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Distress and health-related quality of life in Indonesian type 2 diabetes mellitus outpatients

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Association between patient characteristics and EQ-5D-based utility measures in Indonesian type 2 diabetes mellitus outpatients

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HIGHLIGHTS

What is already known about the topic?

EQ-5D index scores for T2DM have been estimated for some countries in Southeast Asia. In Indonesia, no previous studies have been done to measure generic HRQoL values such as EQ-5D index scores in T2DM outpatients yet.

What does the paper add to existing knowledge?

This is the first population-based study in Indonesian T2DM outpatients providing EQ-5D index scores. These scores can subsequently be used to explore health economics of interventions in T2DM.

What insights does the paper provide for informing health care-related decision making?

Our paper may inform the health utility scores of T2DM in Indonesia which is needed for the health economics analysis purposes. Furthermore, results suggest the urge to implement the specific attention to T2DM patients who are housewives and those who have lower level of education, since the mentioned groups reported lower utilities than other groups in the population.

ABSTRACT

Objectives

To analyse and present EQ-5D index scores for T2DM outpatients based on socio-demographic characteristics and clinical condition.

Methods

Nine hundred and seven participants living in the Java and Sulawesi regions completed the five-level Indonesian version of the EQ-5D instrument (EQ-5D-5L). Socio-demographic data were collected by interviewing the participants, while the clinical data were obtained from the GP or consulting resident of internal medicine, and self-reported data. The participants originated from five primary care facilities, three public hospitals, and one private hospital. Ordinal regression analysis was conducted with the quintiles of the EQ-5D index scores as the dependent variable

to investigate the multivariate association between EQ-5D scores and the participants' socio-demographic characteristics and clinical condition.

Results

The mean age of the participants was 59.32 ± 9.7 years, and 57% were female. The overall EQ-5D index score was 0.77 (0.75–0.79). Males had a better EQ-5D index score compared with females, and the highest percentage of self-reported problems was in the pain/discomfort dimension (60.7%). Five factors were identified in the multivariate model as being independently associated with lower EQ-5D index scores: (i) treatment in secondary care, (ii) lower educational level, (iii) dependency on caregivers, (iv) not undergoing T2DM therapy, and (v) being a housewife.

Conclusion

This study provides estimates of EQ-5D index scores that can be used in health economic evaluations. We recommend to develop a specific approach targeting housewives living with T2DM and T2DM patients with lower levels of education, given their relatively low EQ-5D scores.

Keywords

EQ-5D-5L, Index scores, Type 2 diabetes mellitus, Health-related quality of life, Indonesia.

INTRODUCTION

The World Health Organization (WHO) has estimated that type 2 diabetes mellitus (T2DM) will be the seventh leading cause of death in 2030 [1]. Furthermore, the U.S. Centers for Disease Control and Prevention (CDC) estimated that the mortality in T2DM patients is twice as high as in people of similar age without T2DM [2]. In Indonesia, the number of T2DM patients has increased rapidly, not only in urban but also in rural areas [3], which makes Indonesia one of the countries with the most T2DM cases in the world. In 2011, the International Diabetes Federation (IDF) reported that there were 7.3 million T2DM patients living in Indonesia [4] and this number increased to 10.3 million in 2017 [5].

The Ministry of Health of the Republic Indonesia reported, based on the comparison of T2DM data in 2007 and 2013, that new T2DM cases had doubled from 1.1% to 2.1% [3]. Recently, new cases were found in the younger age group (15-24 years) and relatively more females than males were living with T2DM. As for level of education, the highest percentage of T2DM was found in those who never attended school at 10.4% compared to those with a university degree at 5.9% [3]. With regard to clinical condition, 60% of T2DM patients in Indonesia have at least one T2DM-related complication, with kidney neuropathy and retinopathy being the most common complications [6,7].

T2DM is a serious and complex chronic disease which significantly affects the daily lives of the patients, their families and the general population in terms of premature mortality, health care expenditures, and lower health-related quality of life (HRQoL) [5]. Early treatment has been shown effective to lower the aforementioned burdens as well as T2DM-related complications [8]. End-stage-T2DM-related complications are

related to higher healthcare expenditures and lower HRQoL as compared to those without complications [5]. Well-structured management strategies for T2DM are warranted and interpretation and evaluation of HRQoL can help to evaluate such strategies. As the portfolio of strategies is broad and may comprise various target groups (those with advanced T2DM, those with comorbidities, those with high dependency on the caregiver, etcetera), detailed estimation for subgroups is therefore needed.

To our knowledge, no studies have done to measure generic HRQoL values such as the EuroQoL-5D (EQ-5D) index scores in T2DM outpatients in Indonesia. Therefore, the aim of this study was to present generic EQ-5D index scores based on socio-demographic characteristics and clinical condition and to subsequently investigate the multivariate association between those variables. Since only the 5-level version (EQ-5D-5L) has a value set based on the Indonesian general population [9], we specifically used the EQ-5D-5L instrument in this study. We focused on two major regions in Indonesia, namely Java and Sulawesi. Java is the island with the largest population in Indonesia while Sulawesi has the highest incidence of T2DM over the whole country [3].

METHODS

Study design and setting

A cross-sectional study was carried out in Java and Sulawesi from November 2015 to October 2017 in T2DM outpatients in primary and secondary care settings. The study was approved by the Medical Ethics Committee of Universitas Gadjah Mada in Yogyakarta (KE/FK/1188/EC, 12 November 2014, amended 16 March 2015), and the Ethics Committee of Ahmad Dahlan University in Yogyakarta (011703028, 4 April 2017).

Java region

In the primary care setting, surveys and data collection were conducted in three family doctor clinics in Yogyakarta and a T2DM outpatient community in Surakarta (Central Java). In the secondary care setting, RSUD Dr Moewardi Hospital in Surakarta and Rumah Sehat Terpadu Dompot Dhuafa Hospital in Bogor (West Java) were chosen as the study sites.

Sulawesi region

Data collection was carried out at the Amirah clinic in Luwuk, Banggai (Central Sulawesi) as the study site for the primary care setting. We selected RS Akademis Jaury Hospital in Makassar (South Sulawesi) as our secondary care site.

Participants

Patients were included in the study if they were diagnosed with T2DM by a consulting resident of internal medicine, had a minimum age of 18 years, and were willing to sign the informed consent form. For participants who were illiterate or had other difficulties with reading the form, the consent was given by the caregiver who would also further assist the participant during the subsequent data collection process.

Instrument

The EQ-5D-5L is a generic HRQoL instrument that consists of two pages [10]. The first page is the EQ-5D classification consisting of a descriptive system that comprises five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has five levels: no problems, slight problems, moderate problems, severe problems, and unable/extreme problems. A single digit expresses the level selected for that specific dimension. Therefore, the five-digit number for five dimensions describes a specific health state. For

example, '11111' indicates 'no problems in any of the five dimensions,' while '21134' indicates slight problems in the mobility dimension, no problems in the self-care and usual activities dimensions, moderate problems in the pain/discomfort dimension, and severe problems in the anxiety/depression dimension. Each EQ-5D health state is then mapped to a single index score based on the preference of the relevant general population; i.e. the Indonesian value set in this case [9,11]. For instance, the health state of '11111' corresponds to the maximum EQ-5D index score of 1.00, and '21134' leads to a score of 0.56. The second page of the instrument comprises the visual analogue scale, labelled EQ-VAS. This thermometer-like scale (ranging from 0 to 100) reflects the patient's health in general, representing a more integral measure than the EQ-5D index scores [11]. Also, the EQ-VAS represents the patient perspective whereas the EQ-5D index score, since it uses population preferences, reflects the societal perspective. The participants were asked to rate their own health, where zero indicates the worst imaginable health-state, and 100 indicates the best imaginable health state.

Data collection procedure and data sources

To ensure a smooth process of distributing the EQ-5D-5L instrument to the participants, the researcher asked the general practitioners (GPs) and consulting residents of internal medicine who were responsible for the participants to assist by providing information about ethics, the objective of the research and the importance of participating. Notably, it was hypothesized that participants would be more cooperative in completing the instrument when it was introduced by the treating physician. The process of distributing the instrument took place in the outpatients' waiting rooms in the primary

and secondary care settings concerned. Also, some instruments were distributed when the participants joined the morning exercise in the T2DM community. During the data collection process, most of the elderly participants had to be assisted when they filled in the instrument. Moreover, they often asked for further information on how to differentiate each level in each dimension.

Socio-demographic data such as gender, age, T2DM duration, occupation, level of education, and dependence on a caregiver were obtained from self-reporting. We classified the participants into two age categories based on the retirement age of Indonesian people (56 years): productive age (below 56 years) and retirement age (56 years and above). As for employment status, participants were defined as unemployed if they reported not having a job, and in active employment when they were still actively working. Those whose main responsibilities were for the family members and household chores were classified as housewives.

Data on the clinical condition such as the type of therapy, T2DM-related complications, and comorbidities were obtained from the GPs or consulting residents of internal medicine. Self-reported data from participants was used in the cases data collection through GPs or residents of internal medicine could not be obtained. In the study, participants were defined as having comorbidities if they suffered comorbidities such as cancer, tuberculosis, gastritis, hepatitis, low back pain, urinary tract infections, and tumors. Also, participants with comorbidities and T2DM-related complications were considered as a separate group to be analyzed specifically.

Statistical Analysis

EQ-5D index scores were calculated using the Indonesian value set [9]. Descriptive statistics were computed to compare

EQ-5D index scores among different sub-groups based on sociodemographic characteristics and clinical condition; both means and 95% confidence intervals (CIs) were calculated. Univariate associations between the EQ-5D index score and various participants' characteristics were subsequently tested by Chi-square tests. Next, a multivariate ordinal regression analysis was conducted to explore how this score was associated with the socio-demographic characteristics and the clinical condition. As a dependent variable in this analysis we used the quintiles of the EQ-5D index score. Unlike being categorical variables in the univariate analysis, the T2DM duration, age, fasting blood glucose (FBG), and postprandial blood glucose were entered into the model as continuous variables after comparing the corresponding goodness-of-fit of the regression models. The existence of multicollinearity in our regression model was assessed by the variance inflation factor (a value > 10 indicates multicollinearity). Missing values on T2DM duration, FBG, and postprandial blood glucose were dealt with using multiple imputations [12]. Considering the percentage of missing measurements, 25 imputed datasets were obtained for each measurement. The completed measures were then computed by taking the average values generated from each imputed dataset. When setting up the regression, the independent variables 'gender' and 'T2DM duration' were found to not meet the proportional odds assumption [13] when using the quintile EQ-5D index score. To relax this assumption in the regression model, the effects of these two variables were allowed to be varied across the intervals of the utility score (quintile 1 and 2, quintile 2 and 3, quintile 3 and 4, and quintile 4 and 5). The descriptive statistics with the corresponding tests were performed using IBM SPSS Statistics for Windows, version 25 (SPSS Inc., Cambridge, MA). The ordinal regression model

Table 1. Distribution of participants within different subgroups over reporting problems (slight to extreme problems) on the EQ-5D dimensions

Characteristics	N(%)	Mobility % reporting problems	Self-care % reporting problems	Usual activities % reporting problems	Pain/discomfort % reporting problems	Anxiety/depression % reporting problems	p-value	p-value	p-value
Total respondents	907 (100)	37.4	12.2	23.4	60.7	34.4			
Socio-demographic characteristics									
Region									
Java	499 (55)	37.9	12.6	23.4	57.3	35.5	.760	.020	.482
Sulawesi	408 (45)	36.8	11.8	23.3	65.0	33.1			
Sex									
Male	387 (43)	33.9	10.6	22.0	58.4	31.0	.219	.217	.066
Female	520 (57)	40.0	13.5	24.4	62.5	36.9			
Age (59.32±9.70)									
Productive age (<56 years)	886 (98)	31.5	12.1	24.9	61.2	42.9	1.000	.770	.000
Retirement age (≥56 years)	289 (32)	40.2	12.1	22.4	60.0	30.3			
597 (66)									
Occupation									
Active employment	314 (35)	30.3	8.3	19.4	58.9	32.8	.003	.049	.001
Unemployed	234 (26)	35.9	10.7	18.8	56.0	26.5			
Housewife	359 (39)	44.6	16.7	29.8	65.5	40.9			
Education									
Up to senior high school	698 (77)	41.4	14.8	26.9	64.6	36.7	.000	.000	.008
University degree	209 (23)	23.9	3.8	11.5	47.8	26.8			
Level of health facilities									
Primary care	133 (15)	19.5	3.0	8.3	39.8	40.6	.000	.000	.114
Secondary care	774 (85)	40.4	13.8	26.0	64.3	33.3			
Dependency on a caregiver									
Yes	488 (54)	44.3	15.0	26.8	64.1	36.7	.000	.025	.123
No	419 (46)	29.4	9.1	19.3	56.8	31.7			

Characteristics	N(%)	Mobility		Self-care		Usual activities		Pain/discomfort		Anxiety/depression	
		% reporting problems	p-value	% reporting problems	p-value	% reporting problems	p-value	% reporting problems	p-value	% reporting problems	p-value
Clinical condition											
T2DM duration	805 (89)										
Less than five years	446 (49)	38.1	.219	14.6	.300	28.9	.005	63.0	.713	35.7	.295
More than five years	359 (40)	42.6		12.0		20.3		64.3		32.0	
Therapy											
None (diet, herbal or exercise)	49 (5)	46.9	.000	26.5	.001	40.8	.000	59.2	.037	44.9	.086
OAD (mono and combinations)	490 (55)	31.6		9.6		19.2		57.1		31.6	
Insulin (mono and combination with OAD)	368 (40)	43.8		13.9		26.6		65.8		36.7	
Types of complications and comorbidities											
Complications											
None	269 (30)	32.7	.103	8.2	.002	14.1	.000	57.2	.305	32.7	.152
Macrovascular	290 (32)	38.3		10.6		22.9		58.9		33.2	
Microvascular	140 (15)	35.7		11.4		21.4		64.3		29.3	
Macro and microvascular	30 (3)	46.7		23.3		43.8		56.3		34.4	
Comorbidities	86 (10)	36.0		19.8		36.0		68.6		44.2	
Comorbidities + T2DM complications	92 (10)	48.9		22.0		36.4		67.0		42.0	
Number of T2DM? complications											
None	269 (30)	32.7	.012	8.2	.0323	14.1	.004	57.2	.622	32.7	.462
1 T2DM complication	341 (37)	34.5		11.1		22.2		60.8		30.7	
2 or more T2DM complications	119 (13)	47.9		12.4		28.9		57.9		37.2	
Blood glucose level											
Random blood glucose	147 (16)										
≤200 mg/dl	73 (8)	23.1	.562	8.8	.437	20	.446	37.4	.609	22.4	.283
>200 mg/dl	74 (8)	25.9		11.6		23.1		36.1		27.2	
Fasting blood glucose	685 (76)										
≤126 mg/dl	265 (30)	14.7	.807	4.2	.205	8.2	.245	22.8	.137	10.4	.029
>126 mg/dl	420 (46)	23.9		8.8		15.3		39.6		21.3	
Postprandial blood glucose	570 (63)										
≤200 mg/dl	309 (34)	18.1	.047	4.2	.020	9.5	.023	31.8	.258	15.1	.129
>200 mg/dl	261 (29)	18.9		6.3		11.6		28.9		15.4	

Note: p value: Chi-square

Table 2. Mean (95% CI) EQ-5D index score according to socio-demographic characteristics and clinical condition in Indonesian T2DM outpatients using the Indonesian EQ-5D-5L tariff (n = 907).

Characteristics	N (%)	EQ-5D index score (95% CI)	p-value
Overall study participants	907 (100)	0.77 (0.75 - 0.79)	
Socio-demographic characteristics			
Region			
Java	499 (55)	0.78 (0.75 - 0.80)	.357
Sulawesi	408 (45)	0.76 (0.73 - 0.79)	
Sex			
Male	387 (43)	0.79 (0.75 - 0.81)	.026
Female	520 (57)	0.76 (0.73 - 0.78)	
Age (59.32± 9.70)	886 (98)		
Productive age (<56 years)	289 (32)	0.77 (0.73 - 0.80)	.925
Retirement age (≥56 years)	597 (66)	0.77 (0.75 - 0.80)	
Occupation			
Active employment	314 (35)	0.81 (0.78 - 0.84)	.000
Unemployed	234 (26)	0.79 (0.75 - 0.82)	
Housewife	359 (39)	0.72 (0.69 - .075)	
Education			
Up to senior high school	698 (77)	0.74 (0.72 - 0.76)	.000
University degree	209 (23)	0.86 (0.83 - 0.89)	
Level of health facilities			
Primary care	133 (15)	0.90 (0.87 - 0.92)	.000
Secondary care	774 (85)	0.74 (0.73 - 0.77)	
Dependence on a caregiver			
Yes	488 (54)	0.72 (0.69 - 0.75)	.000
No	419 (46)	0.83 (0.81 - 0.85)	
Clinical condition			
T2DM duration ^a	805 (89)		
Less than five years	446 (49)	0.76 (0.74 - 0.79)	.576
More than five years	359 (40)	0.74 (0.71 - 0.77)	
Therapy			
None (diet, herbal or exercise) ^b	49 (5)	0.61 (0.47 - 0.76)	.000
OAD (mono and combinations)	490 (55)	0.81 (0.79 - 0.83)	
Insulin (mono and combination with OAD)	368 (40)	0.74 (0.71 - 0.77)	
Types of complications and comorbidities			
Complications			
None	269 (30)	0.80 (0.76 - 0.83)	.036
Macrovascular	290 (32)	0.79 (0.72 - 0.82)	
Microvascular	140 (15)	0.77 (0.72 - 0.82)	
Macro and microvascular	30 (3)	0.69 (0.56 - 0.80)	
Comorbidities	86 (10)	0.71 (0.65 - 0.78)	
Comorbidities + T2DM complication(s)	92 (10)	0.70 (0.63 - 0.76)	
Number of T2DM? complications			
None	269 (30)	0.80 (0.76 - 0.83)	.092
1 T2DM complication	341 (37)	0.79 (0.76 - 0.81)	
2 or more T2DM complications	119 (13)	0.74 (0.69 - 0.80)	

Characteristics	N (%)	EQ-5D index score (95% CI)	p-value
Blood glucose level			
Random blood glucose	147 (16)		
<200 mg/dl	73 (8)	0.70 (0.62 – 0.76)	.308
>200 mg/dl	74 (8)	0.63 (0.54 – 0.71)	
Fasting blood glucose	685 (76)		
<126 mg/dl	265 (30)	0.79 (0.75 – 0.82)	.121
>126 mg/dl	420 (46)	0.75 (0.72 – 0.78)	
Post prandial blood glucose	570 (63)		
<200 mg/dl	309 (34)	0.81 (0.78 – 0.84)	.014
>200 mg/dl	261 (29)	0.76 (0.73 – 0.79)	

Note: p value: Mann-Whitney and Kruskal-Wallis test; ^a 11% of respondents did not know the duration of their T2DM; ^b Five participants reported the reason for not taking metformin was because they had experienced the side effects such as dizziness and nausea. Besides that, five participants with normal blood sugar levels but abnormal blood pressure levels requested that they only be given antihypertensive medication because they felt scared if they consumed medicine if it consisted of too many pills (more than three pills); ^c Comorbidities were defined as diseases other than T2DM complications, such as cancer, tuberculosis, gastritis, low back pain, urinary tract infections, and tumors

was built using R (R Foundation for Statistical Computing, software version 3.4.0, Vienna, Austria). A statistically significant association was defined as having two-tailed *p*-value of < .05.

RESULTS

Characteristics of the participants

The socio-demographic characteristics and clinical condition of the participants are shown in Table 1. In total, there were 907 participants (mean age 59.3±9.7 years) included in our study, 57% were female and about 69% of female participants reported that they were housewives. Of the 359 housewives, 60% were 56 years or older and 4% had a university degree. Almost 55% of male participants were still actively working, either for the government, a company or self-employed. In this study, almost 80% of participants had a lower educational level and 66% of participants had already retired. More than 50% of the participants were accompanied by a caregiver and the majority of caregivers comprised of spouses or children.

With regard to clinical condition, almost 50% of participants had been diagnosed

with T2DM in the last five years and nearly 60% were on oral anti-diabetic (OAD) therapy. In addition, 40% of participants used insulin therapy and this was relatively more prevalent among participants in secondary care settings. In this study, 30% of participants did not report any complications and 10% of participants reported comorbidities.

EQ-5D dimensions affected by T2DM

In total, 60.7% of participants reported problems (i.e. level 2, slight problems to level 5, unable/extreme problems) with regard to pain/discomfort and this was found to be the highest proportion among all five dimensions (Table 1). Housewives (compared to active employment and unemployed) and those with lower education (compared to university degree participants) reported a higher percentage of the presence of problems on all dimensions. Participants treated in secondary care (compared to those who were treated in primary care) and participants accompanied by a caregiver (compared to participants who came alone) reported a higher percentage of problems on all dimensions except for anxiety/depression. Retired participants reported a higher percentage of problems in mobility than those

who were still productive, but this was the other way around for the anxiety/depression dimension. Participants on the island of Sulawesi reported a higher percentage of problems in pain/discomfort than those who lived on Java, but no significant differences were found in the other four dimensions.

With regard to clinical condition, the majority of participants on insulin therapy reported problems on the pain/discomfort dimension. In addition, participants with macrovascular and microvascular complications and those with T2DM-related complications and comorbidities reported experiencing problems on the self-care and usual activities dimensions. Moreover, a higher number of T2DM-related complications seemed to be associated with more problems on the mobility and usual activities dimensions. Of the 570 participants who had a post-prandial blood glucose test, participants with blood glucose of >200 mg/dL also reported problems on the mobility, self-care, and usual activities dimensions.

Univariate association between EQ-5D index scores and the participant characteristics

The average EQ-5D index score in Indonesian T2DM outpatients was 0.77 (95% CI: 0.75–0.79), and male participants had a higher EQ-5D index score compared to female participants (Table 2). Based on occupation, housewives had the lowest EQ-5D index score compared to actively employed and unemployed participants. Participants treated in secondary care and those with a lower level of education had a lower EQ-5D index score compared to those in primary care and with higher education respectively. Furthermore, we also found that participants who were accompanied by a caregiver during a visit to a health facility indicated lower EQ-5D index scores compared with participants who came alone.

With regard to clinical condition, the EQ-5D index scores in participants with OADs (mono or combination therapy) were higher than those on insulin therapy or those not undergoing therapy. Furthermore, participants with T2DM-related complications or comorbidities reported lower EQ-5D index scores than those without complications or comorbidities. In addition, participants with controlled blood sugar reported a higher EQ-5D index score compared to those who had uncontrolled blood sugar.

Multivariate association between EQ-5D index scores and the participant characteristics

Table 3 presents the results of the multivariate ordinal regression model. No multicollinearity was detected in the model. Several characteristics of the participants were shown to significantly influence the EQ-5D index score, mostly in line with the results of the univariate analysis presented above. Participants in secondary care had a lower EQ-5D index score compared to those in primary care. Again, higher education contributed to a significantly better HRQoL for the participants in our study. A caregiver accompanying the participant was shown to be negatively associated with HRQoL. In addition, housewives had a lower EQ-5D index score compared to active employees. The variables with regard to clinical condition were all shown to not significantly influence the index score except for the treatment using monotherapy and combinations of OADs. Not surprisingly, participants having treatment using OADs had a two-fold EQ-5D index score compared to those who were not treated using OADs.

DISCUSSION

This is the first population-based study that reported EQ-5D index scores based

Table 3. Association between socio-demographic characteristics, clinical condition and EQ-5D index scores using a multivariate ordinal regression model (n = 886)

Variables	Coefficient (95% CI)	p-value
Socio-demographic characteristics		
From Sulawesi (vs from Java)	0.882 (0.680~1.144)	.344
Secondary care (vs primary care)	0.322 (0.226~0.484)	<.001
Age (productive vs retired)	0.794 (0.597~1.055)	.113
University degree (vs high school)	1.831 (1.327~2.534)	<.001
With caregiver (vs no caregiver)	0.651 (0.505~0.837)	<.001
Retired (vs active employee)	0.858 (0.609~1.209)	.382
Housewife (vs active employee)	0.619 (0.422~0.906)	.014
Female (vs male)	0.963 (0.619~1.497) [quintile 1 and 2]	.886
	0.966 (0.659~1.415) [quintile 2 and 3]	.858
	1.437 (0.979~2.111) [quintile 3 to 5]	.064
Clinical condition (vs no complications/comorbidities)		
One complication	1.089 (0.803~1.477)	.585
Two or more complications	0.739 (0.494~1.107)	.142
Comorbidities	0.733 (0.458~1.174)	.196
Complications and comorbidities	0.706 (0.446~1.117)	.137
Oral antidiabetic (vs none)		
Insulin (vs none)	2.181 (1.223~3.891)	.008
	1.552 (0.856~2.815)	.147
Fasting blood glucose (n=685)		
(≤126 md/dL vs >126 mg/dL)	0.999 (0.996~1.002)	.397
Postprandial blood glucose (n=570)		
(≤200 md/dL vs >200 mg/dL)	0.998 (0.995~1.000)	.074
T2DM duration (less vs more than 5 years)		
	1.004 (0.979~1.030) [quintile 1 and 2]	.730
	0.993 (0.972~1.014) [quintile 2 and 3]	.505
	0.981 (0.958~1.006) [quintile 3 to 5]	.132

on socio-demographic characteristics and clinical conditions in Indonesian T2DM outpatients. We found five factors that independently associated with lower EQ-5D index scores in our multivariate model: treatment in secondary care, lower educational level, dependency on caregivers, occupation as a housewife and not undergoing T2DM therapy. The mean EQ-5D index score in Indonesian T2DM outpatients in this study was estimated at 0.77 (95% CI: 0.75-0.79).

Our main finding: i.e. mean EQ-5D index score of 0.77, is lower than T2DM outpatients' EQ-5D index scores in East China and Korea of 0.94 and 0.92, respectively [14,15]. A possible explanation for this might be the difference in the participants' characteristics, with almost all of our participants already on OAD therapy (5% had stopped due to side effects of pill overload) whereas 30-40% of T2DM patients

in the Chinese and Korean studies were on the non-pharmacologic treatment, such as diet and exercise only, which could imply these studies included patients with less severe disease. Furthermore, there was also a relatively high proportion of male participants in the Korean study and slightly higher percentages of participants with a higher level of education in both other studies. A previous study reported that the variation of EQ-5D index scores was due to the higher number of male participants and the clinical condition of the T2DM patients [16]. Yet, our estimate is in line with what was previously found in a meta-analysis on EQ-5D in mostly T2DM patients at 0.76 (95% CI: 0.75-0.77) [16]. Notably, the meta-analysis comprised populations from various backgrounds, including high, middle and low income countries as well as various stages of disease in DM,

hampering a straightforward comparison with our study.

The EQ-5D dimension with the highest percentage of participants reporting problems was pain/discomfort. This is fully in line with a report on the Indonesian general population [9] and studies on T2DM patients in other Asian countries [17,18]. Also, our finding that the EQ-5D index score in female participants was lower than in males seems to be consistent with previous studies in similar participants [14,15,17,18]. A possible explanation for this might be that female participants are more likely to report anxiety/depression problems as they have been reported to have more diabetes-related worries, less satisfied with treatment regimens, and less ability to cope with their disease [19,20]. However, when we controlled for socio-demographic characteristics and clinical conditions in the multivariate ordinal regression model, the difference between males and females was no longer significant. This may be due to the fact that 69% of the females were housewives (with 96% with lower education) and being a housewife was already independently associated with a lower EQ-5D index score. It could be argued that for Indonesian housewives who have the responsibility for taking care of the family members and household chores, having a chronic illness such as T2DM presents an extra burden in fulfilling these tasks. Percentages in this subgroup reporting problems on all of the EQ-5D dimensions indeed confirmed this being significantly higher than in the other subgroups of actively employed and unemployed.

Our findings showed that higher educational levels lead to higher HRQoL, which was similar to findings from studies in other countries, such as in Korea, Japan and Iran [14,17,18]. It could be argued that participants with a higher level of education might

have better understanding on the T2DM therapy and the impact of T2DM-related complications and therefore have a more conscientious attitude towards their therapy [15].

Participants who were treated in secondary care were found to have lower HRQoL than those who were treated in primary care. This seems reasonable since worse cases are generally referred from the primary to secondary healthcare facilities with higher severity of T2DM. Similar explanations could be given for findings on lower index scores of participants needing help from their caregivers compared to those who did not need such help: a worse condition likely involves more need for help as well as being associated with a lower HRQoL.

Some limitations of this study have to be acknowledged. Firstly, we collected data only on two major islands of Indonesia, namely Java and Sulawesi. Representativeness of the study sample for the whole of Indonesia can obviously not be straightforwardly claimed. Yet, given our choice for the most densely populated central island (Java) and a more remote area (Sulawesi), we did include a spectrum in our sample covering some national variety and some representativeness may definitely exist. Secondly, there were 21 participants that had missing information on their date of birth for privacy reasons. As these 21 participants only constitute a minor part (2%) of the total sample, and also because age was not found to be associated with EQ-5D index scores it is unlikely this has had a profound influence on our results.

CONCLUSION

This study provides estimates of EQ-5D index scores that can be used in health economic evaluations. Five factors were found in our multivariate model to be independently

associated with lower EQ-5D index scores: treatment in secondary care, lower educational level, dependency on caregivers, occupation as a housewife and not undergoing T2DM therapy.

RECOMMENDATION

We recommend the development of a specific approach targeting housewives living with T2DM and T2DM patients with lower levels of education. Given their decrease in HRQoL compared to the average T2DM outpatients in this study, there is urgent need for improvement. Such health promotions could be integrated with existing health programmes, such as Prolanis BPJS/Badan Penyelenggara Jaminan Sosial, a targeted diabetes program run by the social security administrative agency.

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AUTHOR CONTRIBUTIONS

BA, FDP, TvA, QC, PK, and MJP were involved in the conceptualization and the design of the study. BA and DAP carried out the data collection. BA and QC conducted the analyses, and TvA, PK, and MJP were the main consultants in the data analyses. All the authors commented on the final analysis. BA and LI drafted the manuscript, and all the authors revised it. All the authors read and approved the final manuscript.

COMPETING INTERESTS

MJP reports grants and honoraria from various pharmaceutical companies, inclusive those developing, producing and marketing diabetes drug. However, all grants and honoraria were fully unrelated to this specific study. The other authors declare that they have no competing interests related to this specific study and topic.

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