously published to assess the overall sexual functioning in men. However, many of these questionnaires were not suitable because of the following reasons. First, most of the questionnaires did not assess all the different domains of SD. Secondly, some of the questionnaires were too detailed (200 questions) and not suitable for large population based studies [O'Connor DC et al., 2008]. The Sexual function assessment in diabetic men (SAD-MEN) is a 13 item self-administered questionnaire that had been previously validated for use in a multi-ethnic population, to provide a single score for the overall sexual dysfunction (Appendix 12). It contained questions to identify the socio-demographics and the background medical, psychological and sexual history. This questionnaire was designed to be culturally sensitive and was developed in the two dominant languages in Malaysia: English and Malay. The SAD-MEN questionnaire (both English and Malay versions) was found to have a good validity as assessed by face, content, construct and convergent validation in men with diabetes and CVD. The reliability testing showed Cronbach-α values of all above 0.7 for the English and Malay versions. Psychometric

analysis for internal consistency and test-retest reliability showed that this questionnaire had good reliability. The Spearman's test correlation coefficient was 0.853 ($p<0.05$) for the English version and 0.908 ($P<0.05$) for the Malay language version. Hence, the SAD-MEN questionnaire was employed in this study to answer the research questions. The development and validation of SAD-MEN questionnaire was previously sent for publication. Sexual dysfunction score as calculated from the SAD-MEN questionnaire was the primary outcomes evaluated in this study. The total SD score is made up of sum of the component scores (ED score, Libido score and premature ejaculation score). The SD score was further categorized based on their severity as presented in Table 15.

Table 15: SAD-Men Scoring System

Severity	SAD-Men Score
No Sexual Dysfunction	55-65
Mild Sexual Dysfunction	45-54
Mild-moderate Sexual Dysfunction	35-44
Moderate Sexual Dysfunction	25-34
Severe Sexual Dysfunction	13-24

Study Design

The enrolled participants were interviewed by researcher regarding their socio-demographics (age, marital status, ethnicity, education, occupation, and income), medical history, surgical history, use of medications, smoking and alcohol status. All subjects underwent a general physical examination by doctor researcher where the following were assessed: height, weight, waist circumference, blood pressure, signs of heart disease and complications from diabetes such as retinopathy, neuropathy and peripheral vascular disease. Cardiac assessment was performed by physicians or cardiologists at the study sites. Subsequently, random blood (6ml) was obtained via venepuncture for investigation of HbA1c levels. Subjects were randomly selected for a sub-study involving analysis for testosterone levels. All information obtained was recorded in the source notes specific to each patient. The participants then completed the SAD-Men questionnaire.

Method for Glycated hemoglobin (HbA1c) Testing:

Blood samples of approximately 1ml were collected into Ethylenediaminetetraacetic acid (EDTA) tubes, via venepuncture. In-vitro diagnostic test to determine the HbA1c was performed by Affion AS100 Analyzer which had a coefficient of variation of less than 3%. The analyzer reported the HbA1c test results in percentages (%) which were aligned to the assay used in the DCCT (Diabetic Control and Complications Trial) study.

Method for Testosterone Testing:

Blood samples of approximately 6ml were collected in plain tubes via venipuncture and serum was stored immediately at -80^{o}c till analysis. The samples were analyzed at the pathology laboratory in one batch to reduce inter-assay variability. Cobas e411 analyzer was used with Elecsys Testosterone II immunoassay for the in-vitro quantitative determination of

testosterone in the serum sample, coefficient of variation 1.2-4.7%. The normal range for testosterone was quoted as 9.9 nmol/L to 22.9 nmol/L.

Statistical Analysis:

Descriptive and frequency based analysis were employed to identify the characteristics of the participants, medical history and the prevalence of overall SD within the three groups of patients. Chi-Squared test for independence was applied to evaluate for any significant differences in the socio-demographics and to explore the difference in levels of SD, in the three groups of participants. Stepwise multiple regression were used with total SD score and component score as dependent variable after checking for assumptions. Two separate multivariate analysis were performed, one for all participants with DM and another for all participants with CVD. One way between groups ANOVA was used to look for any significant difference in the mean testosterone levels between the three groups. Statistical significance is set at $p<0.05$.

Results:

Demographic data of the 424 patients recruited are shown in Table 16. Out of the total number, 221 (52%) were from the diabetes only group, 98 (23%) from the CVD only group and the other 105 (25%) from the group with both diabetes and CVD. The Malaysian Statistics Department states that of the 28 million population, 60% are Malays, 23% Chinese, 7% Indians. However, the prevalence of diabetes in Malaysia in year 2013 is highest in Indian ethnic group (38%) compared to Malays (24%) and Chinese (18%) [Wan Nazaimoon WM et al., 2013]. This gives a fair representation of the Malaysian population.

Chi-Square test for independence to compare the characteristics of the subjects within the three groups showed no significant difference between the three groups in terms of age,

marital status, alcohol consumption, stress and insomnia. But there was a significant difference between the three groups with regards to ethnicity, BMI, waist circumference, presence of hypertension or dyslipidemia, cigarette smoking and depression. The mean HbA1c for DM only group was 8.2% (n=205) and DM with CVD group was 7.6% (n=102). Mann-Whitney U Test revealed a statistically significant difference in HbA1c between the two groups with a small effect size (U=8853, z=-2.19, p=0.03, r=0.1).

Table 16 Demographic, co-morbidities characteristics of subjects

Variables	All (n=424)		DM only (n=221)		CVD only (n=98)		DM+CVD (n=105)		χ^2
	n	(%)	n	(%)	n	(%)	n	(%)	
Age									
≤40	28	(6)	17	(8)	6	(6)	5	(5)	p=0.407
41-50	94	(22)	53	(24)	19	(19)	22	(21)	
51-60	160	(38)	87	(39)	31	(32)	42	(40)	
61-70	113	(27)	51	(23)	31	(32)	31	(30)	
>70	27	(6)	12	(5)	10	(10)	5	(5)	
Ethnicity									
Malay	226	(53)	120	(54)	53	(54)	53	(51)	p=0.03
Chinese	86	(20)	46	(21)	25	(26)	15	(14)	
Indian	102	(24)	50	(23)	16	(16)	36	(34)	
Marital Status									
Single	22	(5)	13	(6)	6	(6)	3	(3)	p=0.45
Married	393	(93)	201	(91)	91	(93)	101	(96)	
Body Mass Index									
<23	46	(11)	18	(9)	22	(11)	6	(6)	p=0.00
23-27.4	151	(36)	85	(39)	35	(36)	31	(30)	
≥27.5	196	(46)	108	(49)	37	(38)	51	(49)	
Waist Circumference									
<90cm	74	(18)	23	(10)	38	(39)	13	(12)	p=0.00
≥90cm	246	(58)	125	(57)	60	(61)	61	(58)	
Hypertension									
Yes	256	(60)	121	(55)	59	(60)	76	(72)	p=0.01
No	166	(39)	98	(44)	39	(40)	29	(28)	
Dyslipidaemia									
Yes	252	(59)	114	(52)	66	(67)	72	(69)	p=0.04
No	170	(40)	105	(48)	32	(33)	33	(31)	
Smoker									
Yes	89	(21)	43	(20)	24	(25)	22	(21)	p=0.01
No	202	(48)	123	(56)	37	(38)	42	(40)	
Quit	131	(31)	54	(24)	37	(38)	40	(38)	
Alcohol									
Yes	80	(19)	37	(17)	13	(13)	26	(25)	p=0.08
No	346	(81)	183	(83)	85	(87)	78	(74)	
Stress									
Yes	80	(19)	40	(18)	14	(14)	26	(25)	p=0.14
No	340	(80)	178	(81)	84	(86)	78	(74)	
Insomnia									
Yes	54	(13)	22	(10)	14	(14)	18	(17)	p=0.17
No	366	(86)	196	(89)	84	(86)	86	(82)	
Depression									
Yes	18	(4)	13	(6)	0	(0)	5	(5)	p=0.05
No	402	(95)	205	(93)	98	(100)	99	(94)	

The history of CVD for the two groups: CVD only and DM+CVD groups are presented in Table 17. Majority of participants have had CVD for <5 years in both, CVD only group (72%) and DM+CVD group (67%). In the CVD only group, 43% (n=42) participants were treated by oral medication, 51% (n=50) had undergone angioplasty and 6% (n=6) had undergone coronary artery bypass grafting. This was similar to the DM+CVD group were 43% (n=42) were on oral medications, 48% (n=50) had undergone angioplasty and 10%(n=10) had undergone coronary bypass grafting. Chi-square test for independence showed no statistical difference between the two groups for CVD duration (X^2 (2, n=203) =1.1, p=0.57) and treatment (X^2 (2, n=203) =0.9, p=0.65).

Table 17: Characteristics of CVD history group

Variables	CVD only (N=98)		DM + CVD (N=105)		χ^2
	n (%)		n (%)		
CVD Duration					
0-5 years	71	(72)	70	(67)	p=0.57
6-10 years	15	(15)	22	(21)	
>10years	12	(12)	13	(12)	
CVD Treatment					
Medications only	42	(43)	45	(43)	p=0.65
Angioplasty	50	(51)	50	(48)	
CABG	6	(6)	10	(10)	

Stepwise multiple linear regression done with total SD score as dependent variable for all subjects with DM with or without concomitant CVD showed negative association of age, neuropathy, retinopathy, hypertension. The equation generated was Total SD score= 71(Constant)-0.33(Age)-3.43(Hypertension)-4.39(Retinopathy)-5.13(Neuropathy)(Table 18). The R-square value was 0.22, explaining 22% of the total SD score. Excluded variables were BMI, presence of nephropathy, dyslipidemia, hypertension, prostate problems, spinal problems and HbA1c levels.

Table 18 Predictors of total Sexual dysfunction: Stepwise multiple linear regression

Predictor variable	Coefficient ß		95% Confidence Interval		p
	Unstandardized	Standardized	Lower	Upper	
Diabetes (*n=293, R-square=0.22*)					
Constant	65.71		58.19	73.23	0.000
Age	- 0.33	-0.28	-0.47	-0.19	0.000
Neuropathy	-5.13	-0.19	-8.22	-2.04	0.010
Retinopathy	-4.39	-0.17	-7.39	-1.39	0.004
Hypertension	-3.43	-0.14	-6.25	-0.60	0.018

Analysis of the components of SD using stepwise multiple linear regression with ED score as dependent variable for DM only group showed negative predictors of age, glycemic control (HbA1c), retinopathy, insomnia and neuropathy. The formula generated was ED score =40.12(Constant) -0.24(Age) -0.69(HbA1c) -2.32(Retinopathy) -2.71(Insomnia) -3.13(Neuropathy). The R-square value was 0.24, explaining 24% of the total ED score. (Table 19) The CVD only group demonstrated negative association of age to the ED score. Formula generated=29.50(Constant)-0.14(Age). The R-square value was 0.05. As for the DM +CVD group, the formula generated=17.23(Constant) -3.53(Retinopathy) demonstrating negative association of retinopathy on ED score. The r-square value was 0.06. (Table 19)

Analysis of the different groups with libido score as the dependent variables showed similar result for the DM+CVD group. Formula generated was Libido score = 25.96(Constant) -4.94(Retinopathy). The r-squared value was 0.11 explaining 11% of the total libido score. (Table 19) The DM only group showed negative association of age, hypertension and retinopathy. Formula generated, Libido score=39.99(Constant)-0.20(Age)-2.129(Hypertension)-3.41(Retinopathy). The r-square value was 0.21 explaining 21% of the total libido score.

Analysis of the DM only group with PE score as dependent variable showed negative predictors of age, HbA1c, and retinopathy. The formula generated, PE score= 14.93(Constant)-0.07(Age)-0.27(HbA1c)-0.81(Retinopathy). The R-square value was 0.13 explaining 13% of the premature ejaculation score.(Table 19) The CVD only group showed negative association of age. The formula generated, PE score=11.60(Constant)-0.05(Age). The R-square was 0.06. (Table 19) The DM+CVD group showed negative association of retinopathy and nephropathy to premature ejaculation score. The formula generated, PE score=8.93(Constant)-1.24(Retinopathy)-2.95(Nephropathy). The R-square value was 0.11 explaining 11% of the score (Table 19).

Table 19 Predictors of score stratified by groups: Stepwise multiple linear regression

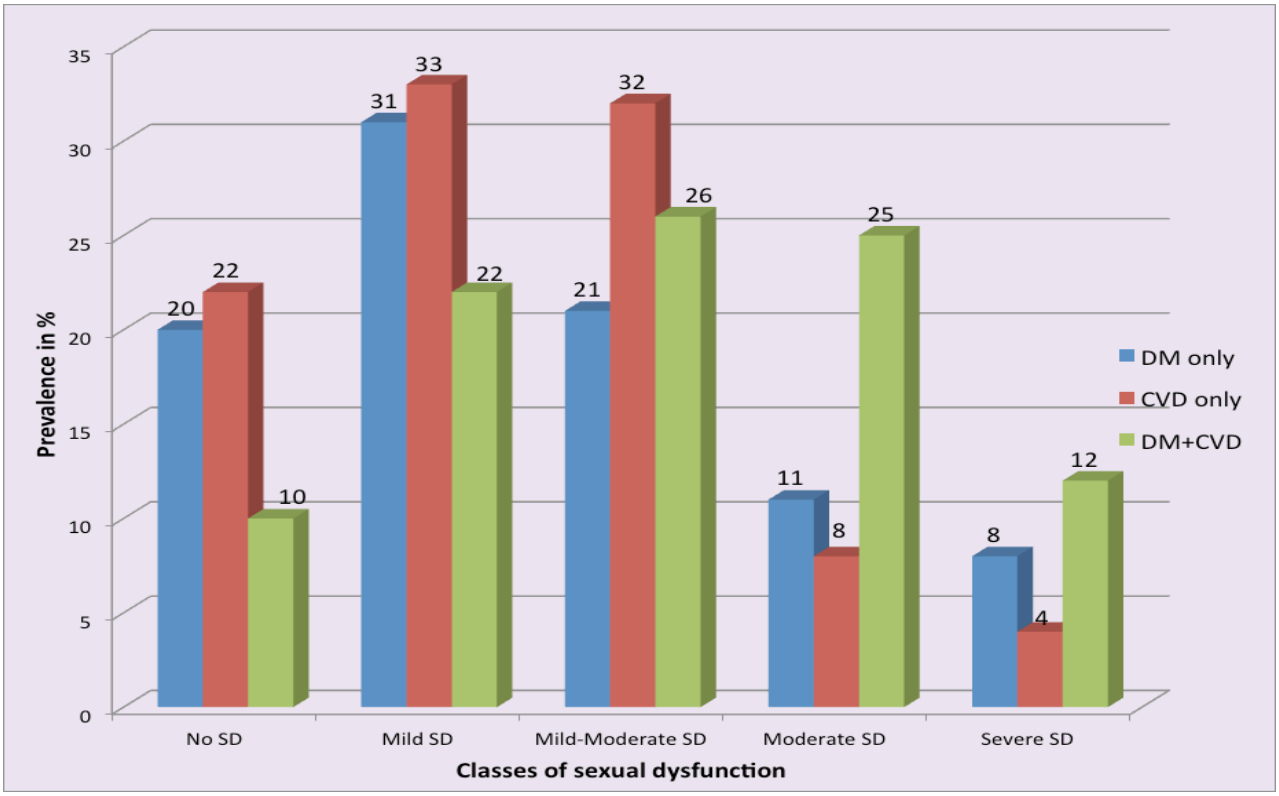
Predictor variable	Coefficient ß		95% Confidence Interval		p
	Unstandardized	Standardized	Lower	Upper	
Dependent variable: ED score					
DM only group (*n*=221, R-square:0.24)					
Constant	40.12		32.43	47.80	0.000
Age	- 0.24	-0.33	-0.33	-0.14	0.000
HbA1c	-0.69	-0.16	-1.24	-0.15	0.013
Retinopathy	-2.32	-0.15	-4.24	-0.40	0.018
Insomnia	-2.71	-0.13	-5.24	-0.19	0.035
Neuropathy	-3.13	-0.19	-5.15	-1.10	0.003
CVD only group (*n*=97, R-square:0.05)					
Constant	29.50		22.03	36.97	0.000
Age	-0.14	-0.22	-0.27	-0.01	0.036
DM+CVD (*n*=73, R-square:0.06)					
Constant	17.23		15.39	19.07	0.000
Retinopathy	-3.53	-0.25	-6.63	-0.44	0.026
Dependent variable: Libido score					
DM only group (*n*=221, R-square:0.21)					
Constant	39.99		35.43	44.56	0.000
Age	-0.20	-0.30	-0.29	-0.12	0.000
Hypertension	-2.12	-0.15	-3.83	-0.41	0.015
Retinopathy	-3.41	-0.24	-5.20	-1.61	0.000

Table 19 Continued

DM+CVD group (*n*=73, R-square:0.11)					
Constant	25.96		24.03	27.89	0.000
Retinopathy	-4.94	-0.32	-8.19	-1.69	0.003
Dependent variable: Premature ejaculation score					
DM only group (*n*=241, R-square:0.13)					
Constant	14.93		12.20	17.66	0.000
Age	-0.07	-0.29	-0.10	-0.04	0.000
HbA1c	-0.27	-0.19	-0.46	-0.07	0.007
Retinopathy	-0.81	-0.19	-0.46	-0.07	0.007
CVD only group (*n*=96, R-square:0.06)					
Constant	11.60		9.00	14.21	0.000
Age	-0.05	-0.24	-0.10	-0.08	0.021
DM+CVD group (*n*=73, R-square:0.11)					
Constant	8.93		8.20	9.65	0.000
Retinopathy	-1.24	-0.22	-2.47	-0.04	0.049
Nephropathy	-2.95	-0.22	-5.85	-0.04	0.047

The prevalence of sexual dysfunction in all subjects was 82%. The prevalence of SD in DM only group, CVD only group and DM plus CVD group was 80%, 78% and 91%, respectively. However, in the DM plus CVD (37%) group a larger proportion of participants have moderate and severe SD compared to the DM only (19%) and CVD only (12%) groups. A Chi-square test for independence revealed a significant difference with a medium effect size, in the severity of sexual dysfunction within the three groups: DM only, CVD only and DM+CVD, χ^2 (8, n=394) =27.9, p=0.00, φ_c=0.2. (Fig.3)

Figure 3 Prevalence of sexual dysfunction in percentage



Univariate Analysis – All CVD participants:

The results of crude logistic regression conducted on all patients with CVD is presented in Table 20. Subjects with CVD, who were more than 50 years age of age, were 3 times more likely to have moderate to severe SD compared to the ones who were 50 years or below. Participants who had CVD with diabetes were 5 times more likely to have moderate to severe SD compared to participants with CVD alone. Men with CVD who consumed alcohol and suffered from stress were 2.5 and 2 times more likely to suffer from moderate to severe SD, compared to those who don't consume alcohol and don't have stress, respectively. Being overweight/ obese, having waist circumference more than 90cm, use of statins/ beta-blockers, cigarette smoking, insomnia and androgen deficiency did not significantly increase the likelihood of moderate to severe SD.

Multivariate Analysis – All CVD participants:

Multiple logistic regression analysis (Table 21) showed no multi-collinearity between the independent variables and the model showed a good fit as tested by Hosmer-Lemeshow Goodness of Fit Test ($p>0.05$). After controlling the confounders, patients with CVD who were more than 50 years old were 3 times more likely to have moderate to severe SD compared to participants who were 50 years or below without CVD (OR=3.23, 95CI 1.11-9.37). Again, after controlling for confounders, participants who had CVD with diabetes were 4 times more likely to suffer from moderate to severe SD compared to participants with CVD alone (OR=4.27, 95CI 2.03-9.00). Alcohol consumption and stress were not significant predictors of moderate to severe SD in diabetic men.

TABLE 20: UNIVARIATE ANALYSIS: ALL CVD PARTICIPANTS							
	No-Mild SD		Moderate-Severe SD		OR	P	95%CI
	n	%	n	%			
Age							
≤50	36	25	5	10	1.00		
>50	107	75	47	90	3.16	0.02	1.17-8.57
Body Mass Index							
<23	20	15	7	15	1.00		
23-27.4	45	35	18	38	1.14	0.80	1.04-3.17
≥27.5	64	50	22	48	0.98	0.97	0.40-0.99
Waist Circumference							
<90cm	41	34	12	27	1.00		
≥90cm	79	66	33	73	1.43	0.36	0.67-3.05
CVD Duration							
≤5years	100	70	35	66	1.00		
>5years	43	30	18	34	1.20	0.60	0.61-2.34
Diabetes							
Yes	58	41	41	77	5.00	0.00	2.43-10.3
No	85	59	12	23	1.00		
Statins							
Yes	104	83	28	76	0.66	0.35	0.27-1.59
No	22	17	9	24	1.00		
Beta-Blockers							
Yes	67	53	18	49	0.85	0.66	0.41-1.77
No	60	47	19	51	1.00		
Smoker							
Yes	31	22	15	28	1.43	0.33	0.70-2.92
No	112	78	38	72	1.00		
Alcohol							
Yes	21	15	16	30	2.51	0.02	1.19-5.30
No	122	85	37	70	1.00		
Stress							
Yes	24	17	15	28	1.96	0.08	0.93-4.11
No	119	83	38	72	1.00		
Insomnia							
Yes	22	15	10	19	1.28	0.56	0.56-2.92
No	121	85	43	81	1.00		
Testosterone							
Low	24	28	8	23	0.77	0.57	0.31-1.92
Normal	62	72	27	77	1.00		

TABLE 21: MULTIPLE LOGISTIC REGRESSION: ALL CVD PARTICIPANTS						
	β	SE	Wald χ^2	OR	P	95%CI
Age (>50 years)	1.17	0.54	4.65	3.23	0.03	1.11-9.37
Diabetes (Yes)	1.45	0.38	14.6	4.27	0.00	2.03-9.00
Alcohol (Yes)	0.68	0.42	2.60	1.96	0.11	0.87-4.46
Stress (Yes)	0.46	0.42	1.18	1.59	0.28	0.69-3.68

A sub-study was conducted in 200 subjects randomly selected from the total 420 men to determine the possible role of testosterone in the various components of SD, Out of 200 participants, 82 were from DM only group, 57 from CVD only group and 61 from DM+CVD group. Overall, 32% of all participants had low testosterone (Normal range: 9.9-22.9 nmol/L) levels (65). In the DM only group, CVD only group and DM+CVD group, 40% (n=33), 22% (n=13) and 31% (n=19) had low testosterone, respectively. Using a one-way between group analysis of variance (ANOVA) was conducted to explore the difference in the testosterone levels between the 3 groups. There was a statistically significant difference at the $p<0.05$ level in testosterone measurement for the three groups: $F(2, 197) = 5.7$, $p=0.00$. However, the difference between mean testosterone levels was quite small as the effect size calculated using eta squared was 0.05. Post-hoc comparison using the Tukey HSD test showed that the mean testosterone level for DM only group was significantly different from that of CVD only group. Testosterone levels for DM plus CVD group did not significantly differ from that of either DM only group or CVD only group.

Discussion

The aim of this study was to determine the predictors of various types of SD in men with DM with or without CVD. The most significant finding of this study was that the predictors were not only different between the components of SD (ED, libido and premature ejaculation) but also between the different groups (DM only, CVD only and DM+CVD). This has never been demonstrated before. When we analyzed the predictors of ED score in the DM only group, we found negative association of age, HbA1c, retinopathy, insomnia and neuropathy. The Action for Health in Diabetes trial also found strong association of ED with presence of neuropathy and vascular complication [Rosen RC et al., 2009]. Romeo JH et al. (2000) conducted a study to evaluate the association of glycemic control (HbA1c) with ED in men with T2DM and found that the mean erectile function score decreased as HbA1c level increased [Romeo JH et al., 2000]. Romeo JH et al. concluded that peripheral neuropathy and HbA1c were independent predictors of ED [Romeo JH et al., 2000]. Our finding of insomnia being an independent predictor of ED score is unique. Little is known about the association of insomnia with ED and SD. However, there is strong evidence linking obstructive sleep apnea syndrome to ED [Margel D et al., 2004; Hirshkowitz M et al., 1990]. Hirshkowitz M et al., (1990) suggested high prevalence of sleep apnea activity (43.8%) among men complaining of ED [Hirshkowitz M et al., 1990]. Margel D et al., (2004) assessed the association of obstructive sleep apnea syndrome and ED found that severe obstructive sleep apnea syndrome is strongly associated with ED with age, morning tiredness and respiratory disturbance index being the predictors [Margel D et al., 2004]. This highlights that sleep disorder could be associated with ED.

When we compare the ED score for the cardiovascular only and CVD+DM group the predictors were different from the DM only group. The main contributors in the DM only group such as HbA1c, insomnia and neuropathy were not associated with ED score in the

CVD only group and the DM+CVD group. In the CVD only group, age was the only predictor while retinopathy listed as the sole predictor for DM+CVD group. Hypertension, hyperlipidemia and depression were not associated with ED in our study. Wei M et al. (1994) examined the relationship between serum cholesterol and ED. They concluded that high levels of total cholesterol and low levels of high-density lipoprotein were associated with ED [Wei M et al., 1994]. The findings were based on general population and not on men with diabetes or cardiovascular disease. The Massachusetts Male Aging Study in year 2000 conducted a population based longitudinal study on 1,709 men and found that the risk of ED was higher in elderly men, lower education, DM, heart disease and hypertension [Johannes CB et al., 2000]. Contradicting to this finding, Siu SC et al, (2001) found that in Hong Kong, highly educated Chinese men with DM were at higher risk of ED [Siu SC et al., 2001]. This could be explained by the better job prospects and higher career position levels among the more educated group and in return greater level of stress. In our study, level of education was excluded from the stepwise regression analysis. This could be due to recruitment of our study population was mainly from urban and sub-urban area with higher education levels compared to the rural population.

Analysis of the libido score showed negative predictors of age, hypertension and retinopathy in the DM only group while retinopathy was negatively associated with libido score in the DM+CVD group. As for the CVD only group, there were no predictors loaded. This highlights the differences between the 3 groups. Hypertension, which was not associated with ED score, strongly predicts libido score for the DM only group. In year 2000, Johannes CB et al, suggested higher risk of ED in men with hypertension [Johannes CB et al., 2000]. In this study, a self-administered questionnaire focusing on ED was used for data collection [Johannes CB etal., 2000]. In our study, usage of a more comprehensive SAD-MEN tool

enabled us to analyze the impact of hypertension on different components of SD and not just ED alone.

Analysis of the premature ejaculation score showed negative predictors of age, HbA1c and retinopathy for the DM only group while retinopathy and nephropathy negatively impacts the score for DM+CVD group. Our findings were similar to those of Dunsmuir WD et al.,(1996) who demonstrated that the 5 most significant associations with impotence were age, retinopathy, peripheral neuropathy, autonomic neuropathy and mode of DM treatment [Dunsmuir WD et al., 1996]. However, this study used erectile function score as the main outcome measure compared to our study that focused on a more comprehensive SD score.

Age, retinopathy, neuropathy and hypertension were found to have negative impact on total SD score in our study. The effect of ageing on decreasing sexual functioning has been shown in previous studies. The likely explanantion for the decrease in function would be the decline in physical health and fitness that occurs with ageing, which could be further aggravated by other comorbid diseases [Nicolosi A et al., 2003]. This study however showed that only age, vascular and neuronal factors made significant contributions to the development of SD in men with DM without CVD. This maybe because neuropathy and vasculopathy has a direct negative influence on the normal mechanism of erection leading to sexual dysfunction [De Angelis L et al., 2001; Nehra A et al., 2001].

The prevalence of SD is high in a multi-ethnic Malaysian population with DM (80%) and this is worse with concomitant CVD (91%). This finding is consistent with a cross-sectional survey on Chinese men with diabetes in Hong Kong by Siu et al. in 2001. They suggested that the prevalence of ED is higher in Asians compared to that of Western population due to cultural differences and association of hypertension and albuminuria [Siu SC et al., 2001]. The high prevalence of SD is consistent with the high prevalence of ED

(70.1%) among urban aging men in Malaysia [Khoo EM et al., 2008]. It is also comparable to our neighboring country, Singapore where a nationwide survey showed the prevalence of ED to be 73% [Chin CM et al., 2002]. However, the focus of the two studies was on ED alone and not on SD as a whole. The prevalence of ED in angiographically diagnosed coronary artery disease patients without DM ranged from 46-49% [Foroutan SK et al., 2007; Montorsi F et al., 2003]. These studies looked specifically at erectile dysfunction while our study considers a more comprehensive sexual dysfunction problem involving erectile, ejaculatory and libido problems together, which account for the higher and more accurate prevalence of SD. Men with concomitant DM and CVD reported more severe SD compared to men with DM or CVD only. This finding is important in view of the increasing trend of CVD and diabetes in the country.

Prevalence of androgen deficiency in diabetic males has been previously estimated to range between 33-50% [Biswas M et al., 2012]. In our sub-study, similar findings were obtained with the prevalence of androgen deficiency being 40% in the DM only group, 22% in CVD only group and 31% in DM with CVD group. This shows that men who had CVD were less likely to be androgen deficient compared to men with diabetes only. Studies had shown that hypogonadism was associated with ED in men with diabetes [Ghazi S et al., 2012; Corona G et al., 2004]. This had resulted in having testosterone replacement therapy as a treatment option in diabetic men with ED [Wang C et al., 2009]. However, the results of our study have shown that androgen deficiency alone is not a significant contributor to SD in men with DM or CVD. The difference in the results may be the study outcome in previous studies mainly focused of erectile problems alone versus the more comprehensive SD in our study.

The main strength of the study is that it was conducted in three major states of Malaysia, including patients from the private and public sectors of general practice clinics, specialist clinics and hospital wards. This allowed a good range of participants from different

socio-economic and ethnic background to be recruited in to the study, making it possible to generalize the results of this study to the general diabetic and CVD population of Malaysia. In addition, this study had extensive assessment of potential contributing factors to the development and aggravation of male SD. In this study, a self-reported questionnaire was employed to obtain data, which have some limitations such as recall and response bias. The topic of sexuality in Asian community is regarded as a very sensitive topic and maybe culturally inappropriate. Hence, this poses a risk of dishonest answers being provided by the participants. Nevertheless as mentioned by Coronoa *et. al.* self-administered questionnaire was the best method to evaluate a sensitive topic such as sexual dysfunction, without having to deal with much embarrassment [Corona G et al., 2006]. The SAD-men questionnaire was developed based on multi-ethnic Asian population and is culturally acceptable for Malaysian. The findings of this study were based on Malaysian population and cannot be generalized for other population until further studies are done.

CHAPTER SIX: GENERAL DISCUSSION AND CONCLUSION

CHAPTER SIX: GENERAL DISCUSSION AND CONCLUSION

Diabetes mellitus (DM) is a chronic condition associated with multiple complications and has profound effects on the social, psychological and physical well-being of a person. DM is associated with multiple complications such as neuropathy, ischemic heart disease, micro albuminuria even at the point of diagnosis [Spijkerman AMW et al., 2003; Spijkerman AMW et al., 2004]. This clearly indicates the insidious onset of organ damage even before diagnosis of DM. One of the earliest large scale study on DM is the UK Prospective Diabetes Study (UKPDS) started in 1977 showed that over 10 years, a difference of HbA1c of 0.9% between the intensively treated versus the conventionally treated group decreased the risk of microvascular complications by 25%; however, no difference was observed for macrovascular complications [UKPDS, 1998]. The UKPDS also found that for every 1% reduction in mean HbA1c, there is a corresponding 21% reduction in DM complications, 21% reduction of deaths related to DM, 14% reduction of myocardial infarction and 37% reduction of microvascular complications [Stratton IM et al., 2000]. Similar findings were found in other studies done on different populations and on Type 1 diabetes [Ohkubo Y et al., 1995; DCCT, 1993]. These studies demonstrated a strong link between good glycemic control and complications of DM.

Post UKPDS and DCCT 10 years follow-up study found that the reduction of risk in developing complications remained lower in the intensively treated group despite similar HbA1c levels to the controls [DCCT/EDIC group, 2005]. This “legacy effect” or “metabolic memory” threw the diabetes management into a glycemic frenzy stage to achieve lowest possible glycemic control in order to reduce complications and cardiovascular events. However, the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, the ADVANCE Collaborative group studies showed contradicting results that lowering the HbA1c level to less than 6.5% significantly increased the mortality and cardiovascular

events. [The Action to Control Cardiovascular Risk in Diabetes group,2008; Ismail-Beigi F et al., 2010; The ADVANCE Collaborative group, 2008; Duckworth W et al.,2009]. Thus, current guidelines support early diagnosis and treatment of DM with 'tailoring' of treatment modalities to target glycemic control. DM management "tailoring" is a broad concept involving multiple factors such as duration of disease, symptoms, presence of complications, age, glycemic control, treatment satisfaction, socio-economic background and etc. How do we judge if the management modality is suitable or is the best for the patient?

Over the years, DM management has undergone rapid evolution and transformation. The focus of DM management was previously more 'gluco-centric' with biochemical and clinical assessment being the only indicator of disease outcome. These measures do not reflect the psychological and social state of patient. This is no longer the case with the progress of medicine. The focus now is more holistic with the aim of maintaining highest possible quality of life for not only people living with diabetes. However, QOL is a subjective perception and the challenge lies in accurately reflecting QOL into objective scores for assessment [WHO, 1997]. In addition, the tool must be sensitive, reliable and relevant to the local population. This is especially difficult for Asia as different languages, races, cultures, religious beliefs and socio-economic progress within the population can influence the outcome. Most of the QOL tool in Asia were translated or adapted from tools developed based on Western population [Cheung YB et al., 2006]. There is a lack of a QOL assessment tool that is sensitive, reliable and stable across the different language, culture, education level, religion and structures of medical care especially in South East and East Asia. Why is Asia so different from the rest of the world?

Asia comprised of Central Asia, East Asia, North Asia, South Asia and South East Asia. It is the most populous continent in the world and bears 60% of the world diabetes population [Chan et al., 2009]. In the 21 st century, Asia is rapidly becoming the epicenter of

the diabetes epidemic [Chan et al., 2009]. What used to be a disease of the West is now serious health crisis in many Asian countries [Wild S et al., 2004]. This is contributed by several causes. Firstly, Asians are more susceptible to develop DM at a younger age, at lower body mass index and with lesser weight gain [Zhang P et al., 2010; Ramachandran A et al., 2010]. Secondly, Asians have a stronger genetic link for T2DM [Mohan V et al., 1985; Ng MCY et al., 2001]. Thirdly, Asians have greater tendency for abdominal obesity resulting in insulin resistance and lastly, the rapid economic growth in many Asian countries propel the shift of lifestyle and diet to a more sedentary and high calorie, high processed food intake [Yoon KH et al., 2006; Hu FB 2011]. The combination of all these factors leads to the DM inferno in Asia. A big challenge for Asia is the vast differences in ethnicity, cultures and socio-economic development within Asia, which can affect the clinical presentation, management, prevention of DM and perception of QOL. In Asia especially South East Asia, there is a strong element of Western culture influence or westernization likely due to the history of colonialism. Westernization represents a lifestyle or behavioral approach to health in epidemiology [Salant T et al., 2003]. DM is considered to be one of the diseases associated with westernization [Fujimoto WY, 1992]. The many different religions and cultures in Asia need to be considered when designing a tool for assessing QOL for Asians as spirituality, religion and personal beliefs is highly correlated to psychological and social domains of QOL [WHO SPRRB Group, 2006]. Special attention to ethnicity and language is particularly important in the assessment of QOL not only due to the subjectivity but also the cultural framework essential to the construct[Guarnnaccia, 1996].

In the age of diabetes epidemic in Asia, QOL is rapidly becoming an important measure of disease outcome. The AsianDQOL was the first tool constructed based on subjects of different ethnicities and their lingua franca i.e English, Malay language and Mandarin. The strong point of this tool is that the construct was based on focus group

interviews for all the three different languages. The focus group's members were of different ethnicities, religion and socio-economic background. This will ensure that the cultural differences are preserved and the tool is acceptable to the local population. Reliability testing demonstrated high internal consistency for all the three languages. Confirmatory factor analysis confirmed the model structure for the English and Malay language version. Although the population was of similar socio-economic background, there were differences in terms of ranking and priority of QOL domains for the different languages. The domain on diet and eating habits played an important role for the English and Mandarin language but were of lesser importance for the Malay language version. This resulted in 3 different QOL tools (English, Malay and Mandarin versions) and not one tool translated into different languages. (English version translated into Malay and Mandarin language).

The scoring system is also unique to the respective language. This gives the tool the advantage of being widely applicable and relevant to many Asian countries such as the English language version for Malaysia, Singapore, Brunei, Indonesia, Philippines, India, Hong Kong, China and Taiwan. The Mandarin version is applicable to Malaysia, Singapore, Hong Kong, China and Taiwan. The Malay language version can be used in Malaysia, Indonesia, Brunei and Southern Thailand. Besides being a stable and reliable tool, the AsianDQOL provides a QOL score that has a good clinical value in the management of DM. This score will enable the clinicians and patient to objectively assess their QOL and to detect for changes over a period of time.

Another important finding in this study is that there are not only differences in perception of QOL between the ethnic groups (Malay, Chinese and Indian) but also within the same ethnic group with different lingua franca (Malay ethnicity speaking Malay language versus Malay ethnicity speaking English language). This clearly stressed the insufficiency of

a single, standard tool for measurement of QOL across the different ethnic groups and their lingua franca in Asia.

In our study, there were significant differences of QOL perception detected within the same ethnic group but with different lingua franca. Analysis demonstrated significant differences between the ethnic groups (Malay, Chinese and Indian) on perception of QOL. In depth analysis of the components of QOL showed differences between the ethnic group's perceptions on diet component. This demonstrates that ethnic differences do exist in a population sharing similar socio-cultural contexts. This finding is similar to Singapore where a population based study by Wee et al. in 2005 showed ethnicity as an important factor influencing QOL in people with diabetes [Wee HL et al., 2006]. However, in the cross-sectional study cross Singapore, a generic tool was used to measure QOL and this could limit the sensitivity in participants with DM. When we compared the different ethnic groups in Malaysia, the predictors of QOL were different in the Malay ethnic group compared to the Chinese and Indian. Within the Malay ethnic group, marked differences were detected with the more English language speaking group (ELS) versus the more traditional Malay language speaking group (MLS). The (ELS) group was primarily concerned about presence of renal impairment while the (MLS) group was affected by the duration of DM and sexual dysfunction. This could be that the ELS group is associated with higher education level (25% have at least secondary education and 75% have above secondary education) compared to the MLS group (54% have at least secondary education and above). Higher education level is associated with better economic security and job prospects. Glasgow et al. in 1997 found that lower education level and lesser income were associated with a lower QOL score [Glasgow RE et al., 1997]. The presence of DM complications was linked to lower QOL score especially for co-existent of microvascular and macrovascular complications [Glasgow RE et al., 1997; UK Prospective Diabetes Study Group, 1999; Coffey JT et al., 2002]. The presence

of chronic kidney disease further worsens the QOL especially in end-stage renal failure and with initiation of dialysis [Perlman RL et al., 2005; Merkus MP et al., 1997]. This is consistent with ELS group with strong negative association of renal impairment on QOL score.

The Chinese ethnic group also showed significant differences between the ELS group versus the traditional Mandarin speaking group. The main determinants of QOL in the ELS group were sexual dysfunction versus HbA1c, hyperlipidemia and sexual dysfunction in the Mandarin-speaking group. The ELS group being more westernized in their behavior and lifestyle could have an impact on their perception compared to the more traditional Mandarin-speaking group. The presence of hyperlipidemia as a determinant of QOL scores in the Mandarin speaking Chinese group is unique. This finding highlights the importance of the eating culture and health among the more traditional Chinese population. A population based study in Hong Kong Chinese population found that the activity of eating was viewed as an important activity signifying good health, social bonding with family and friends [Lau A et al., 1998]. This led to formation of a strong bond between the ability to eat freely, freedom to participate in such social rituals and life satisfaction affecting QOL [Glasgow RE et al., 1997; UK Prospective Diabetes Study Group, 1999; Coffey JT et al., 2002]. Sexual dysfunction severely impacts QOL in the Chinese ethnic group.

The predictors of QOL in the ELS Indian ethnic group were different from the Malay speaking Indians. In the Malay language-speaking group of Indian ethnicity, the mode of treatment and working statues explains 45% of the total QOL score. In this group, having a permanent job is associated with better financial stability and better QOL. Poorer QOL were associated with insulin usage perhaps due to the complications of insulin. This is consistent with findings of Glasgow E et al. in 1996 linking insulin use to poorer QOL [Glasgow RE et al., 1997].

Our study highlights that perception of QOL is not only different across the ethnic groups but also among the more English-speaking and native language-speaking group within the same ethnicity. Perception of QOL is very much influenced by exposure to westernization that can be assessed by their lingua franca. Current study to look at the effect of westernization on perception of QOL among Asian population living in Australia will shed more light into this area.

There is strong evidence to suggest that complications of diabetes were associated with detrimental impact on QOL [Glasgow RE et al., 1997; Stewart AL wt al., 1989; UK Prospective Diabetes Study Group, 1999; Merkus MP et al., 1997]. In our study, sexual dysfunction, retinopathy and nephropathy severely reduced QOL. Sexual dysfunction is also strongly negatively correlated with QOL in all the three major ethnic groups. This is consistent with findings globally that found a strong link between DM, erectile dysfunction and worse QOL [Person DF et al., 2003; De Berardis G et al., 2002]. A comprehensive study done by De Berardis et.al.(2002), found that ED affects 1/3 of patients with diabetes and they have higher depressive symptoms and poorer QOL [De Berardis G et al., 2002]. However, this study takes into account self-reported symptoms with no clinical diagnosis and QOL was assessed using a general assessment tool (SF-36). In women, sexual dysfunction is frequent in patients with DM and is associated with reduction in overall QOL with 77% having lack of libido and 38% with vaginal dryness [Enzlin P et al., 2002; Erol B et al., 2002]. Sexual dysfunctions were found to be associated with poorer QOL outcome in men and women with diabetes from all 3 major ethnic groups. However, very little is known about sexual dysfunction in Malaysia.

Sexual dysfunction is classified as a disorder in one or more of the four stages of sexual response cycle: desire, excitement, orgasm and resolution [DSM IV, 2000]. SD is highly associated with DM in both genders [Berardis GD et al., 2002; Enzlin P et al., 2012;

Erol B et al.,2002]. In our study, the prevalence of SD is associated with negative QOL in English, Malay and Mandarin language group. It is also a strong contributor to poor QOL in Malay speaking Malay ethnic group, Chinese ethnic group of both English and Mandarin speaking and Indian ethnic group of both English and Malay speaking. This finding supports the theory that the prevalence of SD is high among people living with DM and due to the negative impact on QOL it is important for early detection and proper management. However, in Asia SD remains under diagnosed. This is mainly due to the challenge in diagnosing SD. The topic of sexuality in Asian community is regarded as a very sensitive and private topic to discuss even with their doctors. Corona et al in 2006 suggest that self-administered questionnaire is still the best method to evaluate a sensitive topic such as SD, without causing embarrassment [Corona et al, 2006].

The development of a valid and reliable tool to assess all the 4 components of sexual dysfunction is crucial for early detection and proper management. The most widely used tool for assessment of SD is the International Index of Erectile Function-5(IIEF-5) by Rosen et al in 1997. This tool was designed to focus on erectile dysfunction and therefore lack in assessing other areas of sexual dysfunction. In 2004, Rosen et al. designed the Male Sexual Health Questionnaire (MSHQ) to address the ejaculatory disorders and sexual satisfaction component of SD [Rosen et al, 2004]. The IIEF-5 and MSHQ still failed to capture the complete picture of SD which could lead to misconception and under diagnosis. The SADMEN is the first comprehensive assessment tool for SD. It is developed based on a multi-ethnic population similar to many Asian countries and is available in English, Malay language and Mandarin. This will ensure a wide application across Asia and the effect of cultural lost during translation of tool can be avoided.

Utilizing the SAD-MEN questionnaire, we were able to demonstrate that the predictors of SD were not only different between the components of SD (ED, libido and

premature ejaculation) but also between the different groups (DM only, CVD only and DM+CVD). This has never been demonstrated before. Analysis done on the predictors of ED score in the DM only group, showed negative association of age, HbA1c, retinopathy, insomnia and neuropathy. The Action for Health in Diabetes trial also found strong association of ED with presence of neuropathy and vascular complication [Rosen RC et al., 2009]. Romeo JH et al. (2000) conducted a study to evaluate the association of glycemic control (HbA1c) with ED in men with T2DM and found that the mean erectile function score decreased as HbA1c level increased [Romeo JH et al., 2000]. Romeo JH et al. concluded that peripheral neuropathy and HbA1c were independent predictors of ED [Romeo JH et al., 2000]. Our finding of insomnia being an independent predictor of ED score is unique as insomnia is not an indicator of diabetes or its complications. Little is known about the association of insomnia with ED and SD. However, there is strong evidence linking obstructive sleep apnea syndrome to ED [Margel D et al., 2004; Hirshkowitz M et al., 1990]. Hirshkowitz M et al., (1990) suggested high prevalence of sleep apnea activity (43.8%) among men complaining of ED while Margel D et al., (2004) assessed the association of obstructive sleep apnea syndrome and ED found that severe obstructive sleep apnea syndrome is strongly associated with ED with age, morning tiredness and respiratory disturbance index being the predictors [Margel D et al., 2004; Hirshkowitz M et al., 1990]. This supports the theory that sleep disorder could be associated with ED.

When we compare the ED score for the cardiovascular only and CVD+DM group the predictors were different from the DM only group. The main contributors in the DM only group such as HbA1c, insomnia and neuropathy were not associated with ED score in the CVD only group and the DM+CVD group. In the CVD only group, age was the only predictor while retinopathy listed as the sole predictor for DM+CVD group. Hypertension, hyperlipidemia and depression were not associated with ED in our study.

Analysis of the libido score showed negative predictors of age, hypertension and retinopathy in the DM only group while retinopathy was negatively associated with libido score in the DM+CVD group. As for the CVD only group, there were no predictors loaded. This highlights the differences between the 3 groups. Hypertension, which was not associated with ED score, strongly predicts libido score for the DM only group. In year 2000, Johannes CB et al, suggested higher risk of ED in men with hypertension [Johannes CB et al., 2000]. In this study, a self-administered questionnaire focusing on ED was used for data collection [Johannes CB et al., 2000]. In our study, usage of a more comprehensive SAD-MEN tool enabled us to analyze the impact of hypertension on different components of SD and not just ED alone.

Analysis of the premature ejaculation score showed negative predictors of age, HbA1c and retinopathy for the DM only group while retinopathy and nephropathy negatively impacts the score for DM+CVD group. Our findings were similar to those of Dunsmuir WD et al.,(1996) who demonstrated that the 5 most significant associations with impotence were age, retinopathy, peripheral neuropathy, autonomic neuropathy and mode of DM treatment [Dunsmuir WD et al., 1996]. However, this study used erectile function score as the main outcome measure compared to our study that focused on a more comprehensive SD score.

Age, retinopathy, neuropathy and hypertension were found to have negative impact on total SD score in our study. The effect of ageing on decreasing sexual functioning has been shown in previous studies. The likely explanantion for the decrease in function would be the decline in physical health and fitness that occurs with ageing, which could be further aggravated by other comorbid diseases [Nicolosi A et al., 2003]. This study however showed that only age, vascular and neuronal factors made significant contributions to the development of SD in men with DM without CVD. This maybe because neuropathy and

vasculopathy has a direct negative influence on the normal mechanism of erection leading to sexual dysfunction [De Angelis L et al., 2001; Nehra A et al., 2001].

The prevalence of SD is high in a multi-ethnic Malaysian population with DM (80%) and this is worse with concomitant CVD (91%). This finding is consistent with a cross-sectional survey on Chinese men with diabetes in Hong Kong by Siu et al. in 2001. They suggested that the prevalence of ED is higher in Asians compared to that of Western population due to cultural differences and association of hypertension and albuminuria [Siu SC et al., 2001]. The high prevalence of SD is also consistent with the high prevalence of ED (70.1%) among urban aging men in Malaysia [Khoo EM et al., 2008]. It is also comparable to our neighboring country, Singapore where a nationwide survey showed the prevalence of ED to be 73% [Chin CM et al., 2002]. However, the focus of the two studies was on ED alone and not on SD as a whole. The prevalence of ED in angiographically diagnosed coronary artery disease patients without DM ranged from 46-49% [Foroutan SK et al., 2007; Montorsi F et al., 2003]. These studies looked specifically at erectile dysfunction while our study considers a more comprehensive sexual dysfunction problem involving erectile, ejaculatory and libido problems together, which account for the higher and more accurate prevalence of SD. Men with concomitant DM and CVD reported more severe SD compared to men with DM or CVD only. This finding is important in view of the increasing trend of CVD and diabetes in the country.

Prevalence of androgen deficiency in diabetic males has been previously estimated to range between 33-50% [Biswas M et al., 2012]. In our sub-study, similar findings were obtained with the prevalence of androgen deficiency being 40% in the DM only group, 22% in CVD only group and 31% in DM with CVD group. This indicates that men who had CVD were less likely to be androgen deficient compared to men with diabetes only. Studies had shown that hypogonadism was associated with ED in men with diabetes [Ghazi S et al., 2012;

Corona G et al., 2004]. This had resulted in having testosterone replacement therapy as a treatment option in diabetic men with ED [Wang C et al., 2009]. However, the results of our study have shown that androgen deficiency alone is not a significant contributor to SD in men with DM or CVD.

The strength of this study is that is conducted across a multi-ethnic population involving subjects of different ethnicities and ligua franca, religion, socio economic status. This allow a good composition of different layers of society and avoid biasnes. The AsianDQOL and SADMEN questionnaire is available in English, Malay language and Mandarin, making its application wide across many countries in Asia. The limitation is mainly due to the smaller sample size of Chinese with Mandarin speaking subjects due to lack of Chinese Mandarin competent subjects in the recruitment area. In this study, self administered questionnaires were used as the mode for data gathering and this could lead to biasness towards the literature. However, in view of the high literacy rate (93%) among urban Malaysian population, the data capture is adequate[UNICEF, 2013].

Conclusion

In conclusion the AsianDQOL is a valid, reliable and stable tool for assessment of QOL across population with different ethnicities, languages, religions and socio-economic differences. The steps taken to develop and validate the Asian DQOL preserved the cultural differences and should be followed when developing a QOL assessment tool for other Asian countries. This will ensure a more accurate reflection of QOL which is crucial to the management of DM. This study also demonstrated that the perception of QOL is not only different across the ethnic groups but also the different lingua franca of the group. This strongly indicates that in developing a tool for a multi-ethnic population, careful consideration need to be taken not only for ethnicity but for their lingua franca as well. Asian

population cannot be generalized for example in India, a majority of the population are Indians but with different lingua franca ie. Hindi in North India, Punjabi in Punjab. The best way to capture such sensitive data as QOL is to have a tool that is relevant to each sub-population. SD is associated with negative QOL outcome in all major ethnic groups.

It is important to remember that premature ejaculation and libido also play crucial role in determining SD. The predictors of SD were not only different between the components of SD (ED, libido and premature ejaculation) but also between the different groups (DM only, CVD only and DM+CVD). This is the first study that analyzed predictors of the different components of SD and not just ED alone. The presence of microvascular changes is strongly associated with SD. Aging men with diabetes and cardiovascular disease with presence of microvascular changes are at higher risk of developing moderate to severe SD.

The study have contributed new knowledge to the field of diabetes, QOL and SD. Current studies are ongoing to compare the impact of westernization on QOL among Asians living in Australia and Malaysian population. An electronic version of the AsianDQOL is currently being constructed to allow easy access and wider application. Future collaborative studies to validate the AsianDQOL for use in other Asian population such as in Singapore, Brunei, Indonesia, Hong Kong, Taiwan and China will enhance the tool further.

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APPENDICES

Appendix 1: Publication acceptance letter from Asia Pacific Journal of Clinical Nutrition

Date: Fri, 18 Jul 2014 05:31:03 -0400

[redacted]

> Subject: Asia Pacific Journal of Clinical Nutrition - Decision on Manuscript ID APJCN-2014-0114.R1

>
> 18-Jul-2014
>
> Dear Dr. Abdul Kadir:
>
> It is a pleasure to accept your manuscript entitled "Title: Review: Evolution of diabetes management in the 21st century: the contribution of quality of life measurement in Asians." in its current form for publication in the Asia Pacific Journal of Clinical Nutrition.
>
> We also enclose our "manuscript checklist" of items which we have identified that need to be addressed by the authors. (Please refer to the newest Instruction for Authors online.)
>
> Particular points follow for careful consideration:
> 1.Provide authors' full given names and qualifications, fully detail the address of the corresponding author, recommend a running title, and be sure that a statement about approval by an institutional review board of the ethical matters which pertain to the submitted work is included in the manuscript.
> 2.Units: International System of units (SI) should be applied. For litre, "L" is used rather than "l". e.g., mL, dL rather than ml and dl, mol rather than g, etc.
> 3.Initially use the word in full, followed by the abbreviation in parentheses. Thereafter use the abbreviation.
> 4.While 'Spell Check' in Word should be used routinely, make sure to read the manuscript again after the check since inappropriate changes may have been made and be persistent once accepted.
> 5.Significant figures: not more than 3
> 6.Proper footnote for tables
> 7.Concise table heading

> 8.Change all P to p (probability for statistic testing)
> 9.Please refer to the SAMPLE.pdf file attached for the revision of citation format (after but not before period) and Reference list (list all authorship but not et al., and do not include issue number if there is continuous pagination throughout a volume.
> 10.Some references are incomplete.
> 11.Use SD, SE instead of sd and se.
>
> Once the revised manuscript is prepared, you can email us, but not upload it through your Author Center.
[redacted]
>
> Thank you for your valuable contribution. The Editors of the Asia Pacific Journal of Clinical Nutrition, look forward to your continued contributions to the Journal.
>
> Sincerely,
> Prof Mark L Wahlqvist,
> Editor-in-Chief
> Asia Pacific Journal of Clinical Nutrition
> The First Affiliated Hospital of Zhengzhou University
> No.1 Eastern Jianshe Road, Zhengzhou, 450052, China
[redacted]
>

Appendix 2: Poster Presentation at the International Diabetes Congress 2013

IDF 2013 melbourne world diabetes congress 2 - 6 December 2013

Certificate of Attendance

This is to certify that

Dr Goh Shereen (Malaysia)

attended the

World Diabetes Congress Melbourne 2013

2 to 6 December 2013
Melbourne, Australia

[redacted]

Sir Michael Hirst
President IDF Melbourne, 2013

International Diabetes Federation

Diabetes AUSTRALIA

MELBOURNE AUSTRALIA

Appendix 3: Ethical approval from Monash University Human Research Ethical Committee

MONASH University

Monash University Human Research Ethics Committee (MUHREC)
Research Office

Human Ethics Certificate of Approval

Date:	**28 March 2012**
Project Number:	**CF2630 - 2011001537**
Project Title:	**Development, validation and evaluation of a quality of life measurement scale for diabetes mellitus; a prospective interventional study in type 2 diabetics in Malaysia**
Chief Investigator:	**Prof Rusli Nordin**
Approved:	**From: 28 March 2012** **To: 28 March 2017**

Terms of approval

1. The Chief investigator is responsible for ensuring that permission letters are obtained, if relevant, and a copy forwarded to MUHREC before any data collection can occur at the specified organisation. **Failure to provide permission letters to MUHREC before data collection commences is in breach of the National Statement on Ethical Conduct in Human Research and the Australian Code for the Responsible Conduct of Research**.
2. Approval is only valid whilst you hold a position at Monash University.
3. It is the responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval and to ensure the project is conducted as approved by MUHREC.
4. You should notify MUHREC immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.
5. The Explanatory Statement must be on Monash University letterhead and the Monash University complaints clause must contain your project number.
6. **Amendments to the approved project (including changes in personnel):** Requires the submission of a Request for Amendment form to MUHREC and must not begin without written approval from MUHREC. Substantial variations may require a new application.
7. **Future correspondence:** Please quote the project number and project title above in any further correspondence.
8. **Annual reports:** Continued approval of this project is dependent on the submission of an Annual Report. This is determined by the date of your letter of approval.
9. **Final report:** A Final Report should be provided at the conclusion of the project. MUHREC should be notified if the project is discontinued before the expected date of completion.
10. **Monitoring:** Projects may be subject to an audit or any other form of monitoring by MUHREC at any time.
11. **Retention and storage of data:** The Chief Investigator is responsible for the storage and retention of original data pertaining to a project for a minimum period of five years.

[redacted]

Professor Ben Canny
Chair, MUHREC

cc: Dr Khalid Abdul Kadir, Dr Shereen Giap Kah Goh

Postal – Monash University, Vic 3800, Australia
Building 3E, Room 111, Clayton Campus, Wellington Road, Clayton
[redacted]www.monash.edu/research/ethics/human/index/html
ABN 12 377 614 012 CRICOS Provider #00008C

Appendix 4: Study Information Sheet and Informed Consent forms for subjects

MONASH University
Malaysia

Patient Information Sheet (cross-sectional questionnaire study)

Development, validation and evaluation of a quality of life measurement scale for Type 2 diabetes mellitus (Project Number: CF2630-2011001537)

Patient No:

1. STUDY TITLE

Development, validation and evaluation of a health-related quality of life measurement scale for Type 2 diabetes mellitus.

2.WHY IS THIS STUDY BEING DONE?

You are being asked to join this study because you have type 2- diabetes mellitus with or without medication. The aim of this study is to invent and validate a questionnaire that can measure the quality of life in people with diabetes that is suitable for use in Asian countries and to determine the predictors of quality of life.

3. HOW WILL THIS STUDY BE CONDUCTED?

This study will be conducted in Malaysia.

In this study, you will be given two sets of questionnaires to fill. This questionnaire will ask you questions about your diabetes condition, your daily life activities, and inter-personal relationships.

The completed questionnaires will be collected by our researchers and data obtained will be analyzed.

4. WHAT ARE MY RESPONSIBILITIES DURING THE STUDY?

You must follow the instructions given by the doctor closely.

You must complete the questionnaires with the most accurate answer.

5.WHAT ARE THE POTENTIAL BENEFITS FROM PARTICIPATING?

You may or may not benefit from taking part in this study. Possible benefits include improvement in your condition.

The information we obtain from this study may help in the treatment of diabetes in the future.

6. WILL I BE INFORMED ABOUT NEW FINDINGS?

Your study doctor will inform you immediately about all new findings, which are available.

7. WILL THERE BE ANY COSTS FOR ME?

There are **NO** charges applicable to you. The study visits, blood tests, kits and physical examinations will be at no cost to you. The diabetes medication(s) you are currently taking will not be provided.

You will receive reimbursement of RM 5 for this study upon completion of the questionnaires.

8. IS MY PARTICIPATION VOLUNTARY?

Joining this research study is based on voluntary basis. You may refuse to take part or you may stop the study at any point of time for any reason. If you do not want to participate in this study your medical care **will not** be affected in any way.

9.WILL THE DATA BE KEPT CONFIDENTIAL?

All information concerning your participation in this study will be confidential. You will be given a patient number for identification.

Only the researchers and doctors will have access to your information and medical records. In the event that the results of this study are published, your personal data will not be divulged.

Records will be kept in the research center for a period of 2 years of which shall be dispose for destruction.

10. IS THIS A STUDENT RESEARCH PROJECT?

Yes, this study will support ONE postgraduate (Phd) student from School of Medicine and Health Sciences, Monash University Sunway Campus.

11. WHO CAN I CONTACT IF I HAVE ANY QUESTIONS OR COMPLAINTS?

If you have any questions about this study or in case of injury or illness, you should contact study doctor:

i) **Chief Investigator: Prof. Rusli bin Nordin**

Professor of Public Health (Occupational Medicine)

[redacted]

ii) **Investigator: Prof. Dato' Khalid bin Kadir**

Senior Consultant Endocrinology

[redacted]

iii) **Student Researcher: Dr.Shereen G.K. Goh**

Postgraduate (Phd) student , Monash University Malaysia

[redacted]

If you have any complaints regarding this study **(Project Number: CF2630-2011001537)**, kindly contact:

Ms. Joyce Tang,

Head, Planning & Research Management,

Monash University Sunway Campus,

Jalan Lagoon Selatan,

46150 Bandar Sunway,

Selangor Darul Ehsan, Malaysia.

[redacted]

Or

Executive Officer

Monash University Human Research Ethics Committee (MUHREC)

Building 3e Room 111

Research Office

Monash University VIC 3800

[redacted]

Do not sign this consent form unless you have had a chance to ask questions and have received acceptable answers to all your questions.

Appendix 5: World Health Organization Quality of Life Brief Questionnaire (WHO-QOL)(BREF)

WHOQOL-BREF

The following questions ask how you feel about your quality of life, health, or other areas of your life. I will read out each question to you, along with the response options. **Please choose the answer that appears most appropriate.** If you are unsure about which response to give to a question, the first response you think of is often the best one.

Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life **in the last four weeks.**

		Very poor	Poor	Neither poor nor good	Good	Very good
1.	How would you rate your quality of life?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
2.	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about **how much** you have experienced certain things in the last four weeks.

		Not at all	A little	A moderate amount	Very much	An extreme amount
3.	To what extent do you feel that physical pain prevents you from doing what you need to do?	5	4	3	2	1
4.	How much do you need any medical treatment to function in your daily life?	5	4	3	2	1
5.	How much do you enjoy life?	1	2	3	4	5
6.	To what extent do you feel your life to be meaningful?	1	2	3	4	5

		Not at all	A little	A moderate amount	Very much	Extremely
7.	How well are you able to concentrate?	1	2	3	4	5
8.	How safe do you feel in your daily life?	1	2	3	4	5
9.	How healthy is your physical environment?	1	2	3	4	5

The following questions ask about how completely you experience or were able to do certain things in the last four weeks.

		Not at all	A little	Moderately	Mostly	Completely
10.	Do you have enough energy for everyday life?	1	2	3	4	5
11.	Are you able to accept your bodily appearance?	1	2	3	4	5
12.	Have you enough money to meet your needs?	1	2	3	4	5
13.	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
14.	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

		Very poor	Poor	Neither poor nor good	Good	Very good
15.	How well are you able to get around?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
16.	How satisfied are you with your sleep?	1	2	3	4	5
17.	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
18.	How satisfied are you with your capacity for work?	1	2	3	4	5
19.	How satisfied are you with yourself?	1	2	3	4	5

20.	How satisfied are you with your personal relationships?	1	2	3	4	5
21.	How satisfied are you with your sex life?	1	2	3	4	5
22.	How satisfied are you with the support you get from your friends?	1	2	3	4	5
23.	How satisfied are you with the conditions of your living place?	1	2	3	4	5
24.	How satisfied are you with your access to health services?	1	2	3	4	5
25.	How satisfied are you with your transport?	1	2	3	4	5

The following question refers to how often you have felt or experienced certain things in the last four weeks.

		Never	Seldom	Quite often	Very often	Always
26.	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	5	4	3	2	1

Do you have any comments about the assessment?

_____

_____

[The following table should be completed after the interview is finished]

		Equations for computing domain scores	Raw score	Transformed scores*	
				4-20	0-100
27.	**Domain 1**	(6-Q3) + (6-Q4) + Q10 + Q15 + Q16 + Q17 + Q18 ☐ + ☐ + ☐ + ☐ + ☐ + ☐ + ☐	a. =	b:	c:
28.	**Domain 2**	Q5 + Q6 + Q7 + Q11 + Q19 + (6-Q26) ☐ + ☐ + ☐ + ☐ + ☐ + ☐	a. =	b:	c:
29.	**Domain 3**	Q20 + Q21 + Q22 ☐ + ☐ + ☐	a. =	b:	c:
30.	**Domain 4**	Q8 + Q9 + Q12 + Q13 + Q14 + Q23 + Q24 + Q25 ☐ + ☐ + ☐ + ☐ + ☐ + ☐ + ☐ + ☐	a. =	b:	c:

* See Procedures Manual, pages 13-15

Appendix 6: The Asian Diabetes Quality of Life Questionnaire (AsianDQOL) English

English

ID	

MONASH University
Malaysia

AsianDQOL

Asian Diabetes Quality of Life study

Background information

In this section, questions will be asked about your basic personal information such as your age, the area you are living and about your diabetes. The information you provide will be kept confidential at all times.

KINDLY PUT A TICK ' √' IN THE BOX OF YOUR CHOICE.

Example: i) what is the color of your hair?

☑ **black** ☐ **blue** ☐ **yellow** ☐ **green** **OR**

Fill in your answers in the space (_____) provided

Example: i) what year are you born in? Year *1980*

1) Age: _____ (years)

2) Sex

☐ Male ☐ Female

3) Ethnicity: ☐ Malay ☐ Chinese ☐ Indian ☐ Others_____

4) Nationality: _____

5) Marital status:

☐ Married ☐ Single ☐ Divorced ☐ Widowed

6) Education level:

☐ Primary ☐ Secondary ☐ Tertiary and above

7) Are you working?

☐ Working (full time)

☐ Working (part-time/ some days)

☐ Unemployed/ Not working

☐ Retired.

8) Years having diabetes:_____ (years)

Please Turn Over

8) Which following medical problems do you have besides diabetes? (You can tick more than one)

- ☐ Hypertension/ high blood pressure
- ☐ High cholesterol
- ☐ Heart disease/ heart block (previous episodes of heart attack/ chest pain)
- ☐ Visual problems (cataract/ diabetic eye problems)
- ☐ Nerve problems (feeling tingling sensation/ sensation of ants crawling/pain/numbness/ feeling hot on extremities)
- ☐ Problems with achieving/ maintaining erection (**FOR MALES ONLY**)
- ☐ Recurrent vaginal infection/ itchiness (**FEMALES ONLY**)
- ☐ Poor sexual desire
- ☐ Peripheral vascular disease (ulcers on extremities/ amputations/gangrene)
- ☐ Other endocrine problems (thyroid problems)
- ☐ Renal problems (on haemodialysis/ recurrent lower limbs swelling)
- ☐ Others (Please State) _____

9) What type of treatment are you currently on for diabetes?

- ☐ Diet Therapy only
- ☐ Oral medications only (**Proceed to Q10 and Q11**)
- ☐ Insulin only (**Proceed to Q12 and Q13**)
- ☐ Oral medications+ insulin (**Proceed to Q14, Q15 and Q16**)
- ☐ Not on any treatment
- ☐ Others (please state)_____

10) (ORAL MEDICATIONS ONLY)

How many types of medications are you currently taking **for diabetes?** _____

11) (ORAL MEDICATIONS ONLY)

How many times a day you need to take the medications?

_____ **(PROCEED TO QUESTION 17)**

12) (INSULIN ONLY) How long have you been on insulin? _____ year(s)

13) (INSULIN ONLY) How many times a day you need to inject yourself?

_____ time(s) **(PROCEED TO QUESTION 17)**

Please Turn Over

14) (ORAL MEDICATIONS+INSULIN)

How many types of oral medications are you currently taking for diabetes? _____ Type(s)

15) (ORAL MEDICATIONS+INSULIN)

How many times a day you need to take your medications? _____Time(s)

16) (ORAL MEDICATIONS+INSULIN)

How many times a day you need to inject yourself? _____Time(s)

(PROCEED TO QUESTION 17)

17) What supplements/ vitamins are you currently taking? (Please list)

_____

_____

(If NONE please fill in 'NIL' and proceed to QUESTION 18)

18) What type (s) of traditional medicine /herbs are you taking? (Please list)

_____

_____

(If NONE please fill in 'NIL' and proceed to QUESTION 19)

19) How frequent do you monitor your blood sugar at home?

_____Times/ day

_____Times/week

_____Times/month

Others: please specify _____

20) What is your average blood sugar reading?

_____mmol/L

21) How frequent do you experience signs of hypoglycemia (feeling of light-headiness, dizzy, extreme hunger, fainting due to low blood sugar)?

☐Never ☐Once/few months ☐Once/week ☐2-3 times/week ☐Daily

Please Turn Over

22) Where do you go for check-ups/medications for your diabetes?

- ☐ Government clinic/ hospital
- ☐ Private clinic/Hospital
- ☐ Pharmacy
- ☐ Traditional healers / alternative medicine
- ☐ Others: (Please state)_____

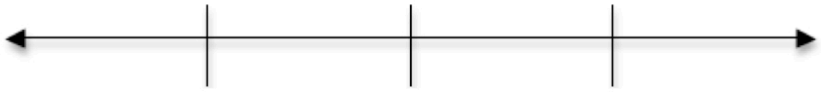
I) DIET AND EATING HABITS (PLEASE CIRCLE)

The following questions will ask you about your daily eating habits and what food you like to take. Please CIRCLE the answer you choose.

EXAMPLE:

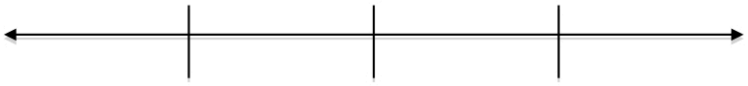
i) What is your favorite food?

1) Chicken rice **2) burgers** **3) noodles** **4) fried rice** **5) cakes**



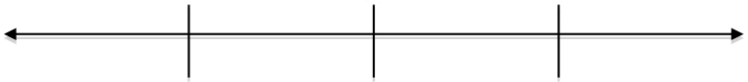
1) How satisfied are you with your current diet? (Please circle below)

1) Very Dissatisfied 2) Dissatisfied 3) Unsure 4) Satisfied 5) Very Satisfied



2) How happy are you with your current eating habits as compared to before the onset of diabetes?

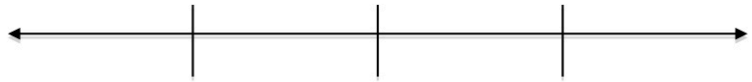
1) Very Unhappy 2) Unhappy 3) Unsure 4) Happy 5) Very Happy



Please Turn Over

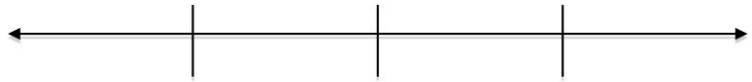
3) Do you find it a burden to follow the diet you are supposed to take?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never



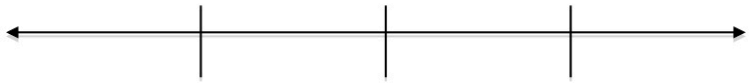
4) Are you still able to enjoy the food you like to eat now, as compared to before the onset of diabetes?

1) Never 2) Sometimes 3) Most of the time 4) Frequently 5) Always



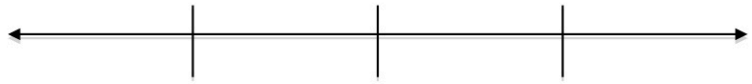
5) Do you feel sad that you are unable to eat freely as before?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never



6) Do you feel left out that you are unable to eat what others do?

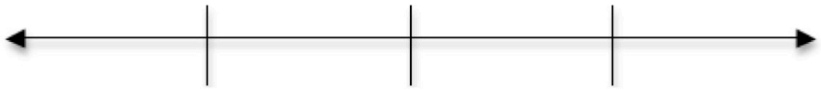
1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never



II) ENERGY

7) **Do you feel weaker/ more tired because of diabetes?**

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never



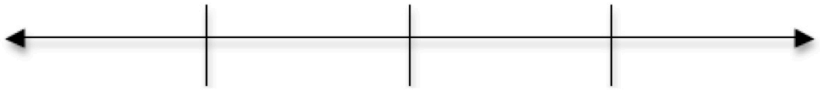
Please Turn Over

8) Do you feel that diabetes have affected the quality of your work or daily activities?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never

9) Do you feel that diabetes prevents you from doing the activities you like or enjoy?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never



III) MEMORY AND COGNITION

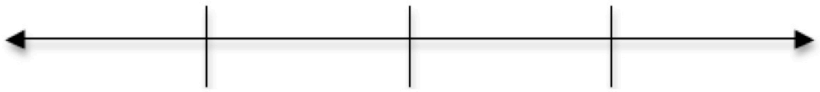
The following questions will ask you about your emotions, decision-making and memory recall power. Please CIRCLE the answer of your choice.

10) How often do you find yourself forgetting recent things?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never

11) Do you find it difficult to recall RECENT events? (Names or things that you have just met or see)

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never



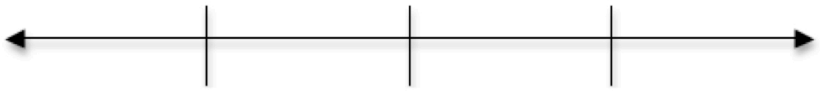
12) Do you find it difficult to recall OLD events? (Events that happened long ago)

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never

Please Turn Over

13) Do you find it difficult to recognize faces, places or numbers?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never



IV) FINANCIAL ASPECTS

This section will ask you questions on your financial aspects. Kindly CIRCLE your answer

14) Do you spend time worrying about your medical cost?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never

15) Do you feel that diabetes have increased your financial burden?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never

16) Do you have difficulties in paying for your medical expenses?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never

17) Do you spend time worrying about your future medical expenses?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never

Please Turn Over

18) Are you in constant fear that you may be a burden financially to your family?

1) Always 2) Frequently 3) Most of the time 4) Sometimes 5) Never

☐

V) INTER-PERSONAL RELATIONSHIP

The questions in this section will ask you about your current relationships. Kindly CIRCLE your answer.

19) How do you find your relationship with your spouse/partner?

☐ **NOT APPLICABLE (kindly proceed to question 20)**

1) Very poor 2) Worse 3) No change 4) Better 5) Much Better

20) How would you describe your sexual relationship now as compared to before the onset of diabetes?

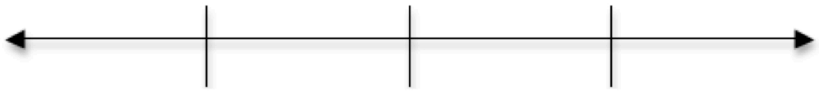
☐ **NOT APPLICABLE (kindly proceed to question 21)**

1) Very bad 2) Worse 3) No change 4) Better 5) Much Better

21) How is your sexual desire as compared to before the onset of diabetes?

☐ **NOT APPLICABLE**

1) Very bad 2) Worse 3) No change 4) Better 5) Much Better



TOTAL SCORE **(For office use only)**	

Appendix 7:The Asian Diabetes Quality of Life Questionnaire (AsianDQOL) Malay Language

MALAY

ID	

MONASH University
Malaysia

AsianDQOL

Asian Diabetes Quality of Life

Maklumat Latar Belakang

Dalam bahagian ini, soalan-soalan mengenai maklumat peribadi asas anda seperti umur, kawasan kediaman dan penyakit kencing manis anda akan ditanya. Maklumat yang anda bekalkan akan dirahsiakan pada setiap masa.

SILA TANDAKAN '√' DALAM KOTAK PILIHAN ANDA.

Contoh: i) Apakah warna ranbut anda?

☑ **Hitam** **c Biru** **c Kuning** **c Hijau**

1) Umur: _____ (tahun)

2) Jantina

☐ Lelaki ☐ Perempuan

3) Bangsa: c Melayu c Cina c India

c Lain-lain_____

4) Kewarganegaraan: _____

5) Taraf perkahwinan:

c Berkahwin c Bujang c Bercerai c Balu / Janda

6) Adakah anda bekerja?

c Bekerja (sepenuh masa)

c Bekerja (sambilan / sesetengah hari)

c Menganggur / Tidak bekerja

c Bersara

7) Tempoh mengidap penyakit kencing manis:_____ (tahun)

8) Tahap pendidikan:

c Tiada c Rendah c Menengah c Kolej/Universiti

Sila Ke Halaman Berikutnya

8) Selain daripada kencing manis, adakah anda masih mempunyai masalah-masalah kesihatan seperti yang berikut? (Anda boleh memilih lebih daripada satu)

- ☐ Hipertensi / Tekanan darah tinggi
- ☐ Kolesterol tinggi
- ☐ Penyakit jantung / Jantung tersumbst (pernah mengalami serangan penyakit jantung / sakit dada sebelum ini)
- ☐ Masalah penglihatan (katarak / masalah mata disebabkan oleh penyakit kencing manis)
- ☐ Masalah saraf (Merasakan perasaan cucukan / perasaan semut merangkak / sakit / kebas / merasa panas pada kaki dan tangan)
- ☐ Masalah dalam mencapai / mengekalkan ketegangan zakar (**UNTUK LELAKI SAHAJA**)
- ☐ Jangkitan / Kegatalan faraj yang berulang (**UNTUK PEREMPUAN SAHAJA)**
- ☐ Nafsu seks yang lemah
- ☐ Penyakit periferi vaskular (bisul pada kaki dan tangan / potong kaki atau tangan / gangren [daging reput])
- ☐ Masalah-masalah lain berkaitan kelenjar endokrin (masalah kelenjar tiroid)
- ☐ Masalah ginjal (menjalani hemodialisis / bengkak yang berulang pada bahagian bawah anggota badan)
- ☐ Lain-lain (Sila Nyatakan) _____

9) Apakah jenis rawatan yang anda terima untuk penyakit kencing manis sekarang?

- ☐ Rawatan pemakanan sahaja
- ☐ Ubat-ubatan secara oral sahaja **(Terus ke soalan 10 dan 11)**
- ☐ Insulin sahaja **(Terus ke soalan 12 dan 13)**
- ☐ Ubat-ubatan secara oral + insulin **(Terus ke soalan 14,15 dan 16)**
- ☐ Tidak menerima sebarang rawatan
- ☐ Lain-lain (sila nyatakan)_____

Sila Ke Halaman Berikutnya

10) (UBAT-UBATAN SECARA ORAL SAHAJA)

Berapa jeniskah ubat-ubatan yang anda makan **untuk penyakit kencing manis** sekarang**?**

_____

11) (UBAT-UBATAN SECARA ORAL SAHAJA)

Berapa kalikah anda perlu memakan ubat dalam satu hari?

_____ **(TERUS KE SOALAN 17)**

12) (INSULIN SAHAJA) Sudah berapa lamakah anda menerima suntikan insulin?

_____ tahun

13) (INSULIN SAHAJA) Berapa kalikah anda perlu membuat suntikan pada setiap hari?

_____ kali **(TERUS KE SOALAN 17)**

14) (UBAT-UBATAN SECARA ORAL + INSULIN)

Berapa jeniskah ubat-ubatan secara oral yang anda makan untuk penyakit kencing manis sekarang? _____ Jenis

15) (UBAT-UBATAN SECARA ORAL + INSULIN)

Berapa kalikah anda perlu makan ubat tersebut pada setiap hari? _____ Kali

16) (UBAT-UBATAN SECARA ORAL + INSULIN)

Berapa kalikah anda perlu membuat suntikan pada setiap hari? _____ Kali

(TERUS KE SOALAN 17)

17) Apakah makanan khasiat tambahan / vitamin yang anda makan sekarang? (Sila senaraikan)

_____

_____

(Sekiranya TIADA, sila tuliskan 'TIADA' dan teruskan ke soalan 18)

18) Apakah jenis ubat tradisional / herba yang anda makan? (Sila senaraikan)

_____

(Sekiranya TIADA, sila tuliskan 'TIADA' dan teruskan ke soalan 19)

Sila Ke Halaman Berikutnya

19) Berapa kerap anda memantau kandungan gula dalam darah anda di rumah?

_____ Kali sehari

_____ Kali seminggu

_____ Kali sebulan

Lain-lain: sila nyatakan _____

20) Apakah purata bacaan kandungan gula dalam darah anda?

_____mmol/L

21) Berapa kerapkah anda mengalami tanda-tanda hipoglisemia (rasa hampir pengsan, pening kepala, kelaparan yang sangat, pengsan disebabkan kandungan gula dalam darah rendah)?

☐ Tidak pernah ☐ Sekali dalam beberapa bulan ☐ Sekali/seminggu

☐ 2-3 kali/seminggu ☐ Setiap hari

22) Di manakah anda mendapatkan pemeriksaan kesihatan / ubat-ubatan untuk penyakit kencing manis anda?

c Klinik / Hospital kerajaan

c Klinik / Hospital swasta

c Farmasi

c Pengamal perubatan tradisional / perubatan alternatif

c Lain-lain: (Sila nyatakan)_____

Sila Ke Halaman Berikutnya

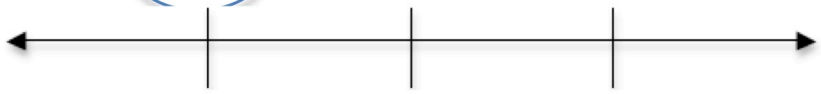
I) PEMAKANAN DAN TABIAT PEMAKANAN (SILA BULATKAN)

Soalan-soalan berikut akan bertanya tentang tabiat pemakanan harian anda dan jenis makanan yang anda gemarkan. Sila BULATKAN jawapan pilihan anda.

CONTOH:

i) Apakah makanan kegemaran anda?

1) Nasi ayam **2) Burger** **3) Mi** **4) Nasi goreng** **5) Kek**



1) Adakah anda berasa mengikuti pemakanan yang sepatutnya untuk anda adalah membebankan?

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5)Tidak Pernah

2) Adakah anda berasa sedih kerana anda tidak dapat memakan sesuka hati seperti dahulu?

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

3) Adakah anda berasa tersisih kerana anda tidak boleh menikmati makanan yang boleh dinikmati oleh orang lain?

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

Sila Ke Halaman Berikutnya

4) **Adakah anda meluangkan masa dalam merisaukan apa yang anda makan akan menjejaskan tahap kandungan gula dalam darah anda?**

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

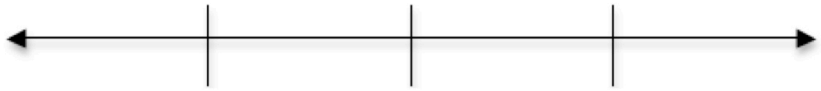
II) TENAGA

5) **Adakah anda rasa lebih lemah / lebih letih disebabkan penyakit kencing manis?**

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

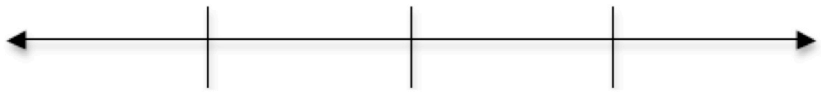
6) **Adakah anda berasa penyakit kencing manis telah menjejaskan mutu kerja atau aktiviti harian anda?**

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah



7) **Adakah anda berasa penyakit kencing manis telah menghalang anda daripada menjalankan aktiviti-aktiviti kegemaran dan kenikmatan anda?**

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah



Sila Ke Halaman Berikutnya

8) Adakah anda berasa kurang bertenaga?

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

III) INGATAN DAN KOGNISI

Soalan-soalan berikut akan bertanya tentang emosi, daya membuat keputusan serta kuasa peringatan semula anda. Sila BULATKAN jawapan pilihan anda.

9) Berapa kerapkah anda menyedari bahawa anda lupa tentang perkara-perkara terkini?

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

10) Adakah anda menghadapi masalah untuk ingat semula peristiwa-peristiwa TERKINI? (Nama orang atau perkara-perkara yang anda baru sahaja bertemu atau nampak)

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

11) Adakah anda menghadapi masalah untuk ingat semula peristiwa-peristiwa SILAM? (Peristiwa-peristiwa yang berlaku lama dahulu)

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

Sila Ke Halaman Berikutnya

12) Adakah anda menghadapi masalah dalam mengenali muka orang, tempat atau nombor yang berlainan?

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

IV) ASPEK KEWANGAN

Bahagian ini akan bertanya soalan-soalan dari segi kewangan anda. Sila BULATKAN jawapan anda.

13) Adakah anda meluangkan masa dalam membimbangkan kos perubatan anda?

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

14) Adakah anda berasa penyakit kencing manis telah menambahkan beban kewangan anda?

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

15) Pernahkah anda menghadapi masalah dalam pembayaran kos perubatan anda?

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

Sila Ke Halaman Berikutnya

16) Pernahkah anda meluangkan masa dalam membimbangkan perbelanjaan perubatan masa depan anda?

1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

17) Adakah anda selalu berasa takut bahawa anda akan menjadi beban dari segi kewangan bagi keluarga anda?

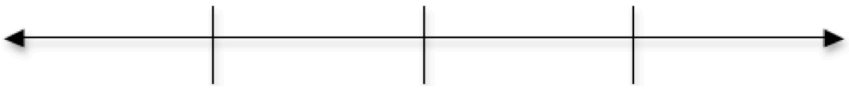
1) Sentiasa 2) Sering 3) Kebanyakan Masa 4) Kadang-kadang 5) Tidak Pernah

V) HUBUNGAN PERIBADI

Soalan-soalan dalam bahagian ini akan bertanya tentang hubungan peribadi terkini anda. Sila BULATKAN jawapan anda.

18) Bagaimanakah hubungan anda dengan ahli-ahli keluarga anda?

1) Lebih Teruk 2) Teruk 3) Tiada Perubahan 4) Baik 5) Lebih baik



19) Bagaimanakah hubungan anda dengan pasangan / teman anda?

c TIDAK BERKAITAN (sila teruskan ke soalan 31)

1) Lebih Teruk 2) Teruk 3) Tiada Perubahan 4) Baik 5) Lebih baik

Sila Ke Halaman Berikutnya

20) Bagaimanakah anda menghuraikan hubungan seksual sekarang dengan pasangan berbanding dengan sebelum dijangkiti penyakit kencing manis?

c TIDAK BERKAITAN (sila teruskan ke soalan 32)

1) Lebih Teruk 2) Teruk 3) Tiada Perubahan 4) Baik 5) Lebih baik

21) Bagaimanakah nafsu seks anda sekarang berbanding dengan sebelum dijangkiti penyakit kencing manis?

c TIDAK BERKAITAN

1) Lebih Teruk 2) Teruk 3) Tiada Perubahan 4) Baik 5) Lebih baik

JUMLAH MARKAH **(Untuk kegunaan pejabat sahaja)**	

Appendix 8: The Asian Diabetes Quality of Life Questionnaire (AsianDQOL) Mandarin Language

MANDARIN

ID

AD-QOL

Asian Diabetes Quality of Life study

MONASH University

School Of Medicine & Health Sciences, Malaysia

谢谢您参与这一次的研究。

以下的问卷需要您花大概 **10** 分钟的时间来完成。

我们将会问您一些关于您个人资料和医疗情况的基本问题。您提供的所有资讯将以绝对保密的方式处理而您也不需要提供您的姓名或者身份证号码。只有研究团队能够获得以下的资讯。

如果您有任何的问题，请随时询问我们任何一位的研究员。

1) Rusli bin Nordin 教授

首席研究员，

新山莫纳斯大学临床医学院主任，

[redacted]

2) 拿督 **Khalid bin Kadir** 教授

首席研究员，

内分泌顾问医生，

[redacted]

3) Shereen G.K Goh 医生

研究员主任

[redacted]

背景资料

在这个部分我们将会问您一些有关您基本的个人资料，例如您的年龄、您居住的地方以及您的糖尿病情况。您所提供的资讯在任何时候都会被保密。

请在您所选的格子中‘ □’画个勾。

例子： **i)** 您的头发是什么颜色？

☑黑色 □蓝色 □黄色 □ 青色

或者

把您的答案填在所提供的空格内 **(_____)**。

例子： **i)** 您在哪一年出生？ ***1980*** 年

1) 年龄： _____(岁数)

2) 性别

□ 男 □ 女

3) 种族： □ 巫裔 □ 华裔 □ 印裔

□ 其他 _____

4) 国籍： _____

5) 婚姻状况：

□ 已婚 □ 单身 □ 离婚 □ 寡妇/鳏夫

6) 您有工作吗？

□ 工作（全职）

□ 工作（兼职/某几天）

□ 失业/不工作

□ 退休

7) 您患有糖尿病多少年：_____ （年）

请翻下页

8) 除了糖尿病以外您还有什么医疗上的问题吗？（您可以勾超过一项）

- □ 高血压
- □ 高胆固醇
- □ 心脏病/心脏传导阻滞（曾经有心脏病发作/胸痛）
- □ 视觉问题（白内障/糖尿病导致的眼部问题）
- □ 神经问题（有刺痛的感觉/蚂蚁在爬的感觉/疼痛/麻痹/四肢感觉烫热）
- □ 达致/维持勃起的问题（只限男性）
- □ 经常性阴道感染/痕痒（只限女性）
- □ 性欲差
- □ 血管周边疾病（四肢溃烂/截肢/坏疽[死亡的肌肉]）
- □ 其他内分泌的问题（甲状腺问题）
- □ 肾脏问题（必须洗肾/经常性下肢肿胀）
- □ 其他（请说明）_____

9) 您现在正在接受哪一些有关糖尿病方面的治疗？

- □ 只有饮食疗法
- □ 只有口服药物（跳到第 10 和 11 题）
- □ 只有胰岛素（跳到第 12 和 13 题）
- □ 口服药物 + 胰岛素（跳到第 14、15 和 16 题）
- □ 没有接受任何治疗
- □ 其他（请说明）_____

10)（只有口服药物）

您现在因为**糖尿病**所服用的药物有几种？ _____

11)（只有口服药物）

您一天需要服用几次药物？

_____ （跳到第 17 题）

12)（只有胰岛素）您注射胰岛素多久了？ _____ 年

13)（只有胰岛素）您一天需要注射多少次胰岛素？

_____ 次 （跳到第 17 题）

请翻下页

14)（口服药物 + 胰岛素）

您现在因为糖尿病所服用的口服药物有几种？ _____ 种

15)（口服药物 + 胰岛素）

您一天需要服用几次药物？ _____ 次

16)（口服药物 + 胰岛素）

您一天需要注射多少次胰岛素？ _____ 次

（跳到第 **17** 题）

17) 您现在正在服用的营养辅助品/维生素有哪些？（请列明）

_____

_____

（如果没有，请填写"无"并跳到第 **18** 题）

18) 您服用的传统药物/草药有哪些？（请列明）

_____

_____

（如果没有，请填写"无"并跳到第 **19** 题）

19) 您在家测试血糖含量的频繁度是多少次？

每天 _____ 次

每个星期 _____ 次

每个月 _____ 次

其他：请注明 _____

20) 您平均的血糖含量读数是多少？

_____ mmol/L

21) 您有多常经历低血糖的迹象（因为血糖低而感觉快要晕厥、头晕、极度饥饿、晕倒）

_____

请翻下页

22) 您会到哪里进行糖尿病检查或获取糖尿病的药物？

□ 政府诊所/医院

□ 私人诊所/医院

□ 药房

□ 传统医师/替代药物

□ 其他：（请列明）_____

I) 饮食和饮食习惯（请画圈）

以下的问题将会问您有关您的饮食习惯和您喜欢吃的食物。请圈出您的选择。

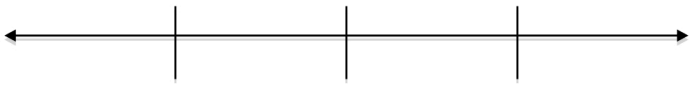
例子：

i) 您最喜欢吃的食物是什么？

1) 鸡饭 **2)** 汉堡包 **3)** 面条 **4)** 炒饭 **5)** 蛋糕

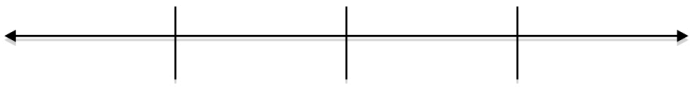
1) 您是否觉得要遵循您所需跟从的饮食这件事是个负担？

1) 总是 2) 经常 3) 大多数的时候 4) 有时候 5) 从不



2) 您是否会因为不能好象以前那样自由选择要吃的食物而觉得难过？

1) 总是 2) 经常 3) 大多数的时候 4) 有时候 5) 从不



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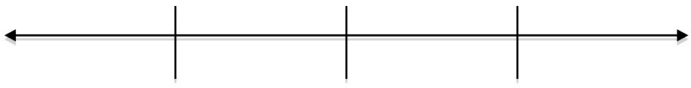
3) 您是否因为不能吃其他人都在吃的食物而觉得被冷落？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不



4) 您是否觉得糖尿病对您喜欢或享受的活动带来了障碍？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

II) 情绪和自我护理

以下的问题将会问您有关您的日常生活以及您的情绪状况和心情。请圈出最能反映您的感觉的答案。

5) 您会因为自己患上糖尿病而觉得比较虚弱/比较疲累吗？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

6) 您是否觉得精神不振？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

7) 您觉得糖尿病是否影响了您工作或日常生活的品质？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

请翻下页

III) 记忆和认知能力

以下的问题会问关于您情绪、决策以及记忆的问题。请圈出您所选择的答案。

8) 您会觉得要想起近期发生的事情很困难吗？（您刚遇见的人的名字或刚看见的事物）

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

9) 您会觉得要识别不同的脸孔、地方或数目字很困难吗？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

IV) 财务方面

以下的部分会问您有关您财务方面的问题。请圈出您的答案。

10) 您是否觉得自己已经成为家里的一个负担？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

11) 您会花时间担忧自己的医疗费用吗？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

请翻下页

12) 您是否觉得糖尿病已经增加了您的财务负担？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

13) 您在支付您的医疗费用方面会有困难吗？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

14) 您会花时间为您将来的医疗费用担忧吗？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

15) 您是否经常担忧您可能会成为家庭里的经济负担？

1) 总是　2) 经常　3) 大多数的时候　4) 有时候　5) 从不

请翻下页

V) 人际关系

这部分的问题将会问到有关您现在的人际关系，请圈出您的答案。

16) 您觉得您和配偶/伴侣的关系如何？

□ 不适用（请跳到第 **31** 题）

1) 更糟糕　2) 糟糕　3) 没有改变　4) 好　5) 更好

17) 和糖尿病发作之前比较，您会如何形容你们现在的性关系？

□ 不适用（请跳到第 **32** 题）

1) 更糟糕　2) 糟糕　3) 没有改变　4) 好　5) 更好

18) 和糖尿病发作之前比较，您现在的性欲如何？

□ 不适用

1) 更糟糕　2) 糟糕　3) 没有改变　4) 好　5) 更好

总分 （仅供办公室用途）	

谢谢您的参与。

请确认您已经答完所有页面的问题。

祝您有美好的一天！

Appendix 9: Invited speaker for Diabetes Asia Conference 2014 for "Quality of Life of Diabetics"

071014

SCIENTIFIC PROGRAMME
'Diabetes Asia 2014' Conference
October 16 - 19, 2014

DAY 1 – OCTOBER 16TH, 2014 (THURSDAY)

0700 – 0830 **REGISTRATION**

0830 – 0915 ***Plenary 1***

PLENARY 1
Chairman: Emeritus Professor Dato' Mustaffa Embong, *National Diabetes Institute*
ADIPONECTIN, DIABETES AND DIABETIC COMPLICATIONS
Speaker : Professor Karen Siu Ling Lam, *HONG KONG*

0915 – 0945 **COFFEE BREAK**

0945 – 1145 ***Concurrent Main Symposium 1***

MAIN SYMPOSIUM 1A
THEME : DIABETES IN ASIA
Chairman: Professor Dato' Anuar Zaini Md Zain, *Monash University Malaysia*

i) **Mutations of KCNJ11 Gene in Chinese Unknown MODY Gene (MODY-X)'s Families**
Professor Limei Liu, *CHINA*

ii) **Quality of Life of Diabetics in Malaysia**
Emeritus Professor Dato' Khalid Abdul Kadir/Dr. Shereen Goh Giap Kah,
Monash University Malaysia

iii) **Unique Feature of Asian T2DM: Strategy for Treatment**
Dr. Zanariah Hussein, *Putrajaya Hospital*

iv) **Panel Discussion**

MAIN SYMPOSIUM 1B
THEME : DIABETES IN PREGNANCY
Chairman: Professor Dato' Nik Mohd Nasri Nik Ismail, *University Science Islam Malaysia*

i) **Diet in Gestational Diabetes**
Datin Farah DiBa Khan, *Prince Court Medical Centre*

ii) **Weight Gain and Pregnancy Outcomes: What is the Evidence?**
Professor Dato' Sivalingam Nalliah, *International Medical University*

iii) **Glucose Control in Diabetic Pregnancy: A Practical Approach**
Professor Chaicharn Deerochanawong, *THAILAND*

iv) **Intrauterine Programming of Diabetes**
Professor Nor Azlin Mohamed Ismail, *National University of Malaysia Medical Centre*

v) **Panel Discussion**

MAIN SYMPOSIUM 1C
THEME : EMERGING RISK FACTORS OF TYPE 2 DM
Chairman: Datuk Dr. Mohamed Badrulnizam Long Bidin, *Kuala Lumpur Hospital*

i) **The Link Between Sleep Disorders and Diabetes**
Associate Professor Tengku Saifudin Tengku Ismail, *KPJ Tawakkal Specialist Hospital*

ii) **Importance of Nutrition in the Prevention of Diabetes**
Ms. Mastari Mohamad, *National Heart Institute*

iii) **Are Chronic Stress & Psychological Traits also to Blame?**
Dr. G. R. Letchuman, *Taiping Hospital*

iv) **Panel Discussion**

Appendix 10: Acceptance letter for oral presentation, Diabetes Asia Conference 2014.

NATIONAL DIABETES INSTITUTE
INSTITUT DIABETES NEGARA [redacted]
No. 1, Jalan SS 3/50, 47300 Petaling Jaya, Selangor, MALAYSIA. http://www.diabetesmalaysia.com.my

25 August 2014

Dear Ms Shereen Goh, *(via email)*

13th CPD: "Diabetes Asia 2014" Conference
October 16-19, 2014
Sunway Pyramid Convention Centre,Selangor,MALAYSIA

Thank you very much for your interest to present a paper at our **'Diabetes Asia 2014' Conference**.

We are pleased to inform that the secretariat have received and accepted your paper entitled:

Is sexual dysfunction worse in men with diabetes and cardiovascular disease? A cross-sectional, population based study using the Sexual dysfunction in Asian Men with diabetes (SAD-Men) Questionnaire.

The Scientific Committee will review all abstracts and you will be notified accordingly via email on whether your abstract has been scheduled for oral or poster presentation. The decision of the Scientific Committee is final. All abstracts accepted will be published in the programme book that will be distributed to all congress attendees.

However please note that all free paper presenters are required to register for the conference. Kindly fill in the registration form and return to us if you have not done so. The organizer reserves the right to refuse publication of your abstract if full payment has not been made before the conference.

Thanking you in advance for helping to make **'Diabetes Asia 2014' Conference** a success.

With best regards,

Yours sincerely,
National Diabetes Institute

[redacted]

PROF. DATO' MAFAUZY MOHAMED
Chairman, Scientific Committee

Organised by
NADI NATIONAL DIABETES INSTITUTE
CENTRE OF EXCELLENCE-DEDICATED TO DIABETICS

Endorsed by
Ministry of Health Malaysia

Certificate OF EXCELLENCE

THIRD PRIZE

Professor Mustaffa Young Investigators Award

October 16-19, 2014
Sunway Pyramid Convention Centre
Selangor, Malaysia

Presented to

DR SHEREEN GOH GIAP KAH

13th Continuing Professional Development (CPD) Series

'Diabetes Asia 2014' Conference

[redacted] Embong
Chairman, Organising Committee

Professor [redacted] Mohamed
Chairman, Scientific Committee

NADI

Appendix 11: 3rd Winner of the Professor Mustaffa Young Investigator's Award

Appendix 12: Sexual Function Assessment in Diabetic men (SAD-MEN) Questionnaire English Language

Sexual Function Assessment in Diabetic Men (SAD-Men)

We are a research group from Monash University under Dato' Professor Khalid Abdul Kadir and we are doing a study on people with diabetes, their status and the co-relation of their disease with sexual dysfunction. We would appreciate your co-operation in answering the following questions.
All the information gathered will be kept anonymous and confidential. Please glance through the questions first and if you are comfortable with the questions asked, please proceed. If you have any other questions or concerns, please approach any one of us.

_____

Age: _____

Marital status:
- ☐ Single
- ☐ Married
- ☐ Divorced
- ☐ Widowed

Ethnicity:
- ☐ Malay
- ☐ Chinese
- ☐ Indian
- ☐ Others (_____)

For doctor's use only:

Date:

Doctor's Code:

Patient's Code:

1. How long have you had diabetes?
   - ☐ 1-5 years
   - ☐ 6-10 years
   - ☐ More than 10 years

2. Is your diabetes under good control?
   - ☐ Yes **Latest HbA1c (if you remember):** _____ %
   - ☐ No Date: _____

3. Are you on any medications for diabetes?
   - ☐ Yes
     - ☐ Oral tablets only
     - ☐ Insulin only
     - ☐ Oral tablets and insulin
   - ☐ No, diet only.

Sexual Function Assessment in Diabetic Men (SAD-Men)

4. Have you experienced any of the following in the **past 6 months**?

   ☐ **Hypoglycaemic epidoses, "low sugar levels"** (i.e BEFORE EATING there is shaking or trembling of hands OR always feeling hungry OR excessive sweating OR fast, and pounding heart OR unclear thinking OR feeling faint AND feels better after taking something sweet OR having low sugar reading levels.)

   ☐ **Hyperglycaemic episodes, "high sugar levels"** (i.e increased thirst OR increased in frequency of urination, especially at night)

   ☐ **Complications from diabetes** (i.e your vision has become worse, your hands and feet feel numb or cold, bubbles in urine OR the urine has become cloudy and less clear)

   ☐ **None of the above**

5. Do you suffer from any of the following?

   ☐ **High blood pressure**. Are you taking medications for it? ☐ Yes ☐ No

   ☐ **High cholesterol**. Are you taking medications for it? ☐ Yes ☐ No

   ☐ **Sinusitis/Allergies**. Are you taking medications for it? ☐ Yes ☐ No

   ☐ **None of the above**

6. Do you have a prostate problem

   ☐ **Yes**.
   Have you been treated for it (ie medications or surgery)? ☐ Yes ☐ No

   ☐ Medications (Name of medication: _____)
   ☐ Surgery

   ☐ **No**

7. Have you experienced any of the following problems with your genitals?

   ☐ Hernia
   ☐ Scrotal swelling
   ☐ Sexually transmitted disease (STD)
   ☐ None of the above

8. Have you ever had any spinal problems?

   ☐ **Yes**. Have you been treated for it (ie medications or surgery)? ☐ Yes ☐ No

   ☐ **No**

Sexual Function Assessment in Diabetic Men (SAD-Men)

9. Do you smoke?

☐ **Yes.** How many cigarettes do you smoke a day?
☐ Less than 1 pack
☐ 1 pack or more

How long have you been smoking?
☐ 0-5 years
☐ 6-10 years
☐ More than 10 years

☐ **Last time, but now stopped.** How many cigarettes do you smoke a day?
☐ Less than 1 pack
☐ 1 pack or more

How long have you been smoking?
☐ 0-5 years
☐ 6-10 years
☐ More than 10 years

☐ **Never**.

10. Do you drink any alcohol?

☐ **Yes.** How much do you drink per week?
☐ 1-3 glasses
☐ 4-10 glasses
☐ More than 10 glasses

How long have you been drinking?
☐ 0-5 years
☐ 6-10 years
☐ More than 10 years

☐ **No**

11. Have you noticed a loss in the amount of pubic hair in the **past 6 months**?

☐ Yes
☐ No

12. Have you noticed a change in shaving patterns (ie shaving your facial hair less than before due to a decrease in facial hair growth) in the **past 6 months**?

☐ Yes
☐ No

13. Have you been feeling any of the following in the past 6 months?

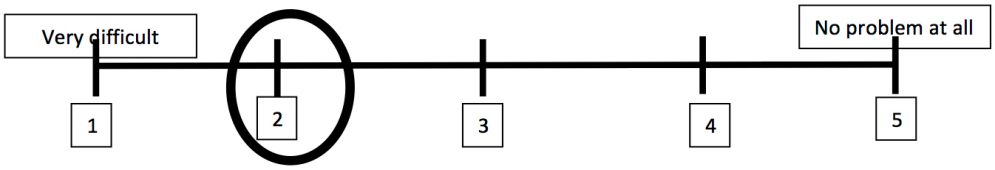
☐	**Stress.** Do you take medications for it?	☐ Yes ☐ No
☐	**Insomnia.** Do you take medications for it?	☐ Yes ☐ No
☐	**Depression.** Do you take medications for it?	☐ Yes ☐ No
☐	**None of the above**	

Questions on Sexual Function

Sexual Function Assessment in Diabetic Men (SAD-Men)

The following questions below would be intimate questions about your sexual life and the erection problems you may/may not face in the last **six (6) months**
Please answer the questions here as honestly as possible.
The questions are in relation to the last **six (6) months.**
If you haven't had sexual intercourse in the past six (6) months, please state your reason. Please continue answering the questions even though you have not had intercourse.

Please **circle** accordingly
Example



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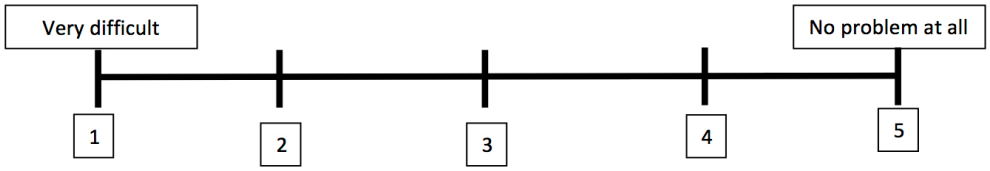
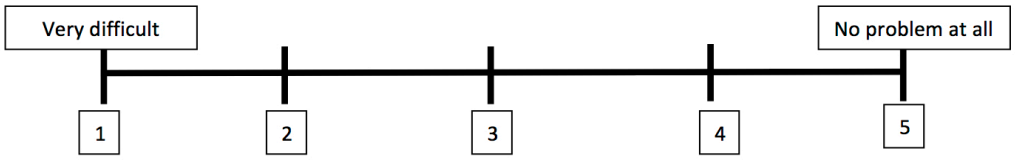
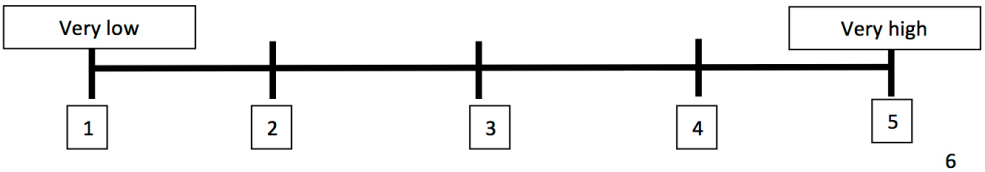
1. When you attempted intercourse, did you find entering your partner difficult?



2. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?

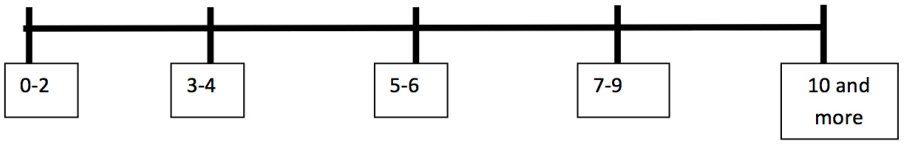


3. How high is your confidence level in achieving and maintaining an erection?

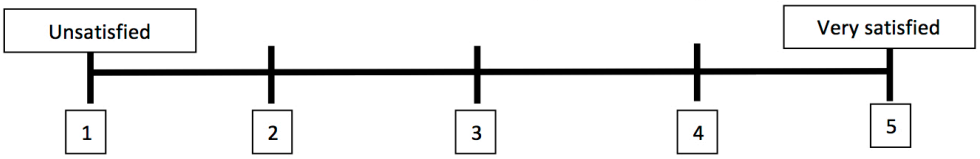


Sexual Function Assessment in Diabetic Men (SAD-Men)

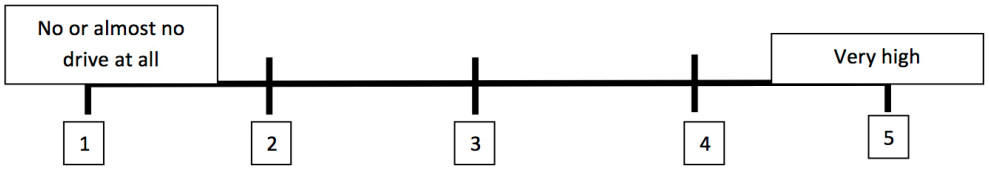
4. How many times have you attempted sexual intercourse (in the last 6 months)?



5. Are you satisfied with the outcome after you have attempted intercourse?



6. How high would you rate your sexual drive?



7. Has any medication made getting and maintaining an erection more difficult?
   - ☐ Yes
   - ☐ No

8. Have you noticed that it requires more stimulation (caressing, foreplay), compared to the past, to achieve an erection?
   - ☐ Yes
   - ☐ No

9. Have you been able to have your morning erections?
   - ☐ Yes
   - ☐ No

10. When do you have problems with erection?
    - ☐ All the time
    - ☐ When with wife only
    - ☐ When with other partner(s) only
    - ☐ No problem

11. Have tried the following medication/methods to increase your sex performance?
    - ☐ Viagra (Levitra, Cialis)
    - ☐ Traditional herb
    - ☐ Traditional massage
    - ☐ Others (please specify:_____)
    - ☐ None

Please tick (/) in the box that applies to you the most

No.	Question	Not at all	Only minimally	Moderately	Slightly more than moderate	Very much
1	How much do you enjoy your sexual intercourse?					
2	How satisfied have you been with your sex life?					

Sexual Function Assessment in Diabetic Men (SAD-Men)

Please tick (/) in the box that applies to you the most

No.	Question	None at all or almost never	Less than half	About half	More than half	Almost always or always
1	How often were you able to get an erection during sexual activity (intercourse, foreplay, or masturbation)?					
2	How often did you ejaculate during any sexual activity (intercourse, foreplay, or masturbation)?					
3	How often did you have the feeling of orgasm or climax when you had sexual activity (intercourse, foreplay, or masturbation)?					
4	How often is there an urge for sex?					
5	Through foreplay, erotic pictures, and videos, are you able to get an erection?					

Sexual Function Assessment in Diabetic Men (SAD-Men)

The following questions below would be about other sexual dysfunctions you may face.

SECTION 1: Paraphimosis/Phimosis/ Balanitis

- ***Paraphimosis****: entrapment of a retracted foreskin behind the glans penis.*
- ***Phimosis****: inability to retract the end of the foreskin over the glans penis.*
- ***Balanitis****: swelling of the foreskin and the head of the penis due to infection.*

1. Have you been diagnosed with the following?
   - ☐ **Phimosis**
     Have you been treated? ☐Yes ☐No
   - ☐ **Paraphimosis**
     Have you been treated? ☐Yes ☐ No
   - ☐ **Balanitis**
     Have you been treated? ☐Yes ☐ No
   - ☐ **None of the above**

SECTION 2: Premature Ejaculation

1. Do you ejaculate too early for the satisfaction of you and your partner/s?
   - ☐ Yes
   - ☐ No [proceed to **SECTION 3**]

2. How long have you been having/had this problem?
   - ☐ Less than a year
   - ☐ 1 to 5 years
   - ☐ More than 5 years

3. Has this been affecting your sex life?
   - ☐ Yes
   - ☐ No

4. Have you been getting treatment for this problem?
   - ☐ Yes
   - ☐ No

5. Did the treatment help?
   - ☐ Yes
   - ☐ No

6. Have you tried massaging your pubic bone and glans penis to delay ejaculation?
   - ☐ Yes
   - ☐ No

SECTION 3: Retrograde Ejaculation

Retrograde ejaculation *is a term used when semen enters the bladder instead of going out through the urethra during ejaculation. You may find there is no semen when you have an orgasm and find semen in your urine. It can be very distressing during and after sex.*

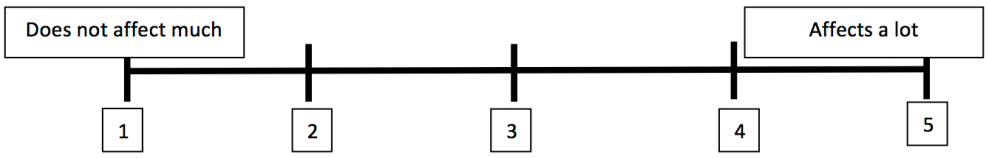
1. Have you been diagnosed with retrograde ejaculation?
   - ☐ Yes
   - ☐ No [proceed to **SECTION 4**]

2. Are you diagnosed with Benign Prostatic Hyperplasia?
   - ☐ Yes
   - ☐ No

SECTION 4: Anorgasmia/ Delayed Ejaculation/ No ejaculation/ No orgasms

1. Are you unable to attain an orgasm, unable to ejaculate, have to wait for a long time to achieve orgasm or ejaculate?
   - ☐ Yes
   - ☐ No [proceed to **SECTION 5**]

2. How much has this problem affect your sex life?



3. Have you been getting treatment?
   - ☐ Yes
   - ☐ No

4. What is the treatment?
   - ☐ Medical- including hormone replacement
   - ☐ Surgery
   - ☐ Psychotherapy
   - ☐ Others (please specify:_____)

5. Has the treatment improved your condition?
   - ☐ Yes
   - ☐ No

SECTION 5: Libido

These following questions below would be about your libido.

1. I have a strong sex drive
   - ☐ 0. Strongly disagree
   - ☐ 1. Disagree
   - ☐ 2. Neutral
   - ☐ 3. Agree
   - ☐ 4. Strongly agree

2. How frequently do you think about having sex?
   - ☐ 0. None at all
   - ☐ 1. Once a month
   - ☐ 2. Once a week
   - ☐ 3. Twice a week
   - ☐ 4. Everyday

3. It doesn't take much to get me sexually excited?
   - ☐ 0. Strongly disagree
   - ☐ 1. Disagree
   - ☐ 2. Neutral
   - ☐ 3. Agree
   - ☐ 4. Strongly agree

Sexual Function Assessment in Diabetic Men (SAD-Men)

Please answer the following questions

Answer these questions if you are concerned about erectile dysfunction.

Over the past six month:

1. How do you rate your confidence that you could get and keep an erection?		Very low 1	Low 2	Moderate 3	High 4	Very high 5	
2. When you had erections with sexual stimulation, how often were your erections hard enough for penetrations?	No sexual activity 0	Almost never/ never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/ always 5	
3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	Did not attempt intercourse 0	Almost never/ never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/ always 5	
4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	Did not attempt intercourse 0	Extremely difficult 1	Very difficult 2	Difficult 3	Slightly difficult 4	Not difficult 5	
5. When you attempted sexual intercourse, how often was it satisfactory for you?	Did not attempt intercourse 0	Almost never/ never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/ always 5	

Appendix 13: Certificate of completion of the ASCEND research network

ASCEND
Research Network

Certificate of Completion

Is presented to

Shereen Goh

For completion of the ASCEND Program

31st of December 2012

[redacted]

ASCEND Program Director & Professor of
International Public Health
Monash University, Australia

[redacted]

Prof Mohamed Shanjahan Yasin
ASCEND Program Director & Director of
Curriculum, Jeffrey Cheah School of Medicine and
Health Sciences
Monash University, Malaysia

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL
MONASH University

Appendix 14: Paper: Development and Validation of the Asian Diabetes Quality of Life Questionnaire (AsianDQOL).

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Development and validation of the Asian Diabetes Quality of Life (AsianDQOL) Questionnaire

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ABSTRACT

Aim: To construct a type-2 diabetes specific quality of life (QOL) tool for Asian populations that is valid and reliable across different ethnicities, languages, and socio-economic backgrounds.

Methods: A focus group determined the domains affecting QOL in consultation with an expert group. A pilot study was conducted to validate the Asian Diabetes QOL (AsianDQOL) in English, Malay and Chinese–Mandarin. The World Health Organization Brief Quality of Life Questionnaire (WHOQOL-BREF) was used for comparison. Exploratory factor analysis (EFA), reliability analysis (RA) using Cronbach's alpha, test–retest reliability, and confirmatory factor analysis (CFA) using structural equation modeling (SEM) was undertaken using the statistical software IBM SPSS Statistics version 20.

Results: EFA with eigenvalues (>1) and factor loadings ≥0.3 for English and Malay language demonstrated 21 items (5 components). CFA (English version) confirmed the model (CMIN 201.08, *p*-value 0.071, GFI 0.88, RMSEA 0.036, CFI 0.978). CFA (Malay version) confirmed the 5-factor model (CMIN 189.39, *p*-value 0.085, GFI 0.937, RMSEA 0.025, CFI 0.987). The Cronbach's alpha scores (English version) were 0.917, 0.818, 0.816, 0.749 and 0.719, respectively. The Malay version scored 0.833, 0.819, 0.816, 0.775, 0.673, respectively, whilst the Chinese/Mandarin version scored 0.890, 0.719, 0.826, 0.862 and 0.759, respectively. Test–retest reliability showed Pearson correlation of 0.600 (English version), 0.700 (Malay version) and 0.500 (Chinese–Mandarin version). A scoring system was generated based on the 25th, 50th and 75th centiles for all the three languages.

Conclusion: The AsianDQOL is a valid, reliable and stable tool for assessing QOL in multi-ethnic and multi-lingual T2DM Asian populations.

1. Introduction

Diabetes mellitus (DM) is a growing worldwide epidemic and Asia will bear 60% of the world diabetic population [1]. Malaysia is a multi-ethnic, multi-cultural and multi-religious country in South-east Asia experiencing the diabetic epidemic. The first National Health and Morbidity Survey (NHMS I) in 1986 showed the prevalence of DM to be 6.3% that has increased to 8.3% in 2006 [2], and escalated to 22.6% by 2010 [3].

Quality of Life (QOL) is defined by the World Health Organization (WHO) as "an individual's perception of his/her

[redacted]

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position in life in the context of the culture and value systems'' [4]. Generic tools cover a range of QOL dimensions in a single questionnaire while disease specific tools measure only relevant dimensions pertaining to the specific illness [5,6]. DM has profound effects on the social, psychological and physical wellbeing of a person making the management of DM a complex and tedious process for both the patient and the health care professionals. Before the development of QOL tools, biochemical or clinical assessment were the only indicators of disease outcome. These measures do not reflect the psychological and social state of the patient. Psychosocial impact of DM is one of the five strongest predictors of mortality in diabetic patients, surpassing the importance of clinical and physiological variables [7]. However, QOL measurement remains elusive with many contributing factors that are dependent on the individual's perception. The challenge lies in accurately reflecting subjective perception of QOL into objective scores for assessment. In order to do this, the tool must be sensitive and relevant to the local population as different languages, races, cultures, socio-economic progress and religious beliefs within the population can have a significant direct or indirect effect on the QOL.

Ethnic disparities are important in determining the prevalence, care, treatment outcomes and QOL of diabetics as shown by many international studies including the San Antonio Heart Study (SAHS) [8–11].

A population-based study in Singapore reported that ethnicity is an important factor influencing QOL [12]. This study was conducted across a multiethnic sample sharing the same sociocultural background similar to Malaysia. The Medical Outcome Study Short form 36 (SF-36) were used [13,14]. The SF-36 English and Mandarin versions were previously validated for use in Hong Kong and Singapore [15,16]. The SF-36 Mandarin version is a direct translation of the English version [16]. The constructs of the questionnaire were mainly based on these Western populations and may not be accurate in the Asian population. A focus group to review the construct of SF-36 as part of the local QOL conceptual measurement will strengthen the usage of this tool [17]. Both questionnaires used in the study were not disease-specific. The Chinese population answering the SF-36 in Chinese was thus not assessed for their cultural differences. In Malaysia, the population is almost similar but there are 65% Malays, 25% Chinese and 10% Indian and others. Many Malaysians, irrespective of their ethnicities, are educated in English and are highly westernized. However, there are also Chinese who are educated in Mandarin and retain their values similar to the Indians who were brought up in Tamil schools. The preferred language usually reflects their cultural values. The early education medium will influence the perception, cognition, behavior and lifestyle of the individual regardless of ethnicity. Having this in mind, we decided to develop a new diabetes QOL tool in English so as to be able to incorporate the different ethnic groups (Malay, Chinese and Indian) to gain their input in the construction of this tool.

We choose the Malaysian population because it gives a fair representation of the diverse composition of different ethnic groups similar to many countries in Asia.

The primary aim is to construct a DM-specific QOL tool built specifically for the Asian population, which is valid, sensitive and reliable across different ethnicities, languages, and socio-economic backgrounds.

2. Methods/design

Ethnics clearance was granted by the Monash University Human Research Ethics Committee (MUHREC), approval no. CF2630–2011001537. Written informed consent was obtained from all participants.

2.1. *Construction of the questionnaire*

The questionnaires were constructed based on focus group discussions. The English language focus group consisted of 30 subjects with T2DM. Ten subjects were of Malay ethnicity, 10 Chinese and 10 Indians. They were of different gender, age groups, duration of DM and socio-economic background with English as their common mode of communication. Individual interviews were conducted to assess factors that they felt would affect their QOL in terms of priority. The Malay language focus group consisted of 10 individuals (6 Malays, 2 Chinese and 2 Indians). The same interview process as for the English language was conducted. The Chinese–Mandarin focus group comprised of 10 Chinese participants. They were mainly Chinese-educated and preferred Mandarin as their main language of communication. The English focus group members were different from the other two languages. The expert group consisting of two endocrinologists, general practitioners, a public health expert and a diabetic nurse were sought on the factors that could affect a patient's QOL. The primary role of the expert group is to edit and supervise the development process. The content of the new QOL tool focused on the important measures of QOL in East Asia population. Existing QOL questionnaires such as the Diabetes Quality of Life Clinical Trial Questionnaire Revised (DQLCTQ-R), Diabetes Specific Quality of Life (DSQOL), Audit of Diabetes Dependent Quality of Life (ADDQoL), SF-36 and World Health Organization Quality of Life Brief (WHOQOL-BREF) were used as references [13,18–29]. An initial questionnaire in English and Malay language were drafted based on findings of the focus group discussion. This initial draft comprised of 30 questions. The choices of answers were in a 5-point rating scale ranging from "very dissatisfied" to "very satisfied". Each answer was given a score. As part of the face validation, the expert group panel commented on the structure of the questions, the choices of answers provided and the relevance of question to our local population. Multiple revisions were made based on the feedbacks and the final draft of the English and Malay language consisted of 21 questions altogether. The initial Chinese–Mandarin version had 25 items in total and 7 items were later removed due to repetition, vague structure and being less important. Subjects participated in the focus group were excluded from participation in the pilot study for validation purpose.

2.2. *Validation of the Asian Diabetes Quality of Life (AsianDQOL) questionnaire in English*

A pilot study was conducted and the WHOQOL-BREF edition 2004 in English was co-administered for comparison [30].

WHOQOL-BREF is a generic tool that was proven to be valid and reliable in chronic diseases such as DM [30,31]. It is also available in English, Mandarin and Malay language [32,33]. Permission was obtained from the WHOQOL group. A total of 136 subjects were recruited. Inclusion criteria were patients with T2DM with or without pharmacological treatment, above 18-years-old have, completed at least primary education and is able to give written consents. Exclusion criteria were subjects with concurrent Parkinson's disease, Alzheimer's disease, dementia or severe visual impairment, or with mental illness and unable to give valid consents. Subjects were recruited from the Monash University Research Centre in Selangor and Johor Bahru, Tropicana Medical Centre in Selangor, Johor Bahru general hospital, Mahmoodiah government polyclinic in Johor Bahru, and private general practitioner clinics in Johor Bahru.

Subjects recruited were English-educated of different races, gender, religion and socio-economic background residing in Malaysia. Basic demographics data collected are shown in Table 1. Medical history taken covers concomitant medical illness, years of having DM, drug and surgical history. Physical examination was done to assess blood pressure, height, weight and signs of diabetic complications. Subjects were given both questionnaires to fill in an area provided to respect their privacy. The questionnaires were given randomly with no specific order of presentation to avoid order effect. The same sets of questionnaires were given to them between 2 weeks to 4 weeks period.

2.3. *Validation of the AsianDQOL (Malay/Indonesia) language and AsianDQOL Chinese (Mandarin) language*

A total of 253 patients with T2DM of different ethnic groups were recruited for validation of the Malay language version. Inclusion and exclusion criteria remained the same as for the validation in the English language version. Medical history and physical examination was done as previous. Subjects then completed the AsianDQOL (Malay) and the same cohort of patients retested on the same questionnaire in 2 weeks to 4 weeks period.

The validation of the AsianDQOL Chinese language in Mandarin involved 62 subjects. They were retested in less than

Table 1 – Demographic, co-morbidities and treatment characteristics of the English, Malay and Chinese–Mandarin groups.

Characteristics	English No. (%)	Malay No. (%)	Chinese Mandarin No. (%)	Significance $p < 0.05$
Gender				0.840
Men	87 (64)	157 (62)	36 (58)	
Women	49 (36)	96 (38)	26 (42)	
Marital status				0.003
Married	120 (88)	226 (89)	49 (79)	
Single	16 (12)	13 (5)	8 (13)	
Others	0 (0)	14 (6)	5 (8)	
Mean age + SD (year)	53 ± 11	53 ± 11	58 ± 12	0.870
Education level				0.740
Secondary school	54 (40)	109 (43)	24 (39)	
Tertiary and above	82 (60)	143 (57)	37 (60)	
Occupation				0.001
Working full-time	77 (57)	134 (53)	22 (36)	
Working part-time	15 (11)	14 (6)	6 (10)	
Unemployed/not working	13 (10)	40 (16)	4 (7)	
Retired	31 (23)	65 (26)	30 (48)	
Duration of DM (year)	16	14	12	0.470
Co-morbidities				
Hypertension	73 (54)	146 (58)	47 (76)	0.011
Hyperlipidemia	66 (49)	115 (46)	39 (63)	0.048
Cardiac disease	36 (27)	39 ((15)	13 (21)	0.030
Visual problems	31 (23)	79 (31)	22 ((36)	0.11
Nerve problems	42 (31)	75 (30)	15 (24)	0.62
Sexual dysfunction	35 (26)	69 (27)	10 ((16)	0.19
Peripheral vascular disease	0 (0)	5 (2)	3 (5)	0.05
Renal problems	5 (4)	8 (3)	2 (3)	0.96
Erectile dysfunction	40 (46)	64 (41)	7 ((19)	0.02
Vaginal problems	6 (12)	18 (19)	6 (24)	0.42
Type of treatment for DM				0.02
Diet therapy alone	7 (5)	22 (9)	0 (0)	
Oral pills only	87 (65)	143 ((61)	46 (74)	
Insulin only	8 (6)	20 (9)	1 (1)	
Oral pills and insulin	29 ((22)	45 (19)	11 (18)	
Not on any treatment	2 (2)	3 (1)	3 (5)	
Diet therapy and pills	0 (0)	0 (0)	1 (2)	

6 weeks apart. The statistical analysis as done before to validate the English version was applied to the Malay and Chinese Mandarin versions as well. Subjects recruited for validation of the English version were different from those in the Malay and Chinese Mandarin group.

2.4. *Statistical analysis*

Data gathered were analyzed using the statistical software IBM SPSS version 20 for validation of the questionnaires. Exploratory factor analysis (EFA) to uncover the underlying structure of a large set of variables was done. Data suitability was tested using the Kaiser Meyer Olkin (KMO) measure of sampling adequacy and Bartlett's test of sphericity. Factors were extracted using the principal component method with Varimax rotation and Kaiser's criteria of eigenvalue >1. Reliability analysis for internal consistency was tested by measuring the Cronbach's alpha coefficient value. A value of ≥0.7 is considered as showing adequate internal consistency. The stability of the tool was measured using the Pearson correlation coefficient for test–retest reliability. Concordant reliability was carried out by comparing the reliability coefficient of the new tool to WHO-QOL BREF. Subjects were given both sets of questionnaire to complete with no specific order. Confirmatory factor analysis (CFA) using structural equation modeling (SEM) was done to confirm the factor structure of the model.

3. Results

Demographic data of the 136 subjects recruited for the English version are depicted in Table 1. Eighty-seven subjects were men (64%) and 49 (36%) women. The mean age was 53.7 and duration of DM was 16 years (Table 1).

Some differences were present for hypertension ($p < 0.05$), hyperlipidemia ($p < 0.05$), cardiac disease ($p < 0.05$), and erectile dysfunction ($p < 0.05$) (Table 1). Demographic data for the Malay language and Chinese–Mandarin language group were depicted in Table 1.

KMO measure for sampling adequacy for English language was 0.761, Malay language 0.798 and Mandarin 0.653. The Bartlett's test of sphericity showed significant *p*-value for all the three languages indicating that the sample size was adequate for factor analysis.

EFA of the English version showed 21 items and 5 components (Table 2). CFA confirmed the model fit (Fig. 1) (CMIN 201.08, *p*-value 0.071, GFI 0.88, RMSEA 0.036, CFI 0.978) (Table A1). Reliability analysis showed component on financial (5 items) scored 0.917, energy levels (3 items) scored 0.818, memory and cognition (4 items) scored 0.816, relationship (3 items) scored 0.749 while diet (6 items) scored 0.719 (Table 5). Analysis done on the total score (English) showed a non-normal distribution, the median score 81, the 25th centile score 74 and 75th centile 88. Based on this, it was decided that for the AsianDQOL (English), a score of 74 points and below is considered poor, 75–81 moderate, 82–88 good and above 88 points is excellent QOL.

Subsequently, EFA for the Malay language demonstrated 21 items and 5 components (Table 3). CFA confirmed the 5-factor model (Fig. 2) (CMIN 189.39, *p*-value 0.085, GFI 0.937, RMSEA 0.025, CFI 0.987) (Table A1). The component on financial scored 0.833, energy levels scored 0.819, memory and cognition scored 0.816, relationship scored 0.775 and diet scored 0.673 (Table 5). The scores from the Malay language were also non-normal with a median of 85, 25th centile of 76, and 75th centile 91 points. The AsianDQOL (Malay) scoring system of 76 points and below is considered poor, 77–85 moderate, 86–91good and above 91 points is excellent QOL, almost similar to that for the English AsianDQOL scoring system.

EFA for the Chinese–Mandarin version showed 5 components with 18 items (Table 4). Component on financial concerns (6 items) scored 0.890. Component on relationship (3 items) scored 0.862, memory (2 items) scored 0.826, diet and activities (4 items) scored 0.759, the final component on energy levels (3 items) scored 0.719 (Table 5). CFA could not be performed due to small sample size. The scoring system of the AsianDQOL Chinese (Mandarin) was also non-normal with the median 71, 25th centile 65, and 75th centile 80. Scores below 65 points is poor, 65 to 70 moderate, 71 to 79 good and above 80 points is excellent QOL.

Significant differences were seen in the Cronbach's Alpha score of the three languages. The component of diet and eating habits were significant in both the English language and Chinese–Mandarin versions but were not in the Malay language. Differences between the three languages in terms

Table 2 – EFA: principal component analysis (English version).

	Component				
	1	2	3	4	5
Financial					
Future medical expenses	0.904				
Medical cost	0.897				
Financial burden family	0.843				
Medical expenses difficulties	0.840				
Financial burden	0.799				
Diet					
Eating habits		0.756			
Satisfied diet		0.065			
Sad about diet		0.692			
Left out		0.675			
Enjoy diet		0.630			
Burden diet		0.500			
Memory and cognition					
Recent recall			0.873		
Old recall			0.773		
Memory			0.799		
Recognition			0.713		
Energy					
Quality of work				0.871	
Activities				0.871	
Weak tired				0.561	
Relationship					
Relationship with partner					0.876
Sexual problem					0.874
Sexual desire					0.669

Rotation: Varimax with Kaiser normalization. Rotation converged in 6 iterations.

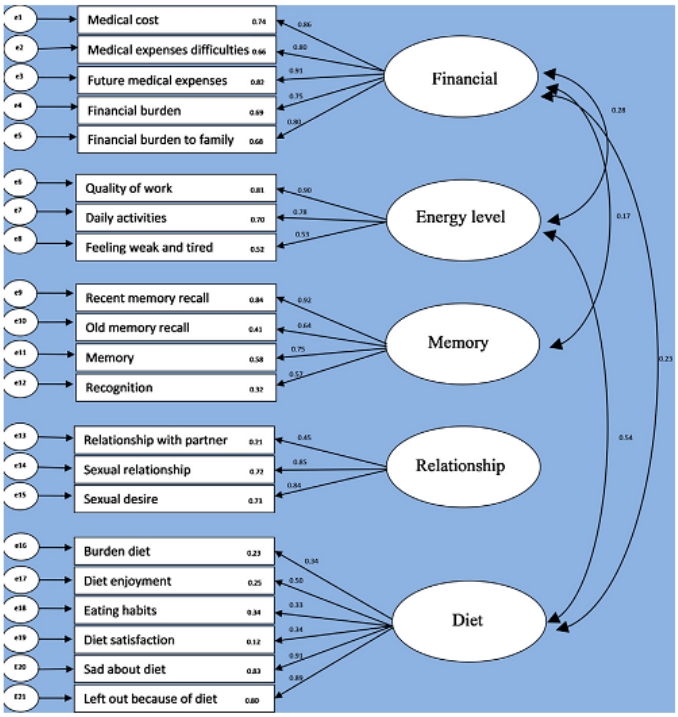

Fig. 1 – Confirmatory factor analysis for English language.

of loading of the questions were accounted for (Table 5). Test–retest reliability with minimum of at least 6 weeks apart for the English, Malay and Mandarin languages were 0.600, 0.700 and 0.500, respectively ($p < 0.01$). Correlation coefficient of 0.5 and above indicates good correlation.

Concordant validity was performed with WHO-QOL (BREF). Domain 1 on physical health was compared to self-care domain of AsianDQOL and showed correlation coefficient of 0.493 while domain 2 of WHO-QOL (BREF) on psychological issues matched against emotional domain on AsianDQOL showed correlation coefficient of 0.520. Domain 3 of WHO-QOL (BREF) on social relations was compared to domain on relationships of AsianDQOL and showed correlation coefficient of 0.387. Overall correlation coefficient comparing the new AsianDQOL to the WHO-QOL (BREF) was 0.612 ($p < 0.01$).

4. Discussion

The present study described the development of a new quality of life assessment tool in English, Malay and Chinese–Mandarin language based on South East Asian population. This resulted in 3 different questionnaires in English, Malay and Mandarin language and not one questionnaire translated into different language. The study design was unique because the core focus was on generating a new quality of life measurement tool that was constructed based on the different ethnic groups and their lingua franca in South East Asian population. The construct of the AsianDQOL was developed based on in-depth focus group interviews. The focus group for the English language version consisted of T2DM subjects of different ethnicities, religion and socio-economic background with English as their lingua franca. The focus group for the Malay version comprised of T2DM of different ethnicities (Malay, Indian and Chinese) with Malay as their preferred language. AsianDQOL takes into consideration the effects of different culture, religion and beliefs on QOL and will play a significant role in diabetes management in terms of reflecting a more accurate QOL.

In Asia, food and eating have complex meanings and implications for different population but in general the activity of eating is viewed in the context of social bonding and interaction, good health, valued leisure activity often involving close friends and family member [34]. The Asians consumes a much higher proportion of carbohydrates that are high in glycemic index such as white rice, noodles and white bread compared to non-Asian populations [35]. The items in our diet component were mainly referring to carbohydrate rich diet that is detrimental to sugar control. As such, people living with diabetes are frequently advised not to consume carbohydrate in their diet. However, for Asians, this has a significant impact on their daily living, life satisfaction and their perception of quality of life.

Table 3 – EFA: principal component analysis (Malay version).

	1	2	3	4	5
Financial					
Future medical expenses	0.822				
Medical cost	0.660				
Financial burden family	0.814				
Medical expenses difficulties	0.721				
Financial burden	0.747				
Diet					
Sad about diet		0.772			
Left out		0.757			
Worry about diet		0.518			
Burden diet		0.642			
Memory and cognition					
Recent recall			0.839		
Old recall			0.808		
Memory			0.771		
Recognition			0.695		
Energy					
Quality of work				0.810	
Activities				0.683	
Weak tired				0.805	
Lack of energy				0.713	
Relationship					
Relationship with partner					0.748
Sexual problem					0.875
Sexual desire					0.858
Relationship with family					0.520

Rotation: Varimax with Kaiser normalization. Rotation converged in 6 iterations.

The topic of sex and sexuality is very sensitive to Asians and not comfortably discussed in public. A study on sexual behavior and dysfunction help seeking patterns across urban populations in China, Taiwan, South Korea, Japan, Thailand, Singapore, Malaysia, Indonesia and the Philippines found that although sexual dysfunction is prevalent, but socio-cultural factors seem to prevent the afflicted individuals from seeking treatment [36]. Self-reported questionnaire is still the best way to capture such delicate information [36,37].

All the five newly developed subscales (English) had high degree of internal consistency with 3 components showing coefficients of >0.8 while the other two components are >0.7. The high degree of factor analysis and internal consistency confirmed the uniform construct of the questionnaire. As for the Malay language version, only one subscale (Diet) scored 0.673, which indicates that this component although showing substantial importance in the other languages may not be the case among Malay speaking population. All the five subscales for the Mandarin version showed high internal consistency with 3 components showing coefficients >0.8 while the other 2 components scored >0.7.

In our study, we found that the components of the three languages were different highlighting the differences in the perception on quality of life. The perception of quality of life was not only influenced by ethnicity but also the lingua franca. This finding is unique and could be contributed by westernization. In Asia especially South East Asia, there is a strong element of Western culture influence or westernization likely due to the history of colonialism. Westernization represents a lifestyle or behavioral approach to health in epidemiology [38]. There is limited data on the impact of westernization on the perception of QOL in a multi-ethnic population. The preferred language of the subject reflecting his or her upbringing may determine the impact of westernization. Those who preferred English language tend to be English educated locally or overseas and have a higher exposure to western culture and lifestyle compared to the more traditional group who are still following local customs, lifestyles and beliefs. Malaysia's population is of the different ethnic group composition. The education system in Malaysia practices multi-lingual concept resulting in a majority of Malaysians who are proficient in more than one language for example Malay language and English or Malay language and Mandarin. Their preferred language is mainly influenced by the medium education and influence of family and social network.

The total score for AsianDQOL is unique to the respective language. The total score is the summation of scores obtained from all the components. This will allow the clinician/doctor to know which components contributed to the poor quality of life or vice versa. The total score can also be used to classify patient's global quality of life score i.e. ''Poor quality of life" or "good quality of life" for clinical assessment purposes. However, this scoring system was based on a small sample and a cross-sectional study with larger sample size is currently in progress to verify the scores.

The AsianDQOL is more suitable for use in Malaysian population compared to DQOL, DQLCTQ-R and DSQOLS because it is disease specific and was constructed based on the Malaysian population. We also recruited subjects of

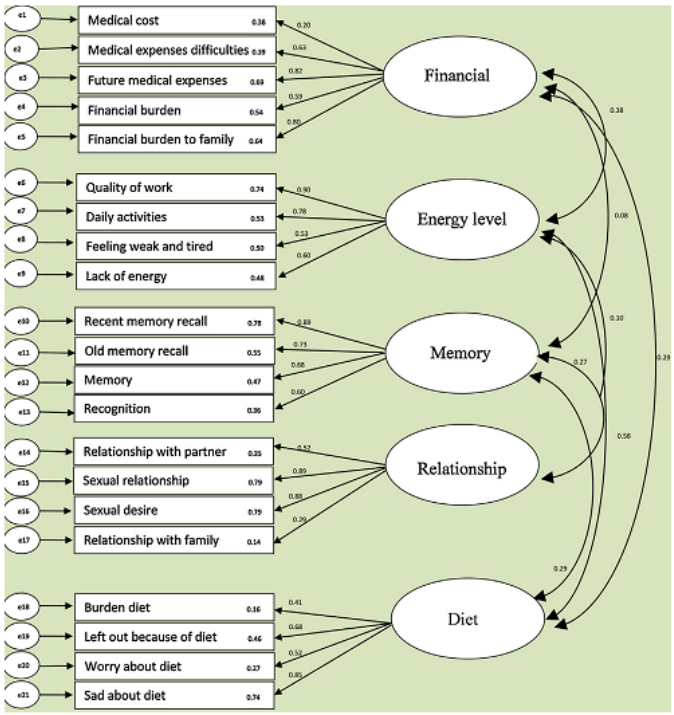

Fig. 2 – Confirmatory factor analysis for Malay language.

Table 4 – EFA: principal component analysis (Chinese/Mandarin version).

	1	2	3	4	5
Financial					
Future medical expenses	0.807				
Medical cost	0.835				
Financial burden family	0.803				
Medical expenses difficulties	0.799				
Financial burden	0.847				
Burden to family	0.588				
Diet and activities					
Sad about diet		0.586			
Left out		0.917			
Activities		0.699			
Burden diet		0.675			
Memory and cognition					
Recent recall			0.880		
Recognition			0.887		
Energy					
Quality of work				0.565	
Weak tired				0.782	
Lack of energy				0.796	
Relationship					
Relationship with partner					0.721
Sexual problem					0.929
Sexual desire					0.930

Rotation: Varimax with Kaiser normalization. Rotation converged in 6 iterations.

Table 5 – Reliability analysis of AsianDQOL using Cronbach's alpha.

Component	Cronbach's Alpha score	No. of items
English		
Financial aspects	0.92	5
Energy levels	0.82	3
Memory	0.82	4
Relationships	0.75	3
Diet	0.72	6
Malay		
Financial aspects	0.83	5
Energy levels	0.82	4
Memory and cognition	0.82	4
Relationships	0.78	4
Diet	0.67	4
Chinese/Mandarin		
Financial aspects	0.89	6
Relationships	0.86	3
Memory	0.83	2
Diet and activities	0.76	4
Energy levels	0.72	3

different ethnicities and this is a better representative sample of our local population.

We found acceptable correlations between AsianDQOL and WHO-QOL (BREF) domains of physical health, psychological aspects and social relations. The QOL score for each language were determined based on the 25th, 50th and 75th centile. The score varied stressing that there are differences between the three languages even though the subjects were from the same country. However, this scoring system will need to be confirmed in larger studies. A population based, cross-sectional study is currently ongoing in 3 different states in Malaysia.

The study demonstrated that across different ethnicities and languages, there are significant differences in factors determining QOL. In the English and Chinese (Mandarin) group, the components of diet and eating habits were shown to have a significant impact on QOL whereas in the Malay language group this component did not achieve a significant impact. We also found that there were differences in the number of items across the 3 languages. This support our theory that subjects of the same ethnic group but of different language group think differently and this was reflected in their perception of QOL. The Chinese–Mandarin language group was smaller in number and this could have effect on the outcome. MacCallum et al. [39] concluded that aspect of sampling (small size) that has detrimental effect receives a low weight if the communalities are high (above 0.6). Results from the analysis showed that the communalities for the Chinese–Mandarin group were all above 0.7 minimizing the effect of sample size. The KMO and Bartlett's test showed adequate sample size for factor analysis [40].

Factors such as financial issues, memory and cognition that were significant in all the three study groups were not discussed much in existing questionnaires. The strength of this study is the ability of AsianDQOL to resolve the limitations faced by other QOL tools in a multi-ethnic population credited to the availability in different languages and the core construct of the tool based on Asian population from different levels of socio-economic background. Our findings were based on Malaysian population of different ethnicities and cannot be applied to other Asian population until further studies are done to assess the suitability in the 3 languages.

In order to further improve the AsianDQOL and assess the suitability for use in Asians outside of Malaysia, studies are currently ongoing in Asian population living in Australia, Singapore and Indonesia using the 3 languages.

Funding for study

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Conflict of interest statement

No conflict of interest declared.

Novelty statement

This study has successfully developed the first valid and reliable quality of life assessment tool for patients with type-2 diabetes mellitus in English, Malay and Chinese/Mandarin that is constructed based on Asian populations. This tool is sensitive across different ethnicities, languages, and socio-economic backgrounds. In view of the rising number of diabetics in Asia, this tool will be able to accurately reflect the quality of life and play a vital role in improving the clinical management of diabetes mellitus.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.diabres.2015.02.009.

Appendix C. Supplementary data

Table A1.

Table A1 – CFA: summary of goodness-of-fit for English and Malay language.

	Recommended value [35]	English	Malay
Model chi-square (p-value)	$p > 0.05$	201 ($p = 0.07$)	189 ($p = 0.09$)
Degree of freedom		173	164
Root mean square error of approximation (RMSEA)	Less than 0.07	0.036	0.025
Goodness of fit (GFI)	Values greater than 0.95	0.88	0.94
Comparative fit index (CFI)	Values greater than 0.95	0.98	0.99

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Appendix 15: Paper: Diabetes Quality of Life perception in a multi-ethnic population.

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Diabetes quality of life perception in a multiethnic population

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Abstract
Aim The aim of this study was to determine ethnic differences and predictors of the perception of quality of life (QOL) in a multiethnic Malaysian population with type 2 diabetes.
Methods A population-based cross-sectional study was done in three different states in Malaysia. The Asian Diabetes Quality of Life (AsianDQOL) tool specific for type 2 diabetes is the primary outcome tool. One-way analysis of covariance was undertaken to examine ethnic differences on the total and component AsianDQOL scores controlling for important covariates. Stepwise multiple linear regression models were used for selecting predictors for the AsianDQOL score with stratification for ethnicity and language.
Results A total of 647 subjects (338 Malays, 160 Chinese and 149 Indians) were recruited. Chinese scored significantly lower (78.1 ± 11.6) on the AsianDQOL (total) score compared to Malays (81.4 ± 9.0) and Indians (81.5 ± 9.2) ($F = 3.060$, $p = 0.049$, $\eta^2 = 0.02$). Likewise, Chinese scored significantly lower (21.0 ± 4.3) on the AsianDQOL (diet) score compared to Malays (22.8 ± 3.6) and Indians (22.5 ± 3.7) ($F = 4.96$, $p = 0.008$, $\eta^2 = 0.04$). The main predictors of AsianDQOL (total) score for the English language group of different ethnicities were sexual dysfunction (−4.5), having visual problems (−3.7), female (−2.8) and glycemic control (−1.6). Sexual dysfunction was negatively correlated with QOL in Malay, Chinese ethnic group and Indian ethnic groups.
Conclusion The perception of AsianDQOL is different across ethnic groups and languages spoken. Significant differences in the English-speaking group and the non-English-speaking group are detected within the same ethnicity. Sexual dysfunction severely impacts AsianDQOL in a multiethnic Asian population and remains an important determinant regardless of ethnicity and language.

Keywords Quality of life · Diabetes · Perception · Sexual dysfunction · Asians

This study assessed ethnic differences and factors predicting quality of life perception in a multiethnic Asian population. There are very limited data on Asian population with diverse culture, ethnic group, religion, language and socioeconomic background.

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Introduction

Quality of life (QOL) measurement apart from physical indices or glycemic control is becoming increasingly important with rapid progression in the field of medicine. QOL has become a crucial outcome measure for management of diabetes (DM). The current available QOL tools are divided into generic and disease specific. In Asia, most of the QOL tools were translated from those developed based on the Western population [1, 2]. The translated versions were then validated for use in the local Asian population [3, 4]. A review of the translation and adaptation process of QOL tools in Asian countries show only 24 % measured the local conception of QOL [5].

QOL is a broad concept, and perception of QOL can be affected by different factors such as the socioeconomic status, culture, population group and even ethnicity [4, 6, 7]. Lau et al. [6] 1998 studied the self-perceived QOL of Chinese elderly people in Hong Kong and concluded that

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general commonalties of health, life satisfaction and social relationships with studies done in Western countries. However, differences in the characteristics and ranking of components are present and must be adjusted or modified for a better reflection of QOL. Several population-based studies in Singapore concluded that ethnicity and socioeconomic status are important in determining QOL in a multiethnic Asian population [4, 7]. There are limited data on the impact of westernization on the perception of QOL in a multiethnic population. The preferred language of the subject reflecting his or her upbringing may determine the impact of westernization on South East Asian countries Malaysia, Singapore, Brunei, Indonesia and the Philippines. Those who preferred English language tend to be English educated locally or overseas and have a higher exposure to Western culture and lifestyle compared to the more traditional group who are still following local customs, lifestyles and beliefs.

Malaysia's population is similar to Singapore in terms of the different ethnic group composition. The education system in Malaysia practices bilingual concept, resulting in a majority of Malaysians who are proficient in more than one language. Their preferred language is mainly influenced by the medium of education and influence of family and social network [8, 9]. Whorf in 2012 explained that language guides our cognition and shaped our conceptual knowledge, and subsequently, there is strong evidence, supporting the theory that language directs thoughts and behavior in human beings [10, 11]. We hypothesized that a population of the same ethnicity but with different preferred language will not share the same perception of QOL. We also want to determine the factors influencing QOL and the impact of DM on QOL in our population with diverse ethnicities and languages.

Methods/design

Study design

A population-based cross-sectional study was conducted across the three most populous states in Peninsular Malaysia. The minimum sample size was calculated for multiple regression based on recommendations by Knofczynski et al. [12] in 2007. The recommended minimum sample size of good prediction level with five predictor variables and medium population correlation coefficients of 0.50 were 65 subjects [12]. The Malaysian statistics department states that of the 28 million population, 60 % are Malays, 23 % Chinese, 7 % Indians and 10 % others. The prevalence of diabetes in Malaysia in 2013 was highest in Indian ethnic group (38 %) compared to Malays (24 %) and Chinese (18 %) [13]. Recruitment sampling takes into consideration these two factors. Convenient sampling method was used, but in order to reduce bias and to cater for the above variables, subjects were recruited from different levels of healthcare facilities across three states in Malaysia. The healthcare system in Malaysia is divided into the private sector and the government section. The government sector is free for all Malaysians while patients in the private sectors will have to bear their own expenses if they are not covered by insurance. According to the Malaysia Health System review by WHO Western Pacific Region in 2012, the government sector (free or subsidized fee) covers 82 % of inpatient and 35 % of outpatient care, while the private sector (self-paying or third party paying) covers 18 % of inpatient and 62 % of outpatient care [14]. The study sample gives a fair representative with 56 % from government sector, 36 % from private sector and 4 % of both. Subjects were also recruited from clinic and hospital with consultants, internal medicine specialist and general practitioner clinics. This is to ensure comprehensive coverage of subjects from all different socioeconomic background and levels of medical care. Subjects were of major ethnic groups residing in Malaysia (Malay, Chinese and Indian) with different preferred language, e.g., English-speaking group of Malay ethnicity. This will ensure a fair representative sample of the Malaysian population who has DM. Patients must have at least 6 years of formal education. The literacy rate in Malaysia (2008–2013) is 93 % [15]. Our study population comprised of the working group and non-working group that consisted of retirees, housewives, students and unemployed. Subjects were from three most populous states in Malaysia (Selangor, Johor and Wilayah Persekutuan), which covered the urban and suburban group. The study population also included patients with long-standing DM (more than 5 years), the newly diagnosed and those who are diagnosed less than 5 years with or without DM complications, on different types of treatment and levels of glycemic control.

The inclusion criteria are subjects with type 2 DM, with or without pharmacological treatment, above 18–80 years old, completed at least 6-year education and able to give written consent. The exclusion criteria were concurrent Parkinson's disease, Alzheimer's disease, dementia and severe visual impairment. The nature of the study was explained to the subjects and a copy of the information consent form. Subjects consenting to the study were given a copy of AsianDQOL in their preferred language to fill. Thorough medical history and physical examination were done by the researcher. Physical examination includes measurement of height, weight, blood pressure, waist circumference body mass index (BMI) and other complications of diabetes. Anthropometric measurements were taken according to the World Health Organization (WHO)

guidelines [16]. BMI was calculated as weight (kg) divided by height (m^2). The waist circumference was taken as between the lowest rib margin and iliac crest. Blood sample for HbA1c levels was taken via venous sampling, and analysis was done using the Arkray Adams HA-8160 (Arkray, Inc., Nakagyo-ku, Kyoto, Japan) Diabetes Control and Complications Trial aligned cation-exchange chromatographer analyzer for HbA1c. Ethnics clearance was granted by the Monash University Human Research Ethics Committee (MUHREC), approval no CF2630–2011001537. Written informed consent was obtained from all participants.

Primary outcome tool

In our previous study, we have developed and validated a QOL assessment tool specific for type 2 DM in Asia. The tool (AsianDQOL) was constructed based on the diverse ethnicity, culture, language, religion and sociodemographic in Malaysian population. This tool shows good reliability and is available in English, Malay/Indonesian language and Chinese-Mandarin. The English and Malay language questionnaire had five components and 21 items, while the Chinese-Mandarin language version had five components with 18 items. The questionnaires showed good reliability with Cronbach's alpha's score of >0.7. Among the domains assessed were diet and eating habits, emotion and self-care, memory and cognition, financial aspects and interpersonal relationships. The scoring system of this questionnaire is such that each component can be assessed individually or as total score. Based on the total score, the subjects can be classified as having 'excellent QOL,' 'good QOL,' 'moderate QOL' or 'poor QOL.'

Statistical analyses

Data were analyzed using the Statistical Package For Social Sciences (SPSS) version 20. A one-way ANOVA was used to analyze mean differences across ethnic groups; Chi-square test was used to analyze categorical differences across ethnic groups. A one-way analysis of covariance (ANCOVA) was used to compare ethnic differences of the AsianDQOL (total) and component scores controlling for significant covariates. Stepwise multiple linear regressions were used to identify significant predictors of the AsianDQOL total score across ethnicities and languages. Statistical significance was set at $p < 0.05$.

Results

The total number of subjects recruited was 704, 57 (8 %) subjects were removed due to incomplete data and the final number for analysis was 647. Table 1 depicts the demographic data, comorbidities and treatment characteristics of the study population by the different ethnic groups. Chinese scored significantly lower (78.1 ± 11.6) on the AsianDQOL (total) score compared to Malays (81.4 ± 9.0) and Indians (81.5 ± 9.2) ($F = 3.060$, $p = 0.049$, $\eta^2 = 0.02$). Likewise, Chinese scored significantly lower (21.0 ± 4.3) on the AsianDQOL (diet) score compared to Malays (22.8 ± 3.6) and Indians (22.5 ± 3.7) ($F = 4.96$, $p = 0.008$, $\eta^2 = 0.04$). A preliminary one way between groups ANCOVA was conducted to analyze the effect of ethnicity and different covariates such as age, gender, working status, duration of DM, education level, types of DM treatment, DM care center and HbA1c on AsianDQOL score. Only HbA1c was significant (Table 2). ANCOVA was used to compare the effect of ethnicity on the perception of QOL. The independent variable was the ethnic groups (Malay, Chinese and Indian), and the dependent variable was the QOL score measured by AsianDQOL. Participant's HbA1c level was used as the only covariate in this analysis. Preliminary checks were conducted to ensure that there was no violation of the assumptions of normality, linearity, homogeneity of variances, regression slopes and reliable measurement of the covariate. Analysis showed significant differences between the ethnic groups on QOL ($F = 3.060$, $p = 0.049$, $\eta^2 = 0.02$) (Table 2). When we analyzed the different components' score as dependent variable, only the diet component showed significant differences between the ethnic groups. This indicates that the perception on diet was different between the ethnic groups (Table 3). The other components such as relationship, memory, energy level and financial were not significant (Table 3). Stepwise multiple linear regressions on the 647 subjects to analyze the possible contributors to QOL score were done. Linear regression done on 292 Malay-language-speaking (MLS) subjects of different ethnicities (255 Malays, 32 Indians and 5 Chinese) showed longer duration of DM, and sexual dysfunction is negatively associated with QOL score (Table 4). The equation generated, QOL = 90 (constant) − 1.8 (duration of DM) − 5.9 (sexual dysfunction). For example, for a subject with diabetes for 10 years with complication of sexual dysfunction would obtain a score of 66. Excluded variables were age, gender, education level, glycemic control (HbA1c), BMI, ethnicity, comorbidities such as heart disease, hyperlipidemia, hypertension, visual problems and nerve problems (Table 4).

Analysis of the 282 English language cohort entailing 83 subjects of Malay ethnicity, 82 Chinese and 117 Indian showed the following equation (Table 4): QOL = 91 (constant) −1.6 (HbA1c) − 2.8 (female) − 3.7 (visual problems) − 4.5 (sexual dysfunction). For example, a male subject with HbA1c score of 10 with sexual dysfunction

Table 1 Demographic, comorbidities and treatment characteristics of the Malay, Chinese and Indians with type 2 diabetes mellitus

Characteristics	Malay No. (%)	Chinese No. (%)	Indian No. (%)	χ^2	df	*p*
Age 0(mean ± SD) (year)	55.0 ± 11.6	57.5 ± 11.2	54.5 ± 10.9			0.24[a]
Gender				2.90	2	0.41
Men	214 (63.3)	103 (64.4)	106 (71.1)			
Women	124 (36.7)	57 (35.6)	43 (28.9)			
Language				453.80	4	0.00
Malay	255 (75.4)	5 (3.1)	32 (21.5)			
English	83 (24.6)	82 (51.2)	117 (78.5)			
Mandarin	0 (0.0)	73 (45.6)	0 (0.0)			
Marital status				4.69	2	0.20
Married	304 (89.9)	133 (83.1)	130 (87.2)			
Not married	34 (10.1)	27 (16.9)	19 (12.8)			
Education level				14.40	2	0.03
Secondary school	137 (40.7)	54 (34.2)	44 (29.5)			
Tertiary and above	200 (59.3)	104 (65.8)	105 (70.5)			
Occupation				16.10	2	0.00
Working	191 (56.5)	91 (56.9)	111 (74.5)			
Not working/retired	147 (43.5)	69 (43.1)	38 (25.5)			
Comorbidities						
Hypertension	198 (58.6)	97 (60.6)	75 (50.3)	4.00	2	0.26
Hyperlipidemia	167 (49.4)	87 (54.4)	70 (47.0)	1.90	2	0.60
Cardiac disease	70 (20.7)	28 (17.5)	37 (24.8)	2.60	2	0.46
Visual problems	96 (28.4)	47 (29.4)	44 (29.5)	4.40	2	0.22
Nerve problems	101 (29.9)	39 (24.4)	48 (32.2)	2.80	2	0.43
Sexual dysfunction	140 (41.4)	58 (36.3)	59 (39.6)	2.00	2	0.58
Peripheral vascular disease	5 (1.5)	4 (2.5)	3 (2.0)	8.50	2	0.04
Renal problems	12 (3.6)	7 (4.4)	9 (6.0)	2.40	2	0.50
Type of treatment				19.90	8	0.34
Diet therapy alone	22 (6.5)	3 (1.9)	7 (4.7)			
Oral pills only	205 (60.7)	110 (68.8)	92 (61.7)			
Insulin only	28 (8.3)	7 (4.4)	13 (8.7)			
Oral pills and insulin	53 (15.7)	26 (16.3)	24 (16.1)			
Not on any treatment	6 (1.8)	5 (3.1)	3 (2.0)			
Duration of diabetes				6.94	4	0.64
Less than 1 year	47 (13.9)	18 (11.2)	19 (12.8)			
Between 1 and 5 years	98 (29.1)	40 (25.0)	45 (30.2)			
>5 to <10 years	80 (23.8)	48 (30.0)	31 (20.8)			
More than 10 years	112 (33.2)	54 (33.8)	54 (36.2)			
Center for diabetes care				27.50	4	0.74
Government sector	195 (60.2)	79 (52.3)	86 (59.7)			
Private sector	115 (35.5)	64 (42.4)	54 (37.5)			
Government and private sector	14 (4.3)	8 (5.3)	4 (2.8)			
HbA1c levels				14.30	6	0.11
Less than 6.5 %	63 (19.4)	29 (19.8)	32 (23.0)			
Between 6.5 and 7.5 %	73 (22.5)	48 (32.9)	42 (30.2)			
Between 7.6 and 8.5 %	67 (20.7)	26 (17.8)	19 (13.7)			
More than 8.5 %	121 (37.4)	43 (29.5)	46 (33.1)			

[a] One-way ANOVA used

will score 70.5. This result demonstrates that having poorer glycemic control, the presence of visual problems and sexual dysfunction predicts a poorer QOL score. When compared to Malay language group, the duration of DM is no longer a determinant of QOL score. Excluded variables were glycemic control (HbA1c), education level, ethnicity, BMI, duration of DM and comorbidities such as hyperlipidemia, heart disease and kidney disease.

Analysis of the 73 Mandarin language group of Chinese ethnicity showed glycemic control, and sexual dysfunction is negatively associated with QOL score, while hyperlipidemia is associated with better QOL score (Table 4). QOL = 71 (constant) + 4.6 (hyperlipidemia) − 1.9 (HbA1c) − 5.9 (sexual dysfunction). For example, a subject with HbA1c of 10 and associated hyperlipidemia and sexual dysfunction will score 50.7. Excluded variables were education level, duration of DM and comorbidities such as hypertension, heart disease, visual problems, nerve and kidney problem.

Analysis of 255 more traditional MLS of Malay ethnicity cohort generated an equation of 98 (constant) − 2.3 (duration of DM) − 6.0 (sexual dysfunction). Sexual dysfunction and duration of DM negatively predict QOL in this group. The R^2 value was 0.14, indicating that the model explained 14 % of total QOL score (Table 5). Analysis of the 83 subjects of the English speaking of Malay ethnicity group showed diabetes renal problems was associated with worse QOL score (Table 5). QOL = 82 (constant) − 22 (renal problems). The R^2 value was 0.13, indicating that the model explained 13 % of the total QOL score. For example, a man of Malay ethnicity with Malay language as his lingua franca and has diabetes for 10 years with chronic kidney disease will obtain a score of 75, while a man of Malay ethnicity with English language as his lingua franca and has diabetes for 10 years with chronic kidney disease will obtain a score of 60.

Analysis of the English-speaking group of Chinese ethnicity revealed negative association of sexual dysfunction and female gender with QOL scores (Table 5). Equation generated: QOL = 90 (constant) − 5.9 (female gender) − 10.0 (sexual dysfunction). The R^2 value was 0.15 explaining 15 % of the total QOL score. The traditional Mandarin-speaking group of Chinese ethnicity group demonstrated positive association of hyperlipidemia and negative association of glycemic control and sexual dysfunction with QOL. The equation, QOL = 71 (constant) + 4.6 (hyperlipidemia) − 1.9 (glycemic control) − 5.9 (sexual dysfunction). The R^2 value was 0.21 explaining 21 % of the total QOL score. For example, a male of Chinese ethnicity with English language as his lingua franca has HbA1c of 10 %, and complications of hyperlipidemia and sexual dysfunction will score 80 points, while a male of Chinese ethnicity with Mandarin language as his lingua franca has HbA1c of 10 %, and complications of hyperlipidemia and sexual dysfunction will score 50.7 points.

The 117 subjects from the English-speaking Indian ethnicity group show strong negative association of experiencing nerve problems and sexual dysfunction with QOL scores (Table 5). The equation formed: QOL = 85 (constant) − 3.8 (sexual dysfunction) − 5.7 (nerve problems). The R^2 value was 0.11 explaining 11 % of the total QOL score. The equation generated from analysis of the Malay-speaking Indian ethnicity group shows 113 (constant) − 8.3 (mode of treatment) − 8.5 (working status). This shows that patient on lesser type of treatment (i.e., oral vs combination of oral and insulin) and those who are working has a higher QOL score. The R^2 value was 0.45 explaining 45 % of the total QOL score.

Discussion

The most significant new finding of the study is that the perception of QOL is different across ethnicity and the lingua franca in a population sharing the same basic socioeconomic background. This has not been demonstrated before. Analysis of this study demonstrated significant differences between the ethnic groups (Malay, Chinese and Indian) on perception of QOL. In-depth analysis of the components of QOL showed significance differences between the ethnic group's perceptions on diet component. This demonstrates that ethnic differences do exist in a population sharing similar sociocultural contexts. This finding is similar to Singapore where a population-based study by Wee et al. in 2005 showed ethnicity as an important factor influencing QOL in people with diabetes [12]. However, a generic tool was used to measure QOL, and this could limit the sensitivity in participants with DM. Only English language tools were used in that study limiting the study population to only those proficient in English. When we compared the different ethnic groups in Malaysia, the predictors of QOL were different in the Malay ethnic group compared to the Chinese and Indian. Within the Malay ethnic group, marked differences were detected with the English-language-speaking group (ELS) versus the more traditional MLS group. The (ELS) group was primarily concerned about the presence of renal impairment, while the (MLS) group was affected by the duration of DM and sexual dysfunction. This could be that the ELS group is associated with higher education level (25 % have at least secondary education and 75 % have above secondary education) compared to the MLS group (54 % have at least secondary education and above). Higher education level is associated with better economic security and job prospects. Glasgow et al. [17] in 1997 found that lower education level and lesser income were

Table 2 One-way analysis of covariance with AsianDQOL (total) score as dependent variable

Independent variable	Mean ± SD	Tests of between-subject effects			Estimated marginal means		
		F	p	η^2	Mean	95 % CI	
						Lower	Upper
Ethnic group		3.06	0.049	0.02			
Malay ($n = 80$)	81.4 ± 9.0				81.50	79.34	83.65
Chinese ($n = 77$)	78.1 ± 11.6				78.17	75.98	80.37
Indian ($n = 114$)	81.5 ± 9.2				81.38	79.57	83.18
HbA1c status		8.32	0.004	0.03			

Dependent variable: AsianDQOL (total) score. Levene's test of equality of error variance: $F = 2.9$ ($p = 0.056$) gender ($F = 0.19$, $p = 0.667$), age ($F = 0.31$, $p = 0.577$), working status ($F = 1.80$, $p = 0.182$), duration of DM ($F = 2.15$, $p = 0.143$), education level ($F = 0.01$, $p = 0.931$), types of treatment ($F = 0.00$, $p = 0.992$) and DM care center ($F = 0.01$, $p = 0.920$)

associated with a lower QOL score. The presence of DM complications was linked to lower QOL score, especially for coexistent of microvascular and macrovascular complications [17, 20, 21]. The presence of chronic kidney disease further worsens the QOL, especially in end-stage renal failure and with initiation of dialysis [22, 23]. This is consistent with ELS group with strong negative association of renal impairment with QOL score.

The Chinese ethnic group also showed significant differences between the ELS group versus the traditional Mandarin-speaking group. The main determinant of QOL in the ELS group is sexual dysfunction versus HbA1c, hyperlipidemia and sexual dysfunction in the Mandarin-speaking group. The ELS group being more westernized in their behavior and lifestyle could have an impact on their perception compared to the more traditional Mandarin-speaking group. The presence of hyperlipidemia as a determinant of QOL scores in the Mandarin-speaking Chinese group is unique. This finding highlights the importance of the eating culture and health among the more traditional Chinese population. A population-based study in Hong Kong Chinese population found that the activity of eating was viewed as an important activity signifying good health, social bonding with family and friends [6]. This led to formation of a strong bond between the ability to eat freely, freedom to participate in such social rituals and life satisfaction affecting QOL [17, 20, 21]. The Chinese ethnic group regardless of the preferred language is severely affected by the presence of sexual dysfunction.

The predictors of QOL in the ELS Indian ethnic group were different from the Malay-speaking Indians. In the Malay-language-speaking group of Indian ethnicity, the mode of treatment and working statues explain 45 % of the total QOL score. In this group, having a permanent job is associated with better financial stability and better QOL. Poorer QOL was associated with insulin usage perhaps due to the complications of insulin. This is consistent with findings of Glasgow et al. [17] in 1996 linking insulin use to poorer QOL.

Our study highlights that perception of QOL is not only different across the ethnic groups but also among the more English-speaking and native language-speaking group within the same ethnicity. This indicates that perception of QOL is very much influenced by exposure to westernization that can be assessed by their lingua franca. Current study to look at the effect of westernization on perception of QOL among Asian population living in Australia will shed more light into this area.

In our study, we did not find any differences of QOL between subjects from private (self-paying, higher income) or government healthcare sector (free, lower income group). The mode of treatment did not affect QOL in our study group. This is consistent with the findings of the UKPDS group via two cross-sectional studies of patients in randomized controlled trials of intensive blood glucose control versus conventional control and tight blood pressure control versus less tight control, stating that the therapeutic policies had no effect on QOL [20]. Other studies done post-UKPDS also found that insulin therapy in poorly controlled type 2 DM had no adverse events on QOL [24] or even higher QOL score in the initiation of insulin phase due to relief of hyperglycemic symptoms [25]. However, there are several studies that detected a lower QOL score in subjects on insulin compared to those on oral medications [17, 26].

Complications of diabetes are associated with detrimental impact on QOL [17–20, 23]. Our study shows that among the complications, sexual dysfunction, retinopathy and nephropathy severely reduced QOL. Sexual dysfunction is also strongly negatively correlated with QOL in all the three major ethnic groups. Sexual dysfunction in this

Table 3 One-way analysis of covariance with component score as dependent variable

Independent variable	Mean ± SD	Tests of between-subject effects			Mean	Estimated marginal means	
		F	p	η^2		95 % CI	
						Lower	Upper
Diet component							
Ethnic group		4.96	0.008	0.04			
Malay ($n = 80$)	22.8 ± 3.6				22.88	22.06	23.69
Chinese ($n = 77$)	21.0 ± 4.3				21.08	20.25	21.91
Indian ($n = 114$)	22.5 ± 3.7				22.39	21.71	23.08
HbA1c status		20.90	0.000	0.07			
Relationship component							
Ethnic group		1.97	0.141	0.02			
Malay ($n = 80$)	8.1 ± 3.2				8.07	7.33	8.81
Chinese ($n = 77$)	8.4 ± 3.7				8.41	7.66	9.16
Indian ($n = 114$)	9.0 ± 3.2				9.01	8.39	9.63
HbA1c status		1.19	0.276	0.00			
Memory component							
Ethnic group		2.37	0.096	0.02			
Malay ($n = 80$)	16.6 ± 2.1				16.59	16.08	17.10
Chinese ($n = 77$)	16.1 ± 2.4				16.13	15.61	16.65
Indian ($n = 114$)	16.9 ± 2.4				16.88	16.45	17.30
HbA1c status		0.03	0.865	0.00			
Energy-level component							
Ethnic group		2.20	0.113	0.02			
Malay ($n = 80$)	12.5 ± 2.1				12.55	11.94	13.16
Chinese ($n = 77$)	11.7 ± 3.0				11.75	11.12	12.37
Indian ($n = 114$)	11.8 ± 3.0				11.80	11.29	12.31
HbA1c status		0.56	0.456	0.02			
Financial component							
Ethnic group		0.52	0.593	0.00			
Malay ($n = 80$)	21.4 ± 3.6				21.42	20.54	22.30
Chinese ($n = 77$)	20.8 ± 4.5				20.81	19.91	21.70
Indian ($n = 114$)	21.4 ± 4.0				21.30	11.29	22.04
HbA1c status		9.69	0.002	0.04			

Levene's test of equality of error variances: Diet component ($F = 1.60$, $p = 0.200$), relationship component ($F = 1.60$, $p = 0.200$), memory component ($F = 1.27$, $p = 0.282$), energy-level component ($F = 3.95$, $p = 0.200$), financial component ($F = 1.01$, $p = 0.370$)

study was taken as having experienced erectile dysfunction (ED), having poor libido, premature ejaculation, vaginal dryness, dyspareunia and anorgasmia. This is consistent with findings globally that found a strong link between DM, ED and worse QOL [27, 28]. A comprehensive study done by De Berardis et al. [28] 2002, across 114 DM outpatient clinics and 112 general practitioners, found that ED affects one-third of patients with diabetes, and they have higher depressive symptoms and poorer QOL. However, this study takes into account self-reported symptoms with no clinical diagnosis, and QOL was assessed using a general assessment tool (SF-36). A year later, Person et al. in year 2003 compared impotent men with DM to those without and found more severe dysfunction and worse QOL in the group with DM [28]. Although the sample size for DM group was relatively small ($n = 20$), but a disease-specific tool was used increasing the sensitivity. In women, sexual dysfunction is frequent in patients with DM and is associated with reduction in overall QOL with 77 % having lack of libido and 38 % with vaginal dryness [29, 30]. We conclude that in a multiethnic Asian population, sexual dysfunction is highly associated with DM and in view of the detrimental effect on QOL, it is important for early detection and proper management to maintain good QOL.

Table 4 Predictors of AsianDQOL (total) score stratified by language: stepwise multiple linear regression

Predictor variable	β coefficient		95 % CI		p
	Unstandardized	Standardized	Lower	Upper	
Malay/Indonesian ($n = 292$, $R^2 = 0.11$)					
Constant	90.30		86.90	93.71	0.000
Duration of diabetes	−1.82	−0.18	−2.98	−0.66	0.002
Sexual dysfunction	−5.87	−0.26	−8.41	−3.33	0.000
English ($n = 282$, $R^2 = 0.11$)					
Constant	90.95		86.24	95.65	0.000
HbA1c	−1.56	−0.18	−2.59	−0.54	0.000
Gender	−2.77	−0.13	−5.35	−0.18	0.036
Visual problems	−3.65	−0.16	−6.40	−0.90	0.010
Sexual dysfunction	−4.49	−0.18	−6.95	−2.03	0.000
Mandarin ($n = 73$, $R^2 = 0.22$)					
Constant	71.45		65.94	76.96	0.000
Hyperlipidemia	4.56	0.27	0.47	8.65	0.029
HbA1c	−1.85	−0.26	−3.55	−0.15	0.034
Sexual dysfunction	−5.87	−0.33	−10.10	−1.65	0.007

Table 5 Predictors of AsianDQOL (total) score stratified by ethnicity and language: stepwise multiple linear regression

Predictor variable	β coefficient		95 % CI		p
	Unstandardized	Standardized	Lower	Upper	
Malay ethnicity Malay language ($n = 255$, R^2: 0.14)					
Constant	97.98		88.44	95.53	0.000
Duration of diabetes	−2.28	−0.23	−3.49	−1.07	0.000
Sexual dysfunction	−6.01	−0.27	−8.68	−3.34	0.000
Malay ethnicity English language ($n = 83$, R^2: 0.13)					
Constant	81.79		79.81	83.76	0.000
Renal problems	−21.79	−0.37	−34.24	−9.26	0.001
Chinese ethnicity Mandarin language ($n = 73$, R^2: 0.21)					
Constant	71.45		65.94	76.96	0.000
Hyperlipidemia	4.56	0.27	0.47	8.65	0.029
HbA1c	−1.85	−0.26	−3.55	−0.15	0.034
Sexual dysfunction	−5.87	−0.33	−10.10	−1.65	0.007
Chinese ethnicity English language ($n = 82$, R^2: 0.15)					
Constant	90.47		81.47	99.48	0.000
Gender	−5.87	−0.24	−11.60	−0.13	0.045
Sexual dysfunction	−9.99	−0.42	−15.49	−4.49	0.001
Indian ethnicity English language ($n = 117$, R^2: 0.11)					
Constant	84.77		82.42	87.12	0.000
Sexual dysfunction	−3.79	−0.20	−7.27	−0.30	0.033
Nerve problems	−5.70	−0.28	−9.38	−2.02	0.003
Indian ethnicity Malay language ($n = 32$, R^2: 0.45)					
Constant	113.27		98.85	127.69	0.000
Treatment	−8.26	−0.66	−11.83	−4.68	0.000
Working status	−8.53	−0.35	−15.56	−1.48	0.019

However, there are limitations that need to be considered. Firstly, using a self-assessment technique by questionnaire for recruitment, only subjects who have basic education are included in the study. In view of the high literacy rate in Malaysia, our study did capture a good sample of the population [15]. Secondly, the number of Chinese-Mandarin language individuals is smaller compared to Malay/Indonesia and English group. This is mainly due to the lack of Chinese-Mandarin competent subjects in the recruitment area. Our findings are based on Malaysian population and may not be applicable to other populations in Asia.

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Conflict of interest None.

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