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ORIGINAL RESEARCH ARTICLE

Does Diabetes Have an Impact on Health-State Utility? A Study of Asians in Singapore

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Abstract

Objective Our objective was to compare the time trade-off (TTO) values of EQ-5D-3L health states elicited from Singaporeans with and without type 2 diabetes mellitus (T2DM) and T2DM patients with and without complications.

Methods The TTO values of ten EQ-5D-3L health states were elicited from a consecutive sample of T2DM patients and a general Singaporean population sample using similar valuation protocols. In face-to-face interviews, T2DM patients and members of the general population were asked to value five and ten health states, respectively. The difference in TTO values between the two samples and between T2DM patients with and without complications was examined using multiple linear regression models.

Results A total of 109 T2DM patients and 46 individuals without T2DM provided data. All ten health states considered, the mean TTO value was −0.02 for the general population sample and −0.04 for T2DM patients, with the unadjusted and adjusted difference being −0.06 (95 % confidence interval [CI] −0.16, 0.03) and 0.02 (95 % CI −0.12, 0.15). The general population sample had systematically lower TTO values for mild health states, with the adjusted difference being −0.13 (95 % CI −0.25, −0.02); while the two samples had similar TTO values for severe health states, with the adjusted difference being 0.02 (95 % CI −0.16, 0.19). T2DM patients without complications had systematically lower TTO values than those with complications, with the adjusted difference being −0.10 (95 % CI −0.23, 0.03).

Conclusions It appears that diabetes and its complications affect patients' valuation of health states. Hence, the EQ-5D-3L health-state values based on the general population may underestimate the utility of health interventions for T2DM.

Key Points for Decision Makers

Diabetic patients tend to consider mild EQ-5D-3L health states more desirable than do members of the general population, although they rate severe health states similarly. As a result, the disutility of mild EQ-5D-3L health problems is lower to diabetic patients than to the general population.

Diabetic patients with complications appear to value both mild and severe EQ-5D-3L health problems as less undesirable than those without complications.

The use of EQ-5D-3L health-state values elicited from the general population may underestimate the effectiveness of health interventions for diabetes.

1 Introduction

Health-state utility values used to estimate quality-adjusted life-years (QALYs) in economic evaluations of

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health technologies are usually elicited from general or patient populations. While there seems to be a consensus that patients should be the source of utility values in the context of clinical decision making [1–3], whose values should be used in analysis intended to inform allocation of societal health resources has long been debated [4–9]. The main argument for using the values elicited from the general population is that members of the general population are the actual payers and potential users of health technologies and services. On the other hand, some researchers, such as Gandjour [9], argued that only utility values from patients have a theoretical foundation in the preference-utilitarian theory and welfare economics. The issue of whose values to use is conditional on the assumption that the health-state preferences of the general population and patient populations differ. Some studies have supported this assumption [10–13]. For example, it was found that the value of colostomy is much higher to patients who live with a stoma than to those who have not undergone colostomies [11]. Also, a meta-analysis suggested that patients gave higher health-state valuations than members of the general public when the time trade-off (TTO) or visual analog scale (VAS) were used [12]. The difference in health-state valuations could be due to the general public's focus illusion and patients' adaptation [14]. However, some other studies [15–18], including a meta-analysis [18], found no or minimal difference in health-state utility elicited from general and patient populations, suggesting that the source of utility values may not be crucial.

The question of whether healthy and unhealthy individuals have similar health preferences has important implications for the application of the EQ-5D-3L, a standardized preference-based instrument [19]. The EQ-5D-3L is designed for determining the utility or benefit of health technologies with a health-state descriptive system and a utility function. The utility function generates values for a total of 243 EQ-5D-3L health states. The values are estimated based on the general population's preferences for a subset of the hypothetical EQ-5D-3L health states elicited using the TTO or VAS method [20]. While the EQ-5D-3L has been widely used in economic evaluations for reimbursement decision making, the appropriateness of using the EQ-5D-3L values estimated based on the general public's heath preferences in clinical decision making is debatable. Studies comparing the values of the hypothetical EQ-5D-3L health states with healthy and unhealthy individuals showed mixed results. Pickard et al. [15] found that individuals with and without self-reported chronic conditions gave similar values using the TTO method; Suarez-Almazor and Conner-Spady [21] found that values elicited from patients with rheumatoid arthritis and the general population were similar when the TTO method was used but the values elicited using the VAS method were different; others found that patients and the general population had significantly different utility values for EQ-5D-3L health states [22–26].

The primary aim of our study was to compare the TTO values of hypothetical EQ-5D-3L health states directly elicited from patients with type 2 diabetes mellitus (T2DM) and the general population to determine whether the values differed, and if so, how they differed. The secondary aim was to explore whether the severity of T2DM impacts on health-state values.

2 Methods

2.1 Study Participants

The current study was approved by the institutional review board of the National Healthcare Group of Singapore. In the study, consecutive outpatients with T2DM were approached and enrolled from the diabetes clinic of a tertiary hospital in Singapore (an urban-state with a population of over 5 million in South-East Asia) from May to December 2012. The inclusion criteria were (1) a diagnosis of T2DM; (2) Singapore citizens/Singapore permanent residents aged 21 years or above; (3) ability to read and converse in English. Consenting T2DM patients were interviewed by a trained interviewer for their preferences for five of ten selected EQ-5D-3L health states in the clinic after their routine consultations. The ten states were divided into two blocks of five states, and equal numbers of the participants were randomly assigned to value the two blocks. This arrangement was made because valuing all ten health states was found to be overly burdensome to T2DM patients. In a pilot study, five T2DM patients from the diabetes clinic were interviewed to assess potential difficulties in conducting the valuation interview in the busy clinic. Two of the five patients complained that the interview was too long when the patients were asked to value a total of ten health states.

A valuation study of the EQ-5D-3L health states in Singapore provided data from a general population sample. The sampling and recruitment procedures used were reported in detail elsewhere [27]. Briefly, a sample of non-institutionalized adult Singaporean residents were recruited and interviewed face-to-face in their homes by a trained interviewer. Each participant was asked to value a total of ten EQ-5D-3L health states. Participants who valued the same ten EQ-5D-3L health states as T2DM patients and who reported having no DM were included in the present study.

2.2 Survey Procedures

Similar interview protocols were used to survey T2DM patients and the general population study to measure the utilities of the EQ-5D-3L health states. The interview started with an example TTO task in which the interviewer demonstrated how the TTO tasks would be conducted using a time board and cards. Five states were presented to T2DM patients in a random order for valuation. T2DM patients' own health status and demographic characteristics were assessed after the TTO valuation tasks.

In TTO tasks, each state was valued using 11 questions each asking the participant's preference for two hypothetical lives: (a) living in the health state for 10 years and then die and (b) living in full health for x years and then die. The x values were integers ranging from 0 to 10, with one integer used in a different question. For each question, the response could be (a), (b), or equal preference (no preference). As previous studies found that TTO values are affected by the starting point of x values [28], two starting points, 0 and 10 years, were used in the valuation tasks in our study. For each health state, half of the T2DM patients started with a question asking them to compare 0 years of full health (i.e. immediate death) versus 10 years of life in the health state, and the length of full health in subsequent questions was increased to 10 years by a step of 1 year (i.e. the bottom-up sequence); the other half of the T2DM patients started with comparing 10 years of full heath versus 10 years of life in the health state, and then the length of full health was decreased to 0 years with a step of 1 years (i.e. the top-down sequence).

If a T2DM patient preferred (b) when the x value was 0 (i.e. immediate death), another 11 questions would be given to the respondents to state preferences, each question asking respondents' preference of two options: (a) living in full health for 10 years followed by 10 years in the health state and then die, and (b) living in full health for y years and then die. The y values were also integers ranging from 0 to 10 and the values varied from 10 to 0 in all interviews. A time board and health-state cards were used as visual aids to help respondents comprehend the different life scenarios.

Both T2DM patients and participants from the general population received a gift voucher worth $20 on completion of the survey.

2.3 Health States Valued

The health states valued in this study was defined by the EQ-5D-3L classification system which comprises five domains (i.e. mobility, self-care, usual activities, pain or discomfort, and anxiety or depression), with each domain having three functional levels: 'no problems' (level 1); 'some problems' (level 2); and 'extreme problems' (level 3). EQ-5D-3L health states can be expressed using a five-digit code, with each digit representing the functional level of one domain. For example, a state in which a person has no problems in mobility and self-care, moderate problems in usual activities, moderate pain or discomfort, and extreme anxiety or depression can be coded as 11223. In this study, three mild (11112, 21112, and 21122), four severe (11223, 23221, 21231, and 23211), and three very severe (23332, 32322, and 33333) health states were selected to represent various severities. These health states were divided into two blocks for T2DM patients: 11112, 21112, 21231, 23221, and 32322 in one block; and 21122, 11223, 23211, 23332, and 33333 in the other block.

2.4 Data Analysis

The TTO value for each health state was calculated for each participant who valued that health state. For health states considered as better than death, the TTO value was $x^*/10$, in which x^* is the x value at which equal preference was stated. If there were multiple x values, x^* was the mean of the values; if there was no value at which equal preference was stated, x^* was mean of the maximum value at which option (a) was preferred and the minimum value at which option (b) was preferred. For example, if option (a) is preferred at 0–5 years, and option (b) is preferred at 6 to 10 years, the TTO value of the health state would be $[(5 + 6)/2]/10 = 0.55$. Similarly, the TTO value of a health state considered as worse than death is given by $(y^* - 10)/10$. Poor data quality was considered if a T2DM patient (or a participant from the general population) rated all five (ten) health states as having the same value or worse than death. Data of poor quality were excluded from further analysis.

The primary objective of the study was to compare TTO values of EQ-5D-3L health states between T2DM patients and the general population. For this purpose, data collected from T2DM patients and the general population sample were pooled for analysis. The characteristics of the two samples were compared using Chi-square tests. Separate linear regression models were used to investigate the difference in TTO values of all health states, mild health states (i.e. 11112, 21112, and 21122), severe health states (i.e. 11223, 23221, 21231, 23211, 23332, 32322, and 33333), and each of the health states between T2DM patients and the general population sample. In all models, the TTO value was regressed on the source of the value (T2DM patients or general population) with and without the adjustment of other factors. The factors adjusted for included age, gender, race, and education. The characteristics of the health states were also adjusted in the three models using the TTO values for multiple health states (i.e.

all, mild, and severe health states). All independent variables were coded into dummy variables. For the health-state characteristics, five dummy variables were generated to specify the existence of any health problems in each of the five domains of a health state. Also, random effect (i.e. random intercept) was built into the three models using TTO values for multiple health states. This was because the multiple TTO values from individuals clustered within individuals and as a result the assumption of independence needed for ordinary least-square models was not fulfilled.

The secondary objective was to compare the TTO values between T2DM patients with and without complications. Two mutually exclusive subgroups (i.e. T2DM patients with and without complications) were compared. The statistical analysis performed was the same as that for comparing T2DM patients and the general population except that only data from T2DM patients were used, and accordingly the dummy variable was coded to indicate whether a patient had any diabetes-related complications in the regression models. Presence of complications was considered if a patient reported that he or she had any of the following conditions: diabetic retinopathy, neuropathy, dermopathy, heart disease, diabetic cerebrovascular disease, peripheral vascular disease, diabetic foot ulcer, and diabetic amputation.

All analyses were performed using SAS (version 9.2). The proc mixed procedure of SAS was used to fit the random effect models.

3 Results

A total of 120 T2DM patients were recruited and interviewed in the study. After excluding patients whose TTO values were either the same ($n = 2$) or negative for all the five health states they valued ($n = 9$), 109 T2DM patients

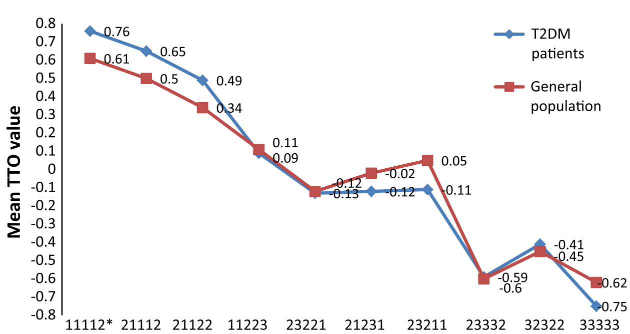

Fig. 1 Mean TTO values for each of the ten EQ-5D-3L health states elicited from T2DM patients and the general population. *The difference in TTO values between T2DM patients and the general population is statistically significant with adjustment of age, gender, education, and ethnicity. *TTO* time trade-off, *T2DM* type 2 diabetes mellitus

were used for comparison analysis. A total of 52 participants without DM in the general population study valued the same health states valued by the T2DM patients. After excluding four participants valuing all states as worse than death and two participants rating all ten states the same, 46 participants were included in the analysis. Compared with the general population, T2DM patients were more likely to be male, older, non-Chinese, and better educated (Table 1).

All ten health states considered, the mean TTO value was 0.04 and −0.02 for the T2DM patients and the general population sample, respectively ($p = 0.1643$). However, after adjusting for covariates, the TTO value for the T2DM patients was 0.02 point lower than the general population sample, which was neither statistically ($p = 0.6527$) nor clinically significant, assuming the minimally important differences in EQ-5D-3L is 0.074 [29]. With and without adjustment of other variables, the mean TTO value of the general population sample was significantly lower than that of T2DM patients for mild health states according to both statistical and clinical criterion. The unadjusted and adjusted mean difference (95 % confidence interval [CI]) between the general population sample and T2DM patients was −0.15 (−0.24, −0.06) and −0.13 (−0.25, −0.02), respectively. On the other hand, with and without adjustment, T2DM patients and the general population sample had similar mean TTO values for severe health states (Table 2).

The mean values of individual health states varied from −0.75 (for 33333) to 0.76 (for 11112) for T2DM patients and from −0.62 (for 33333) to 0.61 (for 11112) for the general population (Fig. 1), with the range being 1.51 and 1.23 for T2DM patients and the general population sample, respectively. With and without adjustment, T2DM patients had systematically higher TTO values for mild health states. On the other hand, there was no systematic difference in the mean values between T2DM patients and the general population sample for severe health states (Fig. 1).

The overall mean value was −0.02 for the patients without complications and 0.08 for the patients with complications ($p = 0.1273$). After adjusting for other variables, the mean difference (95 % CI) between the two groups was −0.10 (−0.22, 0.03), which was not a statistically but clinically significant difference. With and without adjustment, the mean TTO values of T2DM patients without complications was lower than that of T2DM patients with complications for both mild and severe health states (Table 3). The mean values for T2DM patients with complications were systematically higher than those for T2DM patients without complications, although most of the differences were not statistically significant with or without adjustment of other variables (Fig. 2).

Table 1 Characteristics of participants

	T2DM patients (*N* = 109)	General population (*N* = 46)	*p* value
Gender			0.0029
Male	62 (56.9)	23 (50.0)	
Female	47 (43.1)	23 (50.0)	
Age group (years)			<0.0001
21–60	71 (65.1)	35 (76.1)	
>60	38 (34.9)	11 (23.9)	
Education level			0.0007
Tertiary and higher	21 (19.3)	6 (13.0)	
Secondary school or lower	88 (80.7)	40 (87.0)	
Race			<0.0001
Chinese	54 (49.5)	28 (60.9)	
Non-Chinese	55 (50.5)	18 (39.1)	
H_bA_{1c} level (%)			
<6.5	16 (14.7)		
≥6.5	87 (85.3)		
Chronic conditions other than diabetes			
Lung disease	12 (11.0)	0 (0.0)	
Arthritis	19 (17.4)	3 (6.5)	
Depression/anxiety	15 (13.8)	2 (4.3)	
Cancer	10 (9.2)	1 (2.2)	
Musculoskeletal disease	10 (9.2)	0 (0.0)	
Others	15 (13.8)	4 (8.7)	
Diabetes-related complications			
Retinopathy	35 (32.1)		
Neuropathy	30 (27.5)		
Dermopathy	14 (12.8)		
Heart disease	27 (24.8)		
Cerebrovascular disease	17 (15.6)		
Peripheral vascular disease	20 (18.4)		
Foot ulcer	13 (11.9)		
Amputation	8 (7.3)		

Data are presented as *N* (%) unless otherwise indicated

HbA_{1c} glycated hemoglobin, *T2DM* type 2 diabetes mellitus

4 Discussion

We found that the values of EQ-5D-3L states with mild health problems to T2DM patients were higher than for the general population, although the EQ-5D-3L states with severe health problems values were similarly undesirable to these two populations and as a result there was no significant difference between the two populations when all EQ-5D-3L health states were considered. Overall similarities in TTO values of EQ-5D-3L health states between patient and general populations were also observed in two previous studies. Pickard et al. [15] found that chronic conditions including DM have a negligible impact on TTO valuation of EQ-5D-3L health states in the general US population; Suarez-Almazor and Conner-Spady [21] found that patients with rheumatoid arthritis and the general population have similar TTO values of two EQ-5D-3L health states. Also, our finding that T2DM patients rate mild health states better than do the general population is consistent with findings from three previous studies [23, 24, 26]; however, in those studies, patients also rated severe EQ-5D-3L states as better than did the general population, which is inconsistent with the finding about severe EQ-5D-3L health problems in our study. The relatively higher or similar EQ-5D-3L values of patients versus non-patients may be explained by the prospect theory, which assumes that health-state valuation is in a function of the rater's own health [30]. Essentially, individuals with differing health status would rate health states far better or worse than their own health similarly; however, they may rate health states not very different from their health levels differently. Specifically, health states falling between the health levels of two groups would be rated higher by those in lower levels of health but lower by those in higher levels of health. According to this theory, severe health states were rated similarly in our study because they were far worse than the health status of the study subjects; on the other hand, the mild health states were similar to the health status of the study subjects. It should be noted that the

Table 2 Time trade-off values of patients with type 2 diabetes mellitus and the general population

	T2DM patients	General population	Difference between T2DM patients and general population[a]	
	Mean (SD)	Mean (SD)	Unadjusted (95 % CI)	Adjusted (95 % CI)
All health states[b]	0.04 (0.74)	−0.02 (0.75)	−0.06 (−0.16, 0.03)	0.02 (−0.12, 0.15)
States without severe problems[b]	0.64 (0.31)	0.48 (0.50)	−0.15 (−0.24, −0.06)	−0.13 (−0.25, −0.02)
States with severe problems[b]	−0.24 (0.73)	−0.24 (0.71)	0.001 (−0.11, 0.11)	0.02 (−0.16, 0.19)

CI confidence interval, *SD* standard deviation, *T2DM* type 2 diabetes mellitus

[a] Reference group is T2DM patients

[b] Random effect linear regression model, in which age, gender, education, ethnicity, and the characteristics of the EQ-5D-3L health states are adjusted

prospect theory is not supported by some studies [31, 32]. The mixed results from the comparisons of patients and general populations may also be due to the different valuation methods (i.e. TTO and VAS) [33] or elicitation procedure (e.g. mode of administration, search procedures, the use of visual aids, etc.) [34] used in those studies. Therefore, more studies are necessary to investigate the repeatability of the findings of the present study. Also, it should be noted that the mean TTO values of EQ-5D-3L health states elicited from T2DM patients and the general population (i.e. 0.04 and −0.02) in our study were lower than those from other populations [15, 21–26]. This could be for two reasons. First, the negative TTO values in other studies were rescaled before analysis [15, 21–26], but the values in our study were not. Second, Singaporeans may truly consider poor health as more undesirable than do people in other countries [27].

Our results suggest that the utility gain associated with a transition from a severe health state to a mild health state would be greater to T2DM patients than to the general population. For example, according to our study, the utility gain from a transition between 23332 and 21122 would be 1.08 and 0.94 to T2DM patients and the general population, respectively. This means that a health intervention that can achieve such an improvement in health is more attractive to patients than to the general population. This implication of our results is consistent with some previous studies [35–38] but inconsistent with others [21–24]. This is not surprising, as the relative health-state values elicited from patients and the general population or non-patients differed and varied with the severity of the health states to be valued. Given these mixed findings, it might be worthwhile to determine the values of the EQ-5D health states described to patients with a certain condition. In the context of informing resource allocation decisions within a particular patient population, EQ-5D values based on patients' own preferences may be more advantageous than those based on the general public's preferences because the former would be more relevant and accurate. However, it should be noted that an EQ-5D value set based on preferences of patients with a particular condition would not be appropriate for use in analysis to inform society-wide resource allocation. In that context, the conventional EQ-5D value set based on the general public's preferences should be used.

It appears that T2DM patients with complications have systematically higher TTO values for EQ-5D-3L health states than T2DM patients without complications in our study. This could also be explained by the afore-mentioned prospect theory. To the best of our knowledge, this is the first study showing the association between disease severity and health-state valuation. Previous studies [15, 21–26] focused only on comparisons between patients and healthy subjects. However, this finding was from an analysis of a small sample of patients only and therefore should be confirmed in future studies using larger sample sizes.

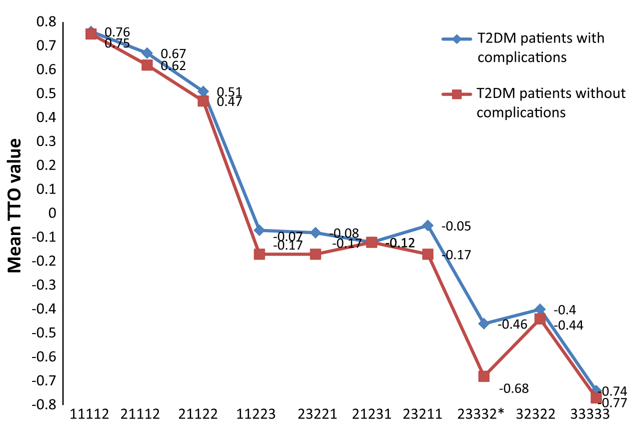

Fig. 2 Mean TTO values for each of the 10 EQ-5D-3L health states elicited from T2DM patients with and without complications. *The difference in TTO values between T2DM patients with and without complications is statistically significant with adjustment of age, gender, education, and ethnicity. *TTO* time trade-off, *T2DM* type 2 diabetes mellitus

Our study has two limitations. First, our sample size is relatively small and may not be representative of the target patient and general populations. Also, the small sample size allowed valuation of only a small number of the EQ-5D-3L health states, which means our results could have

Table 3 Time trade-off values of patients with type 2 diabetes mellitus with and without complications

	With complications ($N = 66$)	Without complications ($N = 43$)	Difference between T2DM patients with and without complications[a]	
	Mean (SD)	Mean (SD)	Unadjusted (95 % CI)	Adjusted (95 % CI)
All health states[b]	0.08 (0.73)	−0.02 (0.74)	−0.10 (−0.22, 0.03)	−0.10 (−0.23, 0.03)
States without severe problems[b]	0.65 (0.29)	0.61 (0.34)	−0.04 (−0.14, 0.05)	−0.06 (−0.15, 0.04)
States with severe problems[b]	−0.20 (0.72)	−0.29 (0.70)	−0.09 (−0.24, 0.05)	−0.09 (−0.24, 0.05)

CI confidence interval, *SD* standard deviation, *T2DM* type 2 diabetes mellitus

[a] Reference group is T2DM patients with complications

[b] Random effect linear regression model, in which age, gender, education, ethnicity, and the characteristics of the EQ-5D-3L health states are adjusted

differed if a different set of health states had been used in the study. Second, as we only recruited outpatients with T2DM, the findings may not be generalized to inpatients with T2DM who may have more severe health problems. Indeed, our study showed disease severity was associated with health-state utility. Due to these limitations, the findings of this study should be treated as preliminary rather than conclusive.

5 Conclusions

Our results indicate that the utility values of mild EQ-5D health states are higher to T2DM patients than to the general population. Therefore, the EQ-5D values based on the general population's preferences could underestimate the effectiveness of health inventions for patients with T2DM. Also, it appears that the values of the EQ-5D-3L health states are higher to T2DM patients with complications than to those without complications.

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All authors have no conflicts of interest that are relevant to the content of the study.

Authors' contributions Wang P: design of the study, data collection, analysis and interpretation of results, drafting of the article, and critical revision of the article for important intellectual content.

Tai ES: study coordination, critical revision of the article for important intellectual content.

Thumboo J: critical revision of the article for important intellectual content.

Vrijhoef HJM: critical revision of the article for important intellectual content.

Luo N: overall guarantor, design of the study, study coordination, interpretation of results, critical revision of the article for important intellectual content.

Appendix

See Tables 4 and 5.

Table 4 Parameter estimates of random-effects regression models of time trade-off values for patients with type 2 diabetes mellitus and participants from the general population

Variables	All health states			Mild health states			Severe health states		
	Estimates	SE[a]	*p* value	Estimates	SE	*p* value	Estimates	SE	*p* value
Intercept	−0.6117	0.0827	<0.0001	0.4396	0.0739	<0.0001	−0.7054	0.1067	<0.0001
Diabetes									
Without	0.0165	0.0686	0.6527	−0.1345	0.0586	0.0128	0.0239	0.0911	0.7036
With	0.0			0.00			0.00		
Age									
Less than 60 years	0.0693	0.0683	0.3105	0.0880	0.0595	0.1410	0.0605	0.0903	0.5031
60 years and above	0.0			0.0			0.0		
Gender									
Male	0.1254	0.0657	0.0565	0.0082	0.0572	0.8861	0.1752	0.0870	0.0445
Female	0.0			0.0			0.0		
Race									
Singaporean Chinese	−0.1379	0.0642	0.0321	−0.0699	0.0557	0.2113	−0.1712	0.0851	0.0447
Non-Chinese Singaporean	0.0			0.0			0.0		
Education level									
Tertiary and higher	0.1489	0.0866	0.0860	0.1222	0.0744	0.1026	0.1827	0.1149	0.1124
Secondary school or lower	0.0			0.0			0.0		
Mobility									
No problem	0.3050	0.0536	<0.0001	0.1368	0.0387	0.0005	0.5980	0.0885	<0.0001
Having problem	0.0			0.0			0.0		
Self-care									
No problem	0.2147	0.0525	<0.0001				0.0831	0.0650	0.2014
Having problem	0.0						0.0		
Usual activity									
No problem	0.7092	0.0706	<0.0001	0.1506	0.0446	0.0009			
Having problem	0.0			0.0					

Table 4 continued

Variables	All health states			Mild health states			Severe health states		
	Estimates	SE[a]	*p* value	Estimates	SE	*p* value	Estimates	SE	*p* value
Pain/discomfort									
No problem	0.1241	0.0474	0.0091				0.1258	0.0731	0.0861
Having problem	0.0						0.0		
Anxiety/depression									
No problem	0.3561	0.0480	<0.0001				0.4569	0.6044	<0.0001
Having problem	0.0						0.0		
AIC value	1666.3			264.0			1223.1		

AIC Akaike information criterion, *SE* standard error

[a] SE; mild health states include 11112, 21112, and 21122; severe health states include 11223, 23221, 21231, 23211, 23332, 32322, and 33333

Table 5 Parameter estimates of random-effects regression models of time trade-off values for patients with type 2 diabetes mellitus with and without complications

Variables	All health states			Mild health states			Severe health states		
	Estimates	SE[a]	*p* value	Estimates	SE	*p* value	Estimates	SE	*p* value
Intercept	−0.7443	0.0930	<0.0001	0.5353	0.0794	<0.0001	−0.8220	0.1203	<0.0001
Diabetes-related complications									
Without	−0.0952	0.0721	0.0864	−0.0569	0.0597	0.4353	−0.0912	0.0965	0.2965
With	0.0			0.00			0.00		
Age									
Less than 60 years	0.1016	0.0726	0.1626	0.0349	0.0575	0.5457	0.1344	0.0971	0.1674
60 years and above	0.0			0.0			0.0		
Gender									
Male	0.1056	0.0730	0.1487	−0.0362	0.0605	0.5522	0.1652	0.0978	0.0925
Female	0.0			0.0			0.0		
Race									
Singaporean Chinese	−0.1087	0.0707	0.1247	−0.0783	0.0588	0.1885	−0.1309	0.0948	0.1682
Non-Chinese Singaporean	0.0			0.0			0.0		
Education level									
Tertiary and higher	0.1858	0.0906	0.0409	0.1462	0.0750	0.0559	0.2492	0.1219	0.0419
Secondary school or lower	0.0			0.0			0.0		
Mobility									
No problem	0.3307	0.0691	<0.0001	0.1545	0.0286	<0.0001	0.6847	0.1228	<0.0001
Having problem	0.0			0.0			0.0		
Self-care									
No problem	0.2795	0.0695	<0.0001				0.1049	0.0909	0.2495
Having problem	0.0						0.0		
Usual activity									
No problem	0.8289	0.0939	<0.0001	0.1098	0.0612	0.0779			
Having problem	0.0			0.0					
Pain/discomfort									
No problem	0.1025	0.0645	0.1124				0.1186	0.1102	0.2827
Having problem	0.0						0.0		
Anxiety/depression									
No problem	0.4231	0.0623	<0.0001				0.4985	0.0830	<0.0001
Having problem	0.0						0.0		
AIC value	880.5			61.0			685.5		

AIC Akaike information criterion, *SE* standard error

[a] SE; mild health states include 11112, 21112, and 21122; severe health states include 11223, 23221, 21231, 23211, 23332, 32322, and 33333

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