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Research Article

The Association of Dry Eye Symptoms with Socioeconomic Factors and Quality of Life

Abstract

Purpose: Dry eye is a common condition with significant morbidity and socioeconomic burden. The associated demographic factors that worsen utility in dry eye patients were not known. There were many questionnaire instruments advocated for dry eye documentation but none of these have been shown to correlate to quality of life (QoL). We aimed at examining the health related utility values in a group of dry eye patients and their associations.

Methods: This was a hospital based prospective cross-sectional study conducted at the dry eye clinic of Singapore National Eye Centre. Patients with dry eye symptoms were randomized to one of the two validated symptom questionnaires, Standard Patient Evaluation of Eye Dryness (SPEED) or Symptom Assessment in Dry Eye (SANDE) questionnaires. All patients underwent an evaluation of socio economic factors and utility was assessed using Time-Trade-Off methodby 4 trained interviewers.

Results: We recruited 178 participants with dry eye symptoms (mean age was 56.4 (SD: 14.1) years, 77% female), 85 were assessed with SPEED and 93 with SANDE. The utility values encountered were skewed with only 52% of patients having a reduced utility (median=1.0) with a mean of 0.984 (SD: 0.11). The mean SPEED was 11.7 (5.6), and the mean SANDE was 56.8 (22.6). A higher symptom score was associated with a utility less than 1 with odds ratio 2.75 (95%CI 1.50-5.04). The correlation between SANDE and utility was r=-0.295 (-0.47 to -0.097) and corresponding correlation for SPEED and utility was not significant. To detect a utility less than 1, SPEED had an area under the curve (AUC) of 0.63 (95%CI 0.51-0.75) and the SANDE, 0.67 (0.56-0.77).

Conclusions: The health related QoL was relatively good in people with dry eye symptoms in this study. Increased symptoms were associated with decreasing QoL but the association was in general weak. This implied that causes of reduced QoL apart from symptoms, such as costs, treatment inconvenience or adverse effects should be explored.

Introduction

Dry eye is a multifactorial condition that affects 5-35% of the population [1]. Common symptoms of dry eyes include irritation of the eye, heaviness of the eyelids, blurring of vision, tearing and light sensitivity [2]. These symptoms can cause a significant reduction in patient health related quality of life (QoL). Clinical studies have shown poor correlation between clinical test symptoms and self-perceived severity of the disease [3]. Studies also have shown that utilities value of more severe dry eye is similar to condition such as class III/IV angina affecting the QoL [4]. Correlation between reduction in QoL and presenting symptoms is unknown compared to other factors such as cost and inconvenience of treatment. This affects physician's decision on the management of the condition. In addition, there is a significant socio-economic burden to treating dry eyes. In 2009, 54,051 patients sought treatment for dry eye in the Singapore National Eye Centre (SNEC) and total costs for dry eye medications amounted to US$1,520,797.80 that year from one pharmacy alone [5].

Although there are different questionnaires used in the assessment of dry eye, to date, there has been no study which evaluates the correlation between the severity and frequency of the symptoms on the questionnaires and QoL. This is particularly important since symptoms of dry eyes are episodic and questionnaires administered at one time point may or may not reflect the true disease morbidity. Two of such questionnaires are the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire which consists of 2 questions graded on a scale of 0-3 on frequency and grade 0-4 on severity and Symptom Assessment in Dry Eye (SANDE) questionnaire which consists of 3 questions based on symptoms of frequency and severity. Both of these questionnaires have been published, validated and utilized in the eye clinic by the investigators [6,7].

Dry eye is a common and growing public health problem with significant morbidity and decrease in health related QoL. Uncertainty in correlation between decreased QoL with presenting symptoms and factors, or the possibility of QoL being associated with factors such as cost and inconvenience of treatment, will affect prioritization in the management of the disease. For instance, if presenting symptoms correlate poorly with the perceived QoL, more emphasis should be placed on making treatment more accessible, convenient and at lower cost. If there is a high correlation, the focus should be making current treatments more efficacious to relieve presenting symptoms, and consequently to improve QoL. The findings of this study will also help us better understand the efficacy of the questionnaires and select appropriate one foruse in future clinical trials.

Utility assessment is a formal method to quantify and understand the impact of a condition. Dry eye has been found to lower the utility value and the mean utilities for mild/moderate and severedry eye were found to be 0.72 and 0.61 respectively in Buchholz et al.'s study. Moreover, the utilities of severe dry eye patients were similar to those who required dialysis or had severe angina [8]. There were many questionnaire instruments advocated for dry eye documentation but none of these have been evaluated for association with QoL.

This study aimed to ascertain:

1. The utility values of dry eye patients in SNEC and demographic, socioeconomic factors that may affect the utility,

2. The association, if any between symptoms of dry eye and the utility, and if this is affected by demographic and socioeconomic factors, and

3. The sensitivity and specificity of the dry eye symptoms in detecting a reduced utility.

Methods

This was a hospital-based prospective cross-sectional study conducted at the dry eye clinic of Singapore National Eye Centre. A total of 178 subjects with dry eye symptoms participated in this study. They were randomized to one of the two validated symptom questionnaires, SPEED or SANDE. Subjects were asked about their general health and the severity and frequency of dry eye symptoms assessed with either the SANDE or the SPEED randomly. Socio-economic status was evaluated using the parameters gross monthly income, highest educational level and type of residential home. Utilities were measured with the time-trade-off method as described below. The interviewers were trained in asking the 2 questionnaires in a standardized way.

Approval was obtained from the institutional review board, and written informed consent was obtained from all subjects. The study complied with the Tenets of the Declaration of Helsinki for human research.

The subjects recruited were 21 years old and above, with symptomatic dry eyes. These inclusion criteria applied to patients referred to the dry eye clinic of Singapore National Eye Center, having been diagnosed as 'dry eye' by another ophthalmologist. Patients with any eye conditions thatwere not dry eye-related such as ocular allergy, infection, irritation, age-related macular degeneration, or intraocular inflammation were excluded from the study. Patients with corrected visual acuity of worse than 6/12 in the better eye were also excluded. Patients with Sjogren syndrome were diagnosed by a rheumatologist. When undiagnosed patients present with dry mouth and dry eye, our protocol was to perform the assays for anti-SSA and anti-SSB antibodies. If these showed a positive result, a referral would be made to the rheumatology department for further evaluation and diagnosis of the systemic condition. Since such patients continued to visit the eye clinic, we were able to classify them as Sjogren syndrome.

51% of patients who participated in this study hadchronic illness such as rheumatoid arthritis, diabetes mellitus, sjogren syndrome or thyroid disease.

The SANDE questionnairerequired subjects to mark an 'X' on a 100 mm horizontal Visual Analogue scale (VAS) based on the frequency and severity of discomfort, blurring of vision and sensitivity to light. The extreme left of thescale representingcomplete absence of symptom, while the extreme right represents severe and constant dry eye symptom. The magnitudes were measured with a ruler and recorded in millimeters. Then, the global SANDE score was obtained by square rooting the multiplication of the frequency and severity of the dry eye symptoms. As the SANDE was applied to the symptoms of discomfort, blurring and photophobia, the worst global score of the symptoms was used in the subsequent analysis [9].

For the SPEED questionnaire, subjects were asked to rate the frequency and severity of dryness, soreness, burning and eye fatigue on a frequency scale of 0 to 3, where 0 being "never" and 3 being "constant". Severity of the symptoms are graded on a scale of 0 to 4, where 0 being "not severe" and 4 being "very severe". The SPEED score was obtained by the summation of the frequency and severity scores with a maximum score of 32. To compare scores with the SANDE, the SPEED scoreswere then normalized to transformed SPEED scores that were comparable with SANDE score. The formula is provided in supplementary file 1.

The utility question was a hypothetical question where subjects were given a "dry eye-free" life scenario and how much of their life expectancy they were willing to trade-off. Theutility values were calculated based on the formula: Utility value=(remaining years of life expected - time trade-off (TTO))/ (remaining years of life), with TTO in years.The remaining years of life expected was computed as the mean life expectancy for men/women subtracting the current age. The closer the utility value was to 1.0, the better the quality of life associated with dry eye symptoms.

SPSS Statistics Version 21 was used to analyze the data. Spearman rho was used in the calculation ofthe confidence intervals for correlation coefficient and the confidence intervalvalues were generated with the online calculator: http://how2stats.blogspot.sg/2011/09/confidence-intervals-for-correlations.html. Binomial confidence intervals were used in the calculation of proportions of subjects with utility value of less than one with the link,http://statpages.org/confint.html.

Results

Overall178 participants were recruited (Table 1), with 85 answering the SPEED questionnaire and 93 the SANDE questionnaire. There was no difference in the gender composition, age, ethnicity, income, and highest level of education attained between participants who were randomized to each questionnaire. The mean presenting corrected visual acuity of the participants was 6/7.5, whereas the mean age was 56.4 (SD: 14.1) years with 77% female.

In this study, 8 subjects had diabetes mellitus, 10 had Sjogren syndrome, 20 had rheumatoid arthritis and 14 had thyroid disease.

A considerable proportion of utility values were close to 1, table 2 shows the proportion of participants who had a utility value of less than 1. The proportions of utility values that were less than 1 were not significantly different between those with different genders, ethnicity,

income, education level and housing type (p>0.05). There were a significantly higher proportion of subjects with ages lesser or equal to 50 years oldhaving a utility of less than 1 (p=0.049).

Supplementary Table 1 shows the mean and SD of the utilities. The mean utility of the participants was skewed with only 52% of patients having a reduced utility from 1. The median utility was 1 and mean was 0.984 (SD: 0.11). The frequency distribution of the utility (histogram) is shown in figure 1. There were no significant difference in the utility between the participants who answered the SANDE and SPEED (p>0.05). We found that 92 out of 178(51.7%) of the participants had a utility value of less than 1.

Table 1: Participants' demographics.

	Total	SPEED	SANDE	P-value
Total	178	85	93	
Female n (%)	137 (77.0)	70 (82.4)	67 (72.0)	0.073
Mean Age (SD)	56.4 (14.1)	57.1 (13.8)	55.7 (14.4)	0.52
Ethnicity				
Chinese n(%)	160 (89.9)	75 (88.2)	85 (91.4)	0.33
Gross Income (monthly)				
Nil (%)	70 (40.0)	40 (47.6)	30 (33.0)	
S$0-S$3000 (%)	61 (34.9)	26 (31.0)	35 (38.5)	0.14
>S$3000 (%)	44 (25.1)	18 (21.4)	26 (28.6)	
Highest education				
Up to A levels (%)	136 (76.4)	63 (74.1)	73 (78.5)	
University or above (%)	42 (23.6)	22 (25.9)	20 (21.5)	0.31
Housing Type				
<=4 room (%)	81 (45.5)	40 (47.1)	41 (44.1)	
5 room/executive (%)	46 (25.8)	19 (22.4)	27 (29.0)	0.59
Private (%)	51 (28.7)	26 (30.6)	25 (26.9)	

Figure 1: Histogram showing the distribution of utility values in this study.

The distribution of dry eye symptoms encountered by the participants is shown in Table 3. The mean symptom score for SPEED was 11.7 (SD: 5.6) in a scale of 0-32, whereas the mean global score in SANDE (worst of 3 symptoms) was 56.8 (SD: 22.6) in a scale of 0-100. 52.7% (49/93) of the participants using SANDE had irritation as the worst of the 3 symptoms, 21 patients had blurring of vision as worst symptom and 23 patients had sensitivity of light. In general, with the exception of housing status, the demographic factors were not associated with the symptoms. The housing level was associated with the symptom score (combining SANDE score and transformed SPEED score) and post hoc testing showsthe participants living in private property reporting more symptoms than those in 4 room flats or smaller apartments (p=0.018). Similar findings were obtained comparing SANDE scores and property type (p=0.011).

The relationship between utility and dry eye symptoms is evaluated in Table 4. Overall the participants with a lower utility than 1 had more symptoms (p=0.001). The significance was also observed in female or Chinese participants, those with agemore than 51 years old, those earning between S$ 0-3000 a month, those with up to A levels education, as well as those living in apartments with 4 rooms or less.

The inverse correlation between utility value and the dry eye symptoms is shown in Table 5. The participants with higher symptoms were correlated to lower QoL (lower utility). In general, the strength of correlation between the utility and the extent of dry eye symptoms was relatively weak, even though statistically significant in a few instances. The correlation between utility and SPEED symptom was -0.198 (-0.394 to 0.016) whereas that between utility and SANDE was -0.295 (-0.470 to -0.097). As in Table 4, the inverse correlation was significant for participants who were Chinese, female, aged 51 and above, earning lesser than S$3000 and with up to A levels of highest education, and those living in apartments with 4 rooms or smaller. An interesting finding was the moderately inversely correlated findings between utility and SANDE for participants living in private apartments (r=-0.52), in 4 rooms or smaller (r=-0.419) and those with income lesser than S$3000 (r=-0.432). There were also weak correlated findings between utility value and SPEED for female participants (r=-0.298) and those with education up to post-secondary level (r=0.282).

Logistic regression was performed with a lowered utility as the outcome (defined as utility value of less than 1) and the symptom score (dichotomized to either above or below the mean) was used as the independent variable. A higher symptom score was associated with reduced utility, with a crude odds ratio (OR) 2.75 (95% CI 1.50-5.04). The odds ratio adjusted for age and gender was the same at 2.70 (1.46-5.00). When adjusted for age, gender, education level, income level and housing status, the adjusted OR was 2.72 (1.44-5.15).

Receiver operating curves are shown for the detection of utility of less than 1 (Figure 2). The SPEED and SANDE questionnaires had areas under the curve (AUC) of 0.63 (95%CI 0.51-0.75) and 0.67 (0.56-0.77) respectively. The most suitable SPEED threshold for predicting a decrease in utility was 11.5 out of a total of 32, with a sensitivity of
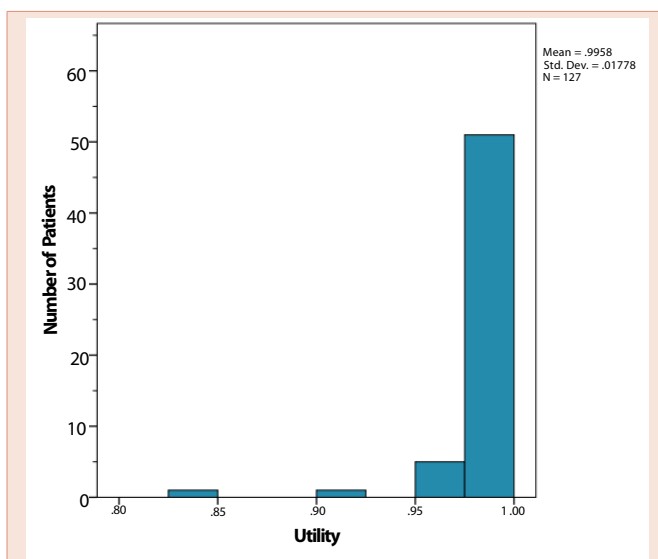
Table 2: Proportions of participants who had utility of less than 1.

| | | All | | | SPEED | | | SANDE | | |
	n	Proportion of utility<1, % (95%CI)		n	Proportion of utility<1, % (95%CI)		n	Proportion of utility<1, % (95%CI)	p value
Total	178	51.7 (44.1 to 59.2)		85	49.4 (38.4 to 60.5)		93	53.8 (43.1 to 64.2)	0.65
Gender										
Male	41	61.0 (44.5 to 75.8)		15	66.7 (38.4 to 88.2)		26	57.7 (37.0 to 76.7)	0.74
Female	137	48.9 (40.3 to 57.6)		70	45.7 (33.7 to 58.1)		67	52.2 (39.7 to 64.6)	0.50
p-value		0.18								
Ethnicity										
Chinese	160	50.0 (42.0 to 58.0)		75	45.3 (33.8 to 57.3)		85	54.1 (43.0 to 65.0)	0.34
Non-Chinese	18	66.7 (41.0 to 86.6)		10	80.0 (44.4 to 97.5)		8	50.0 (15.7 to 84.3)	0.32
p-value		0.18								
Age										
<=50	54	64.8 (50.6 to 77.3)		27	66.7 (46.0 to 83.5)		27	63.0 (42.4 to 80.6)	1.00
51-60	56	50.0 (36.3 to 63.7)		24	41.7 (22.1 to 63.4)		32	56.3 (37.7 to 73.6)	0.42
>60	68	42.6 (30.7 to 55.2)		34	41.2 (24.7 to 59.3)		34	44.1 (27.2 to 62.1)	1.00
p-value		**0.049***								
Gross Income (monthly)										
Nil	70	48.6 (36.4 to 60.8)		40	50.0 (33.8 to 66.2)		30	46.7 (28.3 to 65.7)	0.81
>0 to <S$3000	61	47.5 (34.6 to 60.7)		26	46.2 (26.6 to 66.6)		35	48.6 (31.4 to 66.0)	1.00
>S$3000	44	65.9 (50.1 to 79.5)		18	55.6 (30.8 to 78.5)		26	73.1 (52.2 to 88.4)	0.33
p-value		0.12								
Highest education										
Up to A levels	136	47.8 (39.2 to 56.5)		63	44.4 (31.9 to 57.5)		73	50.7 (38.7 to 62.6)	0.50
University or above	42	64.3 (48.0 to 78.5)		22	63.6 (40.7 to 82.8)		20	65.0 (40.8 to 84.6)	1.00
p-value		0.062								
Housing Type										
<=4 room	81	44.4 (33.4 to 55.9)		40	40.0 (24.9 to 56.7)		41	48.8 (32.9 to 64.9)	0.51
5 room/executive	46	52.2 (37.0 to 67.1)		19	47.4 (24.5 to 71.1)		27	55.6 (35.3 to 74.5)	0.77
Private	51	62.7 (48.1 to 75.9)		26	65.4 (44.3 to 82.8)		25	60.0 (38.7 to 78.9)	0.78
p-value		0.12								

*P values are significant at 95% CI (2 tailed test)

Table 3: Mean and standard deviation of symptoms score.

| | | All† | | | SPEED | | | SANDE |
	n	Symptom score mean (SD)		n	Total score untransformed mean (SD)		n	Global score mean (SD)
Total	178	52.3 (21.2)		85	11.7 (5.63)		93	56.8 (22.6)
Gender								
Male	41	51.6 (21.3)		15	10.7 (6.5)		26	56.6 (19.4)
Female	137	52.5 (21.3)		70	11.9 (5.5)		67	56.8 (23.8)
p value		0.816			0.481			0.972
Ethnicity								
Chinese	160	51.9 (21.3)		75	11.5 (5.48)		85	56.4 (22.7)
Non-Chinese	18	55.8 (21.0)		10	13.3 (6.82)		8	60.5 (22.1)

p value		0.458		0.333		0.626	
Age							
<=50	54	53.9 (18.9)	27	12.8 (5.95)	27	56.9 (19.4)	
51-60	56	49.9 (21.7)	24	10.6 (4.25)	32	53.8 (25.1)	
>60	68	53.0 (21.2)	34	11.6 (5.63)	34	59.5 (22.7)	
p value		0.594		0.382		0.594	
Gross Income (monthly)							
Nil	70	52.5 (20.9)	40	12.0 (5.94)	30	58.2 (21.5)	
>0 to <S$3000	61	47.9 (22.7)	26	10.3 (4.87)	35	51.5 (25.6)	
>S$3000	44	57.5 (18.9)	18	12.3 (5.47)	26	62.5 (19.0)	
p value		0.072		0.365		0.165	
Highest education							
Up to A levels	136	51.6 (22.0)	63	11.1 (5.44)	73	56.8 (23.5)	
University or above	42	54.5 (18.7)	22	13.3 (5.99)	20	56.6 (19.3)	
p value		0.45		0.122		0.978	
Housing Type							
<=4 room	81	47.9 (21.8)	40	11.2 (5.84)	41	50.1 (24.0)	
5 room/executive	46	53.5 (21.0)	19	11.8 (5.52)	27	57.4 (22.1)	
Private	51	58.3 (19.2)	26	12.2 (5.54)	25	67.0 (16.7)	
p value		**0.021***		0.773		**0.011***	

†SPEED scores were transformed to 0-1 from its original scale of 0-32 before computation in this column
*P values are significant at 95% CI (2 tailed test)
*Post hoc bonferroni shows symptom score of private > lesser than/equal to 4 room p<0.05

Table 4: Mean and standard deviation in symptoms score for participants with utility of less than 1 and utility of one.

	Overall†					**SPEED**					**SANDE**				
	n	Utility<1	n	Utility=1	p value	n	Utility<1	n	Utility=1	p value	n	Utility<1	n	Utility=1	p value
Total	92	57.5 (21.14)	86	46.7 (20.0)	**0.001***	42	12.9 (5.5)	43	10.5 (5.6)	**0.05***	50	62.5 (22.8)	43	50.1 (20.6)	**0.007***
Gender															
Male	25	53.1 (21.3)	16	49.4 (21.9)	0.592	10	10.7 (6.48)	5	10.8 (7.36)	0.979	15	59.9 (18.7)	11	52.2 (20.2)	0.327
Female	67	59.1 (21.0)	70	46.2 (19.7)	**<0.001***	32	13.6 (5.07)	38	10.4 (5.43)	**0.016***	35	63.7 (24.5)	32	49.3 (20.9)	0.013
Ethnicity															
Chinese	80	57.3 (21.1)	80	46.5 (20.2)	**0.001***	34	12.9 (5.1)	41	10.3 (5.6)	**0.032***	46	61.5 (23.3)	39	50.4 (20.7)	**0.025***
Non-Chinese	12	58.4 (22.4)	6	50.7 (18.8)	0.480	8	12.9 (7.4)	2	15.0 (5.7)	0.717	4	74.8 (12.4)	4	46.3 (21.1)	0.059
Age															
<=50	35	55.2 (18.2)	19	51.5 (20.3)	0.494	18	12.3 (5.12)	9	13.8 (7.60)	0.547	17	60.9 (19.1)	10	50.1 (18.8)	0.169
51-60	28	57.2 (20.6)	28	42.7 (20.6)	**0.011***	10	12.2 (3.58)	14	9.43 (4.43)	0.117	18	60.7 (23.6)	14	44.8 (24.8)	0.074
>60	29	60.5 (25.0)	39	47.4 (19.3)	**0.017***	14	14.1 (7.03)	20	9.75 (4.96)	**0.04***	15	66.6 (26.5)	19	53.9 (18.1)	0.125
Gross Income (monthly)															
Nil	34	57.0 (22.1)	36	48.3 (19.0)	0.078	20	13.9 (6.55)	20	10.1 (4.72)	**0.047***	14	62.1 (24.3)	16	54.7 (18.8)	0.358
>0 to <S$3000	29	55.9 (22.5)	32	40.5 (20.7)	**0.007***	12	11.9 (4.64)	14	8.86 (4.77)	0.112	17	60.8 (25.3)	18	42.7 (23.2)	**0.034***
>S$3000	29	59.6 (19.0)	15	53.4 (18.6)	0.311	10	12.1 (4.07)	8	12.6 (7.15)	0.847	19	64.4 (20.3)	7	57.2 (15.0)	0.403

Highest education															
Up to A levels	65	58.6 (22.4)	71	45.2 (19.6)	**<0.001***	28	13.3 (5.82)	35	9.37 (4.49)	**0.004***	37	63.3 (24.2)	36	50.1 (21.1)	**0.016***
University or above	27	54.7 (17.8)	15	54.0 (20.7)	0.906	14	12.1 (4.86)	8	15.4 (7.46)	0.221	13	60.4 (19.0)	7	49.6 (19.2)	0.241
Housing Type															
<=4 room	36	56.3 (21.7)	45	41.2 (19.7)	**0.001***	16	13.1 (6.26)	24	10.0 (5.34)	0.105	20	60.1 (23.1)	21	40.5 (21.1)	**0.007***
5 room/ executive	24	55.4 (22.4)	22	51.4 (19.8)	0.525	9	13.7 (5.22)	10	10.2 (5.51)	0.179	15	56.1 (25.6)	12	59.0 (17.7)	0.74
private	32	60.4 (20.0)	19	54.7 (17.7)	0.311	17	12.3 (5.12)	9	12.1 (6.60)	0.938	15	72.2 (17.0)	10	59.3 (13.6)	0.057

†SPEED scores were transformed to 0-1 from its original scale of 0-32 before computation in this column
*P values are significant at 95% CI (2 tailed test)

Table 5: Correlation of utility and symptoms score.

	All†		**SPEED**		**SANDE**	
	n	Correlation coefficient (95%CI)	n	Correlation coefficient (95%CI)	n	Correlation coefficient (95%CI)
Total	178	**-0.246 (-0.38 to -0.10)***	85	-0.198 (-0.394 to 0.016)	93	**-0.295 (-0.470 to -0.097)***
Gender						
Male	41	-0.028 (-0.333 to 0.282)	15	0.018 (-0.499 to 0.525)	26	-0.121 (-0.486 to 0.279)
Female	137	**-0.312 (-0.456 to -0.152)***	70	**-0.298 (-0.498 to -0.068)***	67	**-0.348 (-0.543 to -0.118)***
Ethnicity						
Chinese	160	**-0.233 (-0.375 to -0.081)***	75	-0.199 (-0.408 to 0.029)	85	-0.262 (-0.450 to -0.052)
Non-Chinese	18	-0.388 (-0.724 to 0.096)	10	-0.238 (-0.755 to 0.461)	8	-0.634 (-0.925 to 0.128)
Age						
<=50	54	-0.103 (-0.361 to 0.169)	27	-0.083 (-0.449 to 0.307)	27	-0.179 (-0.523 to 0.216)
51-60	56	**-0.351 (-0.562 to -0.097)***	24	-0.351 (-0.661 to 0.061)	32	-0.325 (-0.605 to 0.027)
>60	68	**-0.257 (-0.467 to -0.020)***	34	-0.199 (-0.503 to 0.149)	34	-0.332 (-0.603 to 0.007)
Gross Income (monthly)						
Nil	70	-0.17 (-0.389 to 0.068)	40	-0.218 (-0.496 to 0.100)	30	-0.138 (-0.475 to 0.234)
>0 to <S$3000	61	**-0.393 (-0.587 to -0.157)***	26	-0.287 (-0.607 to 0.113)	35	**-0.432 (-0.669 to -0.115)***
>S$3000	44	-0.121 (-0.403 to 0.182)	18	-0.106 (-0.546 to 0.380)	26	-0.168 (-0.521 to 0.235)
Highest education						
Up to A levels	136	**-0.312 (-0.456 to -0.152)***	63	**-0.282 (-0.495 to -0.037)***	73	**-0.339 (-0.528 to -0.118)***
University or above	42	0.04 (-0.267 to 0.340)	22	0.147 (-0.293 to 0.535)	20	-0.158 (-0.561 to 0.306)
Housing Type						
<=4 room	81	**-0.35 (-0.528 to -0.143)***	40	-0.244 (-0.516 to 0.073)	41	**-0.419 (-0.644 to -0.128)***
5 room/executive	46	-0.025 (-0.313 to 0.267)	19	-0.149 (-0.565 to 0.327)	27	0.101 (-0.290 to 0.463)
Private	51	-0.185 (-0.438 to 0.095)	26	-0.034 (-0.416 to 0.358)	25	**-0.52 (-0.759 to -0.157)***

†SPEED scores were transformed to 0-1 from its original scale of 0-32 before computation in this column
*P values are significant at 95% CI (2 tailed test)

57% and specificity of 65%. However, to achieve a higher sensitivity, a lower threshold of 8.5 produced a sensitivity of 71%, but this would lower the specificity to only 42%. For the SANDE a threshold of 52 out of 100 produced sensitivity of 66% and specificity of 56%. To attain a higher sensitivity, a lower threshold of 49.3 produced a sensitivity of 78%, but specificity of only 51%.

We repeated the above analyses without including the non-Chinese participants, and essentially the same conclusions were drawn (data not shown).

Discussion

This study found that health related QoL represented by the utility value was relatively high in dry eye patients in the hospital-based Singapore study, with only 51.7% of patients having a utility value of less than 1 (no reduction in QoL). We found that reduction of utility value was associated with younger age of less than or equal to 50 years. In general, socioeconomic and demographic factors did not impact symptoms of dry eye. A reduced utility was associated with more symptoms of dry eye but the strength of the association
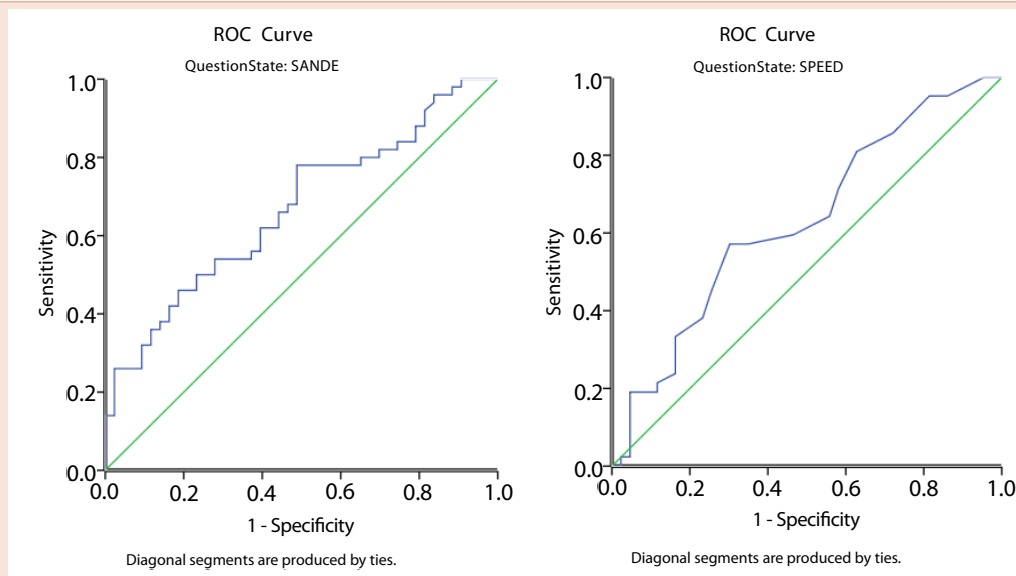
Figure 2: Receiver operating curves for SANDE (left) and SPEED (right) to detect a utility of less than 1.

was weak. Interestingly, the correlation was moderately strong when symptoms were measured with the SANDE for those living in private apartments, those living in 4 rooms or smaller apartment or those earning less than $3000. With worse dry eye symptoms, there was a 3-fold increase in risk for utility to be reduced. The SPEED threshold of 11.5 or SANDE threshold of 52 may be suitable for screening to detect a lowered utility value in dry eye.

Utility value in this study seems much better than Schiff man's study (where even mild dry eye was associated with a mean utility value as low as 0.81). The utility measurement was known to depend on an individual's aversion to risk [4]. It might be that subjects recruited for our study were less willing to take risks, or entertain the concept of death, compared to the participants in Schiff man's study. This may be attributed to cultural or religious differences.

As far as we know, the current study is the first to find a correlation between the magnitude of symptoms and QoL. The relatively weak correlation between symptoms and QoL could be due to other problems faced by people with dry eye that are unrelated to the symptoms. These include socioeconomic burden of dry eye, inconvenience of dry eye treatment and follow up visits at the clinic.

Between 2008 and 2009, the total expenditure of dry eye treatment in our center was found to be US $0.06 million per year per 1,000 patients. However, indirect costs such as loss of productivity were not yet estimated [5]. Dry eye treatment is inconvenient, often requiring instillation of numerous drops a day, with consequently an impact on daily activities. Some patients who were loss to follow up also reported problems with hospital visits (unpublished data). Psychological effects of dry eye were explored previously and it was found that anxiety and depression were correlated with dry eye syndromes [10].

We found a weak correlation between utility and the symptoms of dry eye in participants without systemic disease (as defined in this study), but we failed to elicit any correlation in those with systemic disease. Perhaps people with systemic conditions have decrease in QoL mainly due to those conditions and would not trade-off more time addressing the relatively less impactful dry eye condition. The reason why SANDE scores were more correlated to utility than SPEED could be due to SANDE having continuous variable readings which were more precise than the interval/ordinal measurements in SPEED.

In some scenarios, SANDE may be preferable to SPEED for assessment of dry eye symptoms, especially if the research involved possible changes in symptoms which may have an impact on QoL. However, for screening purposes, SPEED (at a threshold of 11.5), or SANDE (with threshold of 52) may be suitable as a one-time tool to detect a reduced utility.

A limitation of this study is that visual function disturbances often affecting a dry eye patient were not captured. These include forced visual acuity, contrast sensitivity, and non-invasive tear break up time, etc. Another limitation of the study is that we did not evaluate the number of hours on computer use, or attempt to classify the patients based on occupations. These activities may independently affect QoL in addition to the socioeconomics. The study has very few Sjogren syndrome patients, so the results pertaining to QoL may only apply to non-Sjogren syndrome type of dry eye patients.

Conclusion

In conclusion, the health related QoL was relatively high in people with dry eye symptoms in this hospital-based study in Singapore. This implied that apart from symptoms alone, other factors such as costs, treatment inconvenience or adverse effects should be explored as factors that reduce QoL in these patients. With increased magnitude of dry eye symptoms, there is a 3-fold increase in the odds for utility to be reduced. The SPEED threshold of 11.5 or SANDE threshold of 52 may be suitable for screening to detect a lowered utility in dry eye.

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Supplementary Table 1: Mean and standard deviation of utility values.

	All		SPEED		SANDE		
	n	Utility, mean (SD)	n	Utility, mean (SD)	n	Utility, mean (SD)	p value
Total	178	0.984 (0.11)	85	0.996 (0.021)	93	0.973 (0.146)	0.136
Gender							
Male	41	0.968 (0.157)	15	0.984 (0.043)	26	0.959 (0.196)	0.619
Female	137	0.988 (0.087)	70	0.998 (0.011)	67	0.978 (0.123)	0.19
Ethnicity							
Chinese	160	0.983 (0.11)	75	0.995 (0.022)	85	0.972 (0.152)	0.161
Non-Chinese	18	0.992 (0.03)	10	0.998 (0.002)	8	0.983 (0.047)	0.391
Age							
<=50	54	0.993 (0.025)	27	0.992 (0.323)	27	0.995 (0.015)	0.622
51-60	56	0.980 (0.13)	24	0.999 (0.002)	32	0.965 (0.176)	0.349
>60	68	0.979 (0.12)	34	0.996 (0.016)	34	0.962 (0.172)	0.252
Gross Income (monthly)							
Nil	70	0.981 (0.12)	40	0.995 (0.017)	30	0.961 (0.183)	0.318
0-3000	61	0.979 (0.128)	26	1.000 (0.001)	35	0.964 (0.169)	0.29
>3000	44	0.993 (0.03)	18	0.990 (0.038)	26	0.990 (0.038)	0.651
Highest education							
Up to A levels	136	0.981 (0.122)	63	0.998 (0.012)	73	0.967 (0.165)	0.107
University or above	42	0.993 (0.03)	22	0.990 (0.036)	20	0.996 (0.010)	0.445
Housing Type							
<=4 room	81	0.987 (0.11)	40	1.000 (0.001)	41	0.974 (0.156)	0.308
5 room/executive	45	0.972 (0.15)	19	0.995 (0.021)	27	0.956 (0.192)	0.392
Private	51	0.989 (0.03)	26	0.990 (0.033)	25	0.987 (0.033)	0.731

The following method of transformation was designed to ensure that the mean of transformed SPEED has the same mean as the SANDE score.
For SPEED scores greater than its mean, the following formula is used:

$$\text{Transformed SPEED score} = \text{mean SANDE} + \left(100 - \text{mean SANDE}\right) \times \frac{\text{SPEEDscore} - \text{meanSPEED}}{32 - \text{meanSPEED}}$$

Else, the following formula is used: $\text{Transformed SPEED score} = \text{mean SANDE} \times \dfrac{\text{SPEEDscore}}{\text{meanSPEED}}$