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Comparing disease-specific and generic quality of life measures in patients with schizophrenia

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ABSTRACT

The current study aimed to compare the use of a disease-specific and a generic quality of life (QOL) measure in a group 251 outpatients with a schizophrenia spectrum disorder by examining their relationships with symptoms of schizophrenia, psychiatric and medical comorbidities, and other factors, as well as to determine which of these factors will be associated with the measurement discrepancy between the two measures. QOL was assessed with the generic Healthy Utility Index Mark 3 (HUI3) and disease-specific Schizophrenia Quality of Life Scale (SQLS), and symptom severity was determined using the Positive and Negative Syndrome Scale (PANSS). Symptom severity predicted both SQLS and HUI3, while psychiatric comorbidity predicted only the HUI3. Ethnicity, employment and PANSS *depression* factor were significantly associated with the measurement discrepancy. Using domain scores of the two QOL measures, the HUI3 appears to be superior in discriminating PANSS *cognitive* factor scores and medical comorbidity status compared to SQLS. Although the use of disease-specific QOL is generally preferred to track treatment progress in clinical settings, the two types of instruments measure non-overlapping aspects of QOL and the generic scales may better reflect QOL impairment due to overall clinical presentation.

1. Introduction

Schizophrenia is a severe mental illness which affects nearly 1% of the entire population with a median incidence of 15.2 per 100,000 persons (McGrath et al., 2008). It is an extremely disabling disease that affects major life domains (Switaj et al., 2012) and medication non-adherence often results in high relapse rates among those afflicted (Emsley et al., 2013). Further, many remain ill with little or no symptomatic improvement while others experience frequent re-hospitalizations over a prolonged part of their adulthood (Torrey, 2006). The goal of clinicians in the 21st century has shifted from treating and focusing on disorder-specific symptoms alone towards improving broader and more functional outcomes among those suffering from schizophrenia (Liberman and Kopelowicz, 2002).

In order to formulate a more guided healthcare plan for patients with schizophrenia, a number of disease-specific and generic scales have been developed over the years for the evaluation of QOL in schizophrenia. Disease-specific QOL questionnaires, as the name suggests, tend to measure more specific elements of the respective disease and are thus, theoretically, more sensitive to subtle treatment-related changes than generic QOL measures (Wiebe et al., 2003). On the other hand, generic health questionnaires typically assess the physical, social, and emotional dimensions of health and they tend to have the advantage of evaluating QOL for different type of diseases. A study by Zeng et al. (2015) attempted to examine the factors associated with disease-specific and generic QOL measures among individual with schizophrenia and found difference(s) in the determinants of the two types of measures. While we expect disease-specific and generic QOL measures to have different predictors, it is also important to know what makes them differ or in other words, what may be linked to a greater discrepancy between the two measures. Knowledge of the drivers of the QOL discrepancy can aid researchers and clinicians to have a better understanding when using QOL as an outcome measure and facilitate the development of relevant strategies to alleviate predicting factors as measured by both generic and disease-specific QOL, so as to improve overall QOL of patients.

Extensive studies suggest that core symptoms of schizophrenia have implications on QOL (Karow et al., 2014). For example, both negative

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and positive symptoms were found to correlate negatively with QOL in people with schizophrenia (Kao et al., 2011; Norman et al., 2000; Solanki et al., 2008), although the negative syndrome has been identified to have greater impact on QOL relative to the positive syndrome (Rabinowitz et al., 2012; Rocca et al., 2009). Cognitive deficits have also been accepted as a central feature of schizophrenia (Lewis, 2004) and impaired cognitive functioning appears to have direct impact on patients' perceived QOL (Alptekin et al., 2005; Ueoka et al., 2011). In view of all these findings, it can be surmised that the symptom severity of schizophrenia shares an intricate relationship with QOL. In addition to disorder-specific symptoms, other psychiatric and medical comorbidities are also known to be common among individuals with schizophrenia (Buckley et al., 2009; Carney et al., 2006). These co-existing conditions have also been found to lower the levels of QOL among them (Barnes et al., 2012; Bhalla et al., 2018).

While studies on psychometric properties tend to show preference for the disease-specific approach due to its superior construct validity and responsiveness (Mulhern et al., 2014; Papaioannou et al., 2011), it is unclear whether a single disease-specific measure is sufficient in providing a holistic evaluation of QOL in populations with schizophrenia. The current study therefore aimed to compare the use of a disease-specific and a generic QOL measure in a sample of outpatients with primary schizophrenia spectrum disorder by examining their relationships with symptoms of schizophrenia, psychiatric and medical comorbidities, and other factors. We hypothesized that: firstly, symptom severity of schizophrenia will be more strongly associated with disease-specific QoL than generic QoL and secondly, psychiatric and medical comorbidity status will be more strongly associated with generic QOL than disease-specific QoL. To further elucidate our hypothesis, we examined the two types of QOL scales at the domain level and compared their relationships with two important clinical attributes – (1) severity of the symptom clusters of schizophrenia and the (2) psychiatric and medical comorbidity status.

Lastly, we also aimed to determine which of these factors would be associated with the measurement discrepancy between the two measures.

2. Methods

2.1. Participants and procedures

The study employed a convenience sampling strategy and a total of 251 participants were recruited over the period of August 2016–June 2017 from the outpatient clinic of the Institute of Mental Health, the only tertiary psychiatric hospital in Singapore. Posters were placed in the clinic to inform attending patients of the ongoing study with information on eligibility criteria and researchers' contact provided for self-referral by patients. Psychiatrists and other healthcare professionals also helped to refer their patients for the study. Inclusion criteria consisted of: (1) being 21–65 years of age and able to provide consent; (2) clinically diagnosed with a primary schizophrenia spectrum disorder by consulting psychiatrists; (3) literate in the English language. Patients with a history of dementia or intellectual disability were excluded. After providing written informed consent, the patients were asked to complete a battery of self-administered questionnaires that were designed to collect their sociodemographic and clinical information as well as to assess their QOL, while the severity of their schizophrenia symptoms was assessed by a trained interviewer using the Positive and Negative Syndrome Scale (PANSS). Current psychiatric and medical comorbidities were obtained from the participants' medical records. Participants were paid upon the completion of questionnaires. Approval of study was obtained from the institutional ethics committee, the Domain Specific Review Board of National Healthcare Group, Singapore.

2.2. Instruments

Schizophrenia Quality of Life Scale (SQLS) was administered to examine the disease-specific QOL. Its validity and reliability have been well-illustrated in patients with schizophrenia (Rofail et al., 2016; Wilkinson et al., 2000). The scale comprises 30 items which are all self-report questions that offer five response options: "never", "rarely", "sometimes", "often", and "always". A confirmatory factor analysis of the SQLS was conducted among a local outpatient sample with schizophrenia and it demonstrated the validity of assessing QOL under 3 domains: *psychosocial* (fifteen items), *motivation/ energy* (seven items) and *symptoms/ side effects* (eight items) (Luo et al., 2008). The *psychosocial* domain contains items such as "I feel angry" and "I worry about my future", which explore severity of patient's existing emotional problems, and also the patient's perceived obstacles in social situations. Items in the *motivation/ energy* domain (e.g., "I lack the energy to do things" and "I can't be bothered to do things") address issues related to problems of motivation to do things and energy to perform activities, as well as the patient's likelihood of engaging in the positive aspects of life (e.g. "I take part in enjoyable activities"). Lastly, *symptoms/side effects* domain highlights hindrances in patient's life such as sleep disturbances and tardive dyskinesia (e.g., "I am bothered by my shaking/trembling" and "my muscles get stiff") which may be brought about by antipsychotics. The scores of each domain are scaled to a scoring algorithm ranging from 0 to 100, with higher scores indicating worse perceived QOL while SQLS total score was tabulated by averaging the sum of the three domain scores.

Healthy Utility Index Mark 3 (HUI3) was used as a generic QOL measure and it is a well-established QOL instrument that describes the respondent's health status based on eight attributes of functioning (Feeny et al., 2002): *vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain*. The HUI3 has been reported to be suitable in measuring QOL of patients with psychotic disorders (Tempier and Pawliuk, 2007) and being able to assess change in health status over time (Kopec et al., 2001). Its construct validity has also been demonstrated among a local patient population with schizophrenia (Luo et al., 2006). The eight attributes of HUI3 can be scored in two ways, namely the single-attribute utility scores and the multi-attribute utility scores. The single-attribute utility scores were used for domain-level comparisons and they range from 0 to 1, and a score of 0 corresponds to high disability of functioning pertaining to that attribute (e.g., 0 on '*vision*' means completely unable to see), while a score of 1 represents perfect capacity of functioning (e.g., 1 on '*vision*' means perfect *vision*). HUI3 overall utility score was derived with the HUI3's Dead – Perfect Health Scale formula; $u^* = 1.371 \times (b1 \times b2 \times b3 \times b4 \times b5 \times b6 \times b7 \times b8) - 0.371$) (Feeny et al., 2002), where b1–b8 corresponds to the multi-attribute utility scores of the eight physical domains of functioning. HUI3's overall utility scores range from −0.36 to 1, with 0 being defined as dead, negative scores indicating conditions worse than dead and 1 reflecting a state of perfect health.

Positive and Negative Syndrome Scale (PANSS) is an instrument known to be valid and reliable for measuring severity of schizophrenia symptoms (Bell et al., 1994). The five-factor model of PANSS is the most commonly reported and adopted model in literature (Lehoux et al., 2009) and for the purpose of this study, we have used the version by Jiang and colleagues to measure severity of the symptom clusters in our sample as their five factor structure has been validated in a sample of local Chinese patients with schizophrenia (Jiang et al., 2013). In this model, the five factors consist of *positive* factor (P1 delusions, P3 hallucinations, P6 suspiciousness and G9 unusual thought); *negative* factor (N2 emotional withdrawal, N3 poor rapport, N4 passive social withdrawal, N6 lack of spontaneity and flow of conversation and G7 motor retardation); *cognitive* factor (G10 disorientation and G12 lack of judgment and insight); *excitement* factor (P4 hyperactivity, P7 hostility and G14 poor impulse control); and *depression* factor (G2 anxiety, G3 guilt feelings and G6 depression).

2.3. Statistical analyses

All statistical analyses were carried out using the IBM SPSS software version 23.0. Statistical significance was set at $p < 0.05$ level using two-sided tests. Descriptive statistics were tabulated for the overall sample. Mean and standard deviation were calculated for continuous variables, and frequency and percentage for all other categorical variables. To determine the factors associated with the measurement discrepancy between the generic and disease-specific QOL measures, reverse scoring was first applied to SQLS total scores so that higher scores indicate better QOL; new total scores of SQLS and overall utility scores of HUI3 were then converted into *Z*-scores; and finally, *Z*-scores difference (i.e., measurement discrepancy) was obtained by subtracting *Z*-scores of HUI3 from that of SQLS (Hayhurst et al., 2014). When a *Z*-scores difference deviates further away from 0, it implies higher discrepancy between the two QOL scores. A positive value of the *Z*-scores difference indicates tendency of respondents to score higher levels of QOL on SQLS than HUI3 while a negative value indicates vice versa. For each of the QOL outcome (SQLS total score, HUI3 overall utility score and *Z*-score difference), we ran hierarchical linear regression models with patients' sociodemographic (age, gender, ethnicity, education, employment and marital status) and clinical characteristics (illness duration, hospitalization in the past one year and smoking history) included as independent variables in the first model; followed by adding comorbidity status (both psychiatric and medical disorders) in the second model and finally, adding PANSS factors in the final model. For further comparison between the two types of QOL measures and testing of their relationships with select clinical attributes, independent *t*-tests were conducted to examine difference in QOL domain scores due to comorbidity status while Pearson's correlation tests were performed to examine relationships between PANSS factors and the QOL domain scores.

3. Results

3.1. Participants

Table 1 shows the profile of the study sample. In terms of sociodemographic characteristics, participants were mostly males (56.2%), Chinese (58.6%), had completed up to secondary education (49.4%), employed (51.8%) and not married (75.3%). Their mean age and duration of illness were 39.9 and 14.5 years, respectively. In terms of clinical characteristics, the majority did not have a history of smoking (55.8%) or hospitalization in the past one year (66.9%). For comorbidities, most did not have any co-existing psychiatric disorder (69.7%) but had a co-existing medical disorder (62.2%). The mean (SD) PANSS total score was 47.8 (15.3).

3.2. Disease-specific and generic QOL scores

For the disease-specific SQLS, the mean (SD) of the total score was 32.6 (17.7) and domain scores (in order of increasing QOL) were 36.5 (17.5) for *energy/ motivation*, 34.9 (22.7) for *psychosocial*, and 26.5 (19.8) for *symptoms*.

For the generic HUI3, the mean (SD) of overall utility score was 0.65 (0.31) and domain scores (single-attribute utility functions in order of increasing QOL) were 0.83 (0.24) for *cognition*, 0.88 (0.20) for *emotion*, 0.90 (0.19) for *speech*, 0.91 (0.17) for *pain*, 0.91 (0.16) for *vision*, 0.96 (0.17) for *hearing*, 0.97 (0.10) for *ambulation* and 0.97 (0.11) for *dexterity*.

Upon conversion to *Z*-scores, the HUI3 overall utility scores and SQLS total scores were moderately correlated; $r = 0.667$, $p < 0.001$.

3.3. Factors associated with QOL outcomes

Table 2 shows the factors associated with SQLS total score, HUI3 overall utility score and their measurement discrepancy. Multicollinearity among all the predictors was assessed, with variance inflation factors reported to be below 2 across all the final models. For SQLS, being non-Chinese (vs. Chinese) and unemployed (vs. employed) were associated with higher total scores (i.e., lower perceived QOL) while all PANSS factors, except *excitement* and *cognitive* factors, were positively associated with the total scores (i.e., the higher the symptom severity on PANNS, the lower the perceived QOL measured by SQLS). For HUI3, having a psychiatric comorbidity (vs. no psychiatric comorbidity), higher PANSS *positive* and *depression* factor scores were associated with lower overall utility score (i.e., lower QOL). Ethnicity, employment and PANSS *depression* factor were found to be significantly associated with the measurement discrepancy.

Table 1
Profile of sample ($N = 251$).

		n	%
Gender	Male	141	56.2
	Female	110	43.8
Ethnicity	Chinese	147	58.6
	Non-Chinese	104	41.4
Education	Secondary and Below	124	49.4
	Post Sec to Pre-U	88	35.1
	University	39	15.5
Employment	Employed	130	51.8
	Unemployed	121	48.2
Marital status	Married	62	24.7
	Not married	189	75.3
Hospitalization in the past year	Yes	83	33.1
	No	168	66.9
Smoking history	Yes	111	44.2
	No	140	55.8
Psychiatric comorbidity	Yes	76	30.3
	No	175	69.7
Medical comorbidity	Yes	156	62.2
	No	95	37.8
	Mean	**SD**	
Age	39.9	10.2	
Illness duration	14.5	10.6	
PANSS positive factor	8.18	5.02	
PANSS negative factor	7.59	3.68	
PANSS excitement factor	4.29	1.97	
PANSS depressive factor	6.08	3.30	
PANSS cognitive factor	2.87	1.47	

3.4. QOL domains: Correlations with PANSS factors (Table 3)

For SQLS, all PANSS factors (except the *cognitive* factor) were significantly and positively correlated with all SQLS domains (*psychosocial, motivation/ energy* and *symptoms/ side effects*).

For HUI3, significant correlations with PANSS factors were all in the negative direction (i.e. higher symptom severity correlated with lower perceived QOL). *Positive* factor correlated with all HUI3 domains except *hearing; negative* factor correlated with all HUI3 domains except *hearing, ambulation and dexterity; excitement* factor correlated with all HUI3 domains except *vision, hearing* and *cognition; depression* factor correlated with all HUI3 domains except *hearing* and *dexterity*; and lastly *cognitive* factor correlated with only HUI3 *speech* and *cognition* domains.

3.5. QOL domains: Relationship with comorbidity status (Table 4)

For SQLS, only the *psychosocial* domain was able to differentiate psychiatric comorbidity status.

For HUI3, psychiatric comorbidity status could be differentiated by the *emotion* and *cognition* domains while medical comorbidity status could be differentiated by the *ambulation* domain.

Table 2
Factors associated with QOL and measurement discrepancy.

		SQLS			HUI3			*Z* scores difference		
Model		Adj. R^2	*F*	*P*-Value	Adj. R^2	*F*	*P*-Value	Adj. R^2	*F*	*P*-Value
1. General characteristics		0.078	3.122	0.001	0.014	1.358	0.201	0.030	1.761	0.068
2. Comorbidities		0.081	2.836	0.001	0.045	1.984	0.026	0.036	1.786	0.051
3. PANSS		0.485	14.830	<0.001	0.291	7.038	<0.001	0.079	2.263	0.004
Variables		**B**	**95% CI**	**P-value**	**B**	**95% CI**	***P*-value**	**B**	**95% CI**	**P-value**
Gender	Male	–	–	–	–	–	–	–	–	–
	Female	0.026	−3.576–3.629	0.989	0.018	−0.056–0.093	0.630	−0.060	−0.282–0.162	0.595
Ethnicity	Chinese	–	–	–	–	–	–	–	–	–
	Non-Chinese	4.048	0.358–7.738	0.032	0.025	−0.051–0.102	0.512	−0.310	−0.537–0.082	0.008
Education	Secondary and below	–	–	–	–	–	–	–	–	–
	Post sec to pre-U	−1.111	−4.891–2.668	0.563	−0.012	−0.091–0.066	0.754	0.103	−0.130–0.335	0.386
	University	1.308	−3.817–6.434	0.616	0.016	−0.090–0.122	0.768	−0.125	−0.440–0.191	0.437
Employment	Employed	–	–	–	–	–	–	–	–	–
	Unemployed	5.349	1.987–8.710	0.002	−0.06	−0.075–0.064	0.874	−0.284	−0.491–0.077	0.007
Marital status	Married	1.644	−2.359–5.647	0.419	−0.014	−0.097–0.069	0.736	−0.047	−0.294–0.199	0.706
	Not married	–	–	–	–	–	–	–	–	–
Hospitalization (past year)	Yes	−0.595	−4.066–2.877	0.736	−0.018	−0.089–0.054	0.628	0.090	−0.124–0.304	0.407
	No	–	–	–	–	–	–	–	–	–
Smoking history	Yes	−0.780	−4.451–2.891	0.676	−0.002	−0.078–0.074	0.965	0.049	−0.177–0.275	0.667
	No	–	–	–	–	–	–	–	–	–
Psychiatric comorbidity	Yes	2.508	−1.161–6.178	0.179	−0.114	−0.190–0.038	0.003	0.222	−0.004–0.448	0.054
	No	–	–	–	–	–	–	–	–	–
Medical comorbidity	Yes	–	–	–	–	–	–	–	–	–
	No	−0.207	−3.909–3.494	0.912	0.046	−0.030–0.123	0.234	−0.137	−0.365–0.091	0.238
Age		−0.092	−0.311–0.126	0.407	0.000	−0.004–0.005	0.860	0.004	−0.010–0.017	0.568
Duration of illness		0.003	−0.203–0.209	0.976	−0.001	−0.005–0.003	0.692	0.003	−0.010–0.015	0.691
PANSS *positive* factor		1.180	0.775–1.585	<0.001	−0.022	−0.030–0.013	<0.001	0.003	−0.022–0.027	0.842
PANSS *negative* factor		0.595	0.112–1.078	0.016	−0.008	−0.018–0.002	0.119	−0.008	−0.038–0.022	0.589
PANSS *excitement* factor		−0.231	−1.125–0.663	0.611	0.001	−0.017–0.020	0.891	0.009	−0.046–0.064	0.750
PANSS *depression* factor		2.149	1.540–2.759	<0.001	−0.020	−0.032–0.007	0.003	−0.059	−0.096–0.021	0.002
PANSS *cognitive* factor		−1.201	−2.398–0.004	0.049	−0.002	−0.027–0.023	0.884	0.074	−0.000–0.147	0.050

4. Discussion

There has been a shift in mental health care services from an emphasis on treatment that focused on reducing disorder-specific symptoms to focus on improving the quality of life (QOL) of those suffering from chronic diseases such as schizophrenia. There is, therefore, a growing interest in the development of QOL measures to provide useful information for planning and evaluating clinical interventions in patients with schizophrenia. In the current study, we examined the relationship of predictor variables with disease-specific and generic QOL and attempted to understand the drivers of the discrepancy between the two which is a previously under-researched topic. Both the SQLS and HUI3 were selected as our choice of QOL measures as they have been validated in local populations with schizophrenia. In addition, the generic HUI3 covers a wide spectrum of major life domains (including those that examine physical health and general functioning) that are distinct from those of the disease-specific SQLS, which would thus provide us with a greater difference for comparison. A significant but only moderate correlation ($r = 0.667$) was found between the two scales in our sample of patients with schizophrenia ($n = 251$) and this confirms the existence of differing constructs in defining QOL by the two QOL measures.

4.1. Sociodemographic factors

Our study revealed two sociodemographic variables- ethnicity and employment- to be the main drivers for the discrepancy between the two QOL measures. A closer examination of the findings from the regression analyses for SQLS and HUI3 outcomes revealed that non-Chinese and those unemployed were more likely to rate their levels of QOL worse on the disease-specific SQLS than Chinese and those employed, respectively but with non-significant differences on the generic

Table 3
Correlations between QOL domains and PANSS factors.

		PANSS *positive* factor	PANSS *negative* factor	PANSS *excitement* factor	PANSS *depression* factor	PANSS *cognitive* factor
SQLS	*Psychosocial*	0.537**	0.227**	0.181**	0.635**	0.055
	Energy/Motivation	0.413**	0.285**	0.126*	0.448**	0.089
	Symptoms/Side effects	0.545**	0.176**	0.193**	0.541**	0.073
HUI3 (single-attribute utility scores)	*Vision*	−0.257**	−0.159*	−0.065	−0.192**	−0.042
	Hearing	−0.062	−0.041	−0.060	0.101	0.016
	Speech	−0.365**	−0.207**	−0.164**	−0.242**	−0.175**
	Emotion	−0.358**	−0.141*	−0.134*	−0.435**	−0.007
	Pain	−0.190**	−0.126*	−0.202**	−0.175**	0.007
	Ambulation	−0.220**	−0.052	−0.258**	−0.231**	−0.061
	Dexterity	−0.159*	−0.076	−0.150*	0.009	−0.095
	Cognition	−0.339**	−0.144*	−0.023	−0.390**	−0.218**

*$p < 0.05$, **$p < 0.01$.

Table 4
Relationships between QOL domains and comorbidity status.

		Other psychiatric disorder			Other medical disorder		
		Yes	No	*P*-Value	Yes	No	P-Value
SQLS	*Psychosocial*	41.32 ± 23.25	32.12 ± 21.96	0.003	34.94 ± 23.41	34.84 ± 21.62	0.972
	Energy/ Motivation	39.61 ± 16.95	35.08 ± 17.54	0.059	37.25 ± 18.11	35.15 ± 16.32	0.357
	Symptoms	29.65 ± 19.82	25.16 ± 19.76	0.100	27.74 ± 19.62	24.51 ± 20.16	0.211
HUI3 (single-attribute utility scores)	*Vision*	0.89 ± 0.19	0.91 ± 0.14	0.284	0.90 ± 0.17	0.91 ± 0.15	0.569
	Hearing	0.94 ± 0.20	0.96 ± 0.14	0.494	0.94 ± 0.19	0.97 ± 0.10	0.207
	Speech	0.87 ± 0.21	0.90 ± 0.17	0.254	0.88 ± 0.19	0.91 ± 0.17	0.252
	Emotion	0.82 ± 0.25	0.90 ± 0.17	0.006	0.88 ± 0.18	0.87 ± 0.22	0.752
	Pain	0.90 ± 0.13	0.91 ± 0.18	0.788	0.90 ± 0.18	0.91 ± 0.15	0.565
	Ambulation	0.95 ± 0.11	0.97 ± 0.09	0.101	0.95 ± 0.12	0.98 ± 0.05	0.032
	Dexterity	0.96 ± 0.11	0.97 ± 0.10	0.623	0.96 ± 0.11	0.97 ± 0.10	0.391
	Cognition	0.75 ± 0.27	0.86 ± 0.21	0.001	0.82 ± 0.25	0.84 ± 0.22	0.513

HUI3. A study among patients with schizophrenia in an Asian population also found that being Chinese was associated with better QOL ratings on mental health component compared to the Malays and Indians but there was no ethnic difference in terms of QOL on their physical health component (Osman et al., 2009). Additional analyses with our data revealed that although the two major ethnic groups did not score differently in terms of PANSS total and domain scores, non-Chinese scored significantly worse on the *symptoms/ side effects* domain but not the *psychosocial* and *motivation/ energy* domains compared to the Chinese, suggesting that non-Chinese may experience greater side effects such as disturbed sleep, shaking/trembling or dizzy spells due to their condition and medications despite having similar core symptom severity as the Chinese. Nonetheless, further research will need to be conducted to explore such ethnic differences.

The result for employment status is not surprising given that unemployment tends to have a greater impact on one's mental health and psychological well-being (better measured by disease-specific QOL) rather than physical health states (better measured by generic QOL) (Pharr et al., 2012).

4.2. Symptom severity of patients with schizophrenia measured by PANSS

To the best of our knowledge, only one existing study had also looked at the predictors of disease-specific and generic QOL among individuals with schizophrenia (Zeng et al., 2015). In this study by Zeng and colleagues, only monthly household income and subjective social support were significant predictors of generic QOL while monthly household, social support factors, current hospitalization duration, PANSS negative and general psychopathology symptoms were significant predictors of disease-specific QOL. Firstly, in terms of correlates of disease-specific QOL, we observed similar findings where most of our PANSS factors were found to be associated with SQLS. However, in terms of correlates of generic QOL, two PANSS factors *(positive* and *depression)* were found to be associated with HUI3 in our study while none of PANSS subscales was associated with the World Health Organization Quality of Life – Brief Form in Zeng's study. The disparity in findings may be due to the use of a different generic measure, PANSS factor structure, set of confounding variables, and even patient group. For a PANSS score range of 30–210, the study by Zeng and colleagues was conducted among inpatients with more severe schizophrenia symptoms (mean PANSS total score of 63.27) while our study was conducted among outpatients who required less intense care (mean PANSS total score of 47.79).

It was also observed that the disease-specific QOL scale may be more sensitive in measuring PANSS *depression* factor than the generic QOL scale. However, it is unclear why other core symptoms of schizophrenia such as *positive* and *negative* symptoms did not significantly predict the discrepancy despite literature lending support to the use of disease-specific QOL measures to assess treatment efficiency given their superior psychometric properties in measuring disorder-specific symptomatic change (Mulhern et al., 2014; Papaioannou et al., 2011; Wiebe et al., 2003). Our correlation analyses revealed that although PANSS *positive, negative, excitement, and depression* factors were found to be significantly correlated with all three domains of SQLS, each of these PANSS factors was also significantly correlated with at least five different domains (except *hearing*) of HUI3, suggesting that the generic scales may also be useful for capturing QOL impairment due to some of these PANSS factors in our sample. Nonetheless, the five PANSS factors did explain higher percentage of QOL variation (based on R^2 change in Table 2) in the disease-specific SQLS compared to the generic HUI3.

Lastly, our results showed PANSS *cognitive* factor to be almost significant ($p = 0.05$) in predicting the discrepancy measure. PANSS *cognitive* factor was also found to correlate significantly with the *speech* and *cognition* domains of the HUI3 but not with any domain of the SQLS, suggesting that the HUI3 may be more sensitive in measuring cognitive dysfunction than the SQLS. As mentioned, cognitive dysfunction has been viewed as a core feature of schizophrenia and is associated with real world functional performance independent of psychotic symptoms or mood states (Bowie and Harvey, 2006). *Cognitive* factors were also found to predict quality of life among schizophrenia patients (Ritsner, 2007) and yet, the disease-specific SQLS did not appear to perform better than the generic HUI3 in detecting change in cognitive scores. Overall, our results may suggest that the generic QOL measure may be able to perform as well as the disease-specific QOL measure in terms of their abilities to reflect symptom severity as assessed by PANSS in patients with schizophrenia.

4.3. Psychiatric and medical comorbidity

Another noteworthy finding from the current study and that of Zeng's (Zeng et al., 2015) was that both studies did not find medical comorbidity to be significantly associated with generic QOL and this contradicts our hypothesis. The inclusion of a heterogeneous class of chronic medical conditions including any metabolic, skin, pain or other disorders with no measure of the duration or severity may explain this inability to predict the generic QOL. One other possibility could be that the patients' primary psychiatric condition (i.e., schizophrenia) has been ranked among one of the top ten leading causes of disease-related disability in the world (Tandon et al., 2008) and thus in comparison, patients' co-existing medical conditions may have a lesser, negative impact on their QOL. Although medical comorbidity also did not significantly predict the discrepancy measurement in our regression analysis, analyses conducted using individual domain scores of both the disease-specific and generic QOL measures showed that those having co-existing medical condition(s) did score significantly lower on the *ambulation* domain of the HUI3 than those without. Scorings on the SQLS domains were, on the other hand, unable to reflect any difference due to physical comorbidity. In terms of psychiatric comorbidity, the generic HUI3 does seem to be a better measure for capturing QOL difference due to this status. Psychiatric comorbidity was not only

found to be significantly associated with HUI overall utility scores but it also approached significance ($p = 0.054$) in terms of predicting the discrepancy measurement. Furthermore, those with a secondary psychiatric disorder scored lower on the *emotion* and *cognition* domains of HUI3 than those without. Overall, our study demonstrated that generic instruments may be more useful than the disease-specific instruments for assessing QOL impairment due to psychiatric and medical comorbidity in patients with schizophrenia.

4.4. Limitations

While this study aids in better understanding of the factors associated with the disease-specific and generic QOL scales and their measurement discrepancy in patients with schizophrenia, there are some limitations that should be taken into consideration when interpreting the findings. First, the direction of causality among variables cannot be determined due to the cross-sectional study design. Second, the current findings on the statistical predictors of QOL measure discrepancy may not apply to discrepancies between other disease-specific and generic QOL measures. We also did not examine other factors such as the effects of antipsychotics, coping style and social support which are known to have an impact on the QOL of patients with schizophrenia. Lastly, the convenience sampling strategy adopted for recruiting our participants limits generalizability of our findings. As demonstrated from the difference in findings with the study by Zeng and colleagues, our study may only be generalizable to the outpatient population with less acute schizophrenia symptoms.

5. Conclusion

In this study, we examined the determinants of the generic and disease-specific QOL measures and found PANSS factors to be associated with both generic QOL and disease-specific QOL while psychiatric comorbidity was found to be associated with only generic QOL. Improving clinical symptoms severity remains the key factor for enhancing overall quality of life while treating comorbid psychiatric conditions may additionally promote better generic QOL in patients with schizophrenia. Besides ethnicity and employment status, only PANSS *depression* factor was found to significantly predict the difference in the scores of the two QOL measures. In other words, change in PANSS *depression* factor score is associated with a much larger change in rating on the disease-specific SQLS total score compared to rating on the generic HUI3 overall utility score. Further analyses using QOL domain scores revealed domains of the generic HUI3 to be more useful than those of the disease-specific SQLS in differentiating PANSS *cognitive* factor and medical comorbidity status. While it is known that the use of disease-specific QOL measures allow clinicians to target and systematically follow specific symptoms, gauge illness severity, or track treatment outcomes, our study recommends the combined use with generic QOL measures in clinical practice for a more accurate and holistic assessment of the well-being of these patients. Considering that individuals with schizophrenia are at higher risk of having other comorbid problems which may further impair their functioning and QOL and that our findings suggest that generic HUI3 can perform as well as the disease-specific SQLS in assessing the impact of PANSS symptoms severity, the use of generic QOL scales may be preferred for measuring QOL as they encompass the overall clinical presentation instead of only the disorder-specific symptoms.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgment

Not applicable.

Data statement

For access to data, please contact Dr Edimansyah Abdin via edimansyah_abdin@imh.com.sg.

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