



Quality of Life in Schizophrenia: A Meta-Analysis of Comparative Studies

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Published online: 22 May 2019

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Abstract

Studies and findings regarding the impact of schizophrenia on quality of life (QOL) has been highly variable. This meta-analysis compared QOL between schizophrenia subjects and healthy controls with a focus on standardized measures. A systematic literature search was conducted through Pubmed, PsycINFO, EMBASE, Cochrane Library and Web of Science databases. Only studies using the World Health Organization Quality of Life (WHOQOL) or its brief version or the Short Form-36 Health Survey (SF-36) were included. Fifteen case-control studies with 2195 schizophrenia subjects and 1508 healthy controls were included in this meta-analysis. The WHOQOL/WHOQOL-BREF score was significantly lower in physical health (SMD = -1.80, 95% CI: -2.31 to -1.28, $P < 0.001$), psychological health (SMD = -1.28, 95% CI: -1.72 to -0.83, $P < 0.001$), social relationships (SMD = -1.60, 95% CI: -2.05 to -1.15, $P < 0.001$), and environment domains (SMD = -0.98, 95% CI: -1.38 to -0.59, $P < 0.001$) in schizophrenia subjects compared to controls. The SF-36 score was significantly lower in both physical (SMD = -1.09, 95% CI: -1.41 to -0.76, $P < 0.001$) and mental health domains (SMD = -2.08, 95% CI: -3.58 to -0.59, $P = 0.006$) in schizophrenia subjects than in controls. Subgroup and meta-regression analyses found that age, male gender, illness duration and income have significant moderating effects on QOL. The meta-analysis of studies with standardized measures confirmed that QOL in schizophrenia subjects is significantly lower than healthy controls. Effective interventions should be developed to improve QOL for this population.

Keywords Schizophrenia · Quality of life · Meta-analysis

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Introduction

Schizophrenia is a severe, chronic psychiatric disorder characterized by delusions, hallucinations and cognitive impairment [1], with the lifetime prevalence of 0.4% worldwide [2]. Schizophrenia is usually associated with significant functional impairment [3, 4] which hinders reintegration into the community for those affected [5] even after being clinically stable. In addition, stigma and discrimination [6] and medication-induced side effects, such as metabolic syndrome [7], are added burden on the illness.

Quality of life (QOL), is defined as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” by the WHO [8]. QOL scales which usually consist of physical health, psychological state, social relationships and environmental domains, have widely been used as major outcome measures in the treatment of schizophrenia [9, 10]. Findings on the QOL between schizophrenia subjects and healthy controls have been varied [11–15]. Both demographic (such as gender, age and education) and clinical characteristics (such as psychopathology, use of psychotropic medications and side effects) have been found to influence QOL in schizophrenia patients [16]. To date there have been no meta-analysis or systematic review to compare QOL between schizophrenia subjects and healthy controls.

Further, studies of QOL have employed various types of QOL measures which make direct comparison between studies difficult. Examples of standardized QOL measures include the World Health Organization Quality of Life (WHOQOL) [17] or its brief version (WHOQOL-BREF) [8] or Short Form-36 Health Survey (SF-36) [18]. These are generic QOL measures used to assess the “general” QOL of patients with any diseases and healthy subjects. Generic instruments can compare between different conditions, but are not sensitive enough to identify small QOL changes.

This meta-analysis aimed to compare QOL between schizophrenia subjects and healthy controls. In order to reduce study heterogeneity and allow data from different studies to be meta-analyzed, only those using the two most widely used generic QOL measures, i.e., the WHOQOL/WHOQOL-BREF and SF-36, were included for analyses.

Methods

This meta-analysis was performed according to the guidelines recommended by the Meta-analysis of observational studies in epidemiology [19].

Search Strategy

Two researchers (MD and LL) independently searched publications via PubMed, PsycINFO, EMBASE, Cochrane Library, Web of Science from their inception date until September 26, 2017. The search terms included: (“World Health Organization Quality of Life” OR “WHOQOL” OR “36-Item Short Form Health Survey” OR “SF-36”) AND schizophrenia. In addition, we browsed relevant review articles to identify potentially eligible studies. The same two researchers independently screened the titles and abstracts, followed by reading the full texts of identified studies. The potentially eligible studies were double-checked to assess their eligibility. Any disagreement was resolved by involving a third researcher (YTX). The literature selection procedure was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PEISMA) flow diagram [20].

Inclusion and Exclusion Criteria

Studies were included in this meta-analysis if they fulfilled the following criteria: [1] Participants: adult patients with schizophrenia according to any diagnostic criteria, such as the Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV) [21], the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) [22] or the Chinese classification of mental disorders (CCMD) [23]; [2] Intervention: not applicable; [3] Comparison: healthy controls; [4] Outcomes: QOL assessed using the (WHOQOL) or WHOQOL-BREF or SF-36 [5] Study design: case-control or cohort studies (only baseline data of cohort studies were included); [6] having meta-analyzable data. Exclusion criteria were as follows: [1] studies focused on special populations (e.g. elderly patient or university students); [2] case reports/series. If more than one publication was based on the same dataset, the publication with complete information was included.

The WHOQOL/WHOQOL-BREF covers four QOL domains: physical and psychological health, social relationships and environmental factors [17]. The SF-36 [24] addresses eight domains: physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems and mental health. Traditionally, the first four SF-36 domains were collapsed into a physical, whereas the remaining four formed a mental component score in clinical studies.

Data Extraction

Two researchers (MD and LL) extracted relevant information from the included studies and recorded on a standardized data collection form, including the first author's name, publication year, study site, study design, sample size, diagnostic criteria, source and mean age of participants, proportion of males, assessment tool on QOL, total and subscale scores of QOL expressed as mean/standard deviation (SD). We contacted authors of included studies by emails for necessary data if needed. If the WHOQOL-BREF and WHOQOL-100 were used concurrently in one paper, the score of WHOQOL-BREF were extracted in order to avoid inter-dependence.

Quality Assessment

The methodological quality of included studies was assessed independently by two researchers (MD and LL) using the Newcastle-Ottawa Scale (NOS) [25], which has a maximum score of 9, and with 7 and above as “high quality” [26].

Statistical Analysis

All data analyses were conducted with the Review Manager Software Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration) and Comprehensive Meta-Analysis Software Version 2.0 (Biostat Inc., Englewood, New Jersey, USA). Heterogeneity of studies was quantified using I^2 statistic [27], with large heterogeneity defined as $I^2 > 50\%$. The random effects model was used in all meta-analyzable outcomes. Standardized mean differences (SMDs) and their 95% confidence intervals (CIs) were used in the analyses. Significant level was set at 0.05 (2-tailed). Potential publication bias was assessed by visually inspecting of funnel plots and Egger's test [28].

Sensitivity and subgroup analyses and meta-regression were conducted in order to examine the potential sources of heterogeneity. Three subgroup analyses were performed according to: [1] illness duration (years): ≤ 9.6 vs. > 9.6 years (using median splitting method of illness duration); [2] PANSS total score: ≤ 61.7 vs. > 61.7 (using median splitting method of PANSS total score); [3] income of study site (country): high income vs. upper middle income vs. lower middle income (according to World Bank list of economies) [29]. Two meta-regression analyses were performed to examine the moderating effects of mean age and proportion of male gender.

Results

Literature Search

The procedure of literature search is shown in Fig. 1. The original search yielded 2201 electronic hits but 1373 unduplicated studies were removed by title and abstract and 75 studies were read in full-text. Finally, 15 studies met the study entry criteria and were included in this meta-analysis.

Study Characteristics and Quality Assessment

The characteristics of included studies are shown in Table 1. Fifteen studies (14 case-control and 1 cohort studies with total $n = 3703$) compared schizophrenia subjects ($n = 2195$) and healthy controls ($n = 1508$). Publication year ranged between 2004 and 2016, and mean age ranged between 27.3 and 41.2 years in schizophrenia group and between 29.6 and 42.1 years in control group. The mean years of education ranged from 11.3 to 12 years in schizophrenia group and ranged from 11 to 15.8 years in control group. Illness duration was available in 9 studies, ranging from 4.3 to 16.3 years. One study included inpatients, 9 studies included outpatients, and 2 studies included both; 13 studies used the WHOQOL/WHOQOL-BREF while 2 studies used SF-36. The NOS scores of the 15 studies ranged from 4 to 9 (median = 6.9) (Table 1); 10 studies were rated as “high quality” (NOS ≥ 7).

QOL in Schizophrenia

Using random effects models, compared with the control group the WHOQOL/WHOQOL-BREF score in the schizophrenia group was significantly lower in all its four domains including physical health (SMD = -1.22, 95% CI: -2.01 to -0.96, $P < 0.001$), psychological health (SMD = -1.00, 95% CI: -1.31 to -0.69, $P < 0.001$), social relationships (SMD = -1.13, 95% CI: -1.34 to -0.92, $P < 0.001$), and environment (SMD = -1.07, 95% CI: -1.60 to -0.54, $P < 0.001$) (Fig. 2). Similarly, the SF-36 scores in the schizophrenia group were also significantly lower in both physical (SMD = -1.09, 95% CI: -1.41 to -0.76, $P < 0.001$) and mental health domains (SMD = -2.45, 95% CI: -3.24 to -1.66, $P < 0.001$) than the control group (Fig. 2).

Publication Bias and Sensitivity Analyses

The Egger’s test did not identify any publication bias in the physical health ($t = 0.16$, $P = 0.87$) and social relationships domains ($t = 0.93$, $P = 0.37$), but identified bias in psychological health ($t = 2.80$, $P = 0.02$) and environment ($t = 3.05$, $P = 0.01$) domains. The trim and fill method

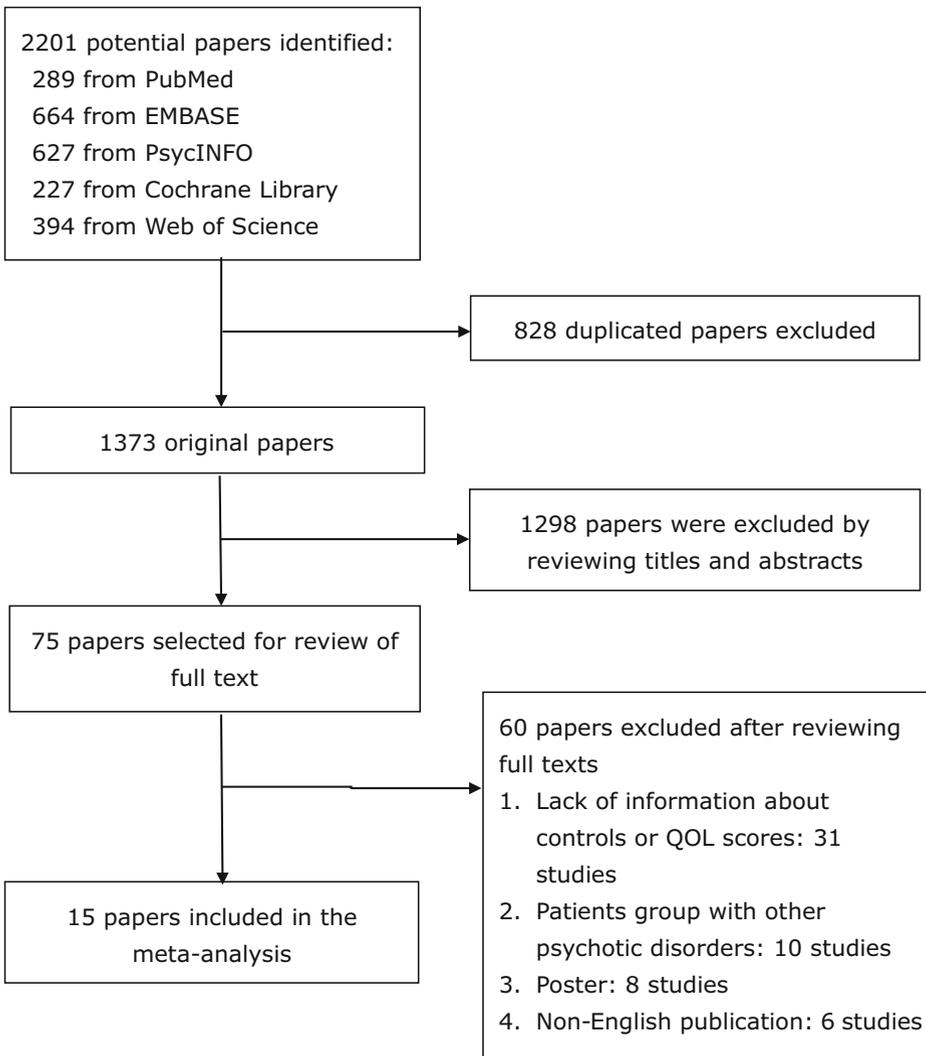


Fig. 1 Flowchart for study selection

revealed that the estimated numbers of missing studies was 7 in psychological health (adjusted random effects: SMD = -1.01, 95% CI: -1.32 to -0.70) and 5 in environment domains (adjusted random effects: SMD = -0.88, 95% CI: -1.07 to -0.69) (Fig. 3) [30]. After removing each study individually, the results did not change significantly for all domains of WHOQOL-BREF.

Subgroup Analyses and Meta-Regression

Subgroup analyses revealed that shorter illness duration (<9.6 years) was associated with better psychological and lower environmental QOL, while higher income was associated with lower social and environmental QOL. Severity of psychotic symptoms as measured by the PANSS was not associated with any QOL domains (Table 2).

Table 1 Characteristics of the studies included in the meta-analysis

NO.	Principal author	Publication year	Country	Design	N	n (S/C)	Schizophrenia patients				NOS score				
							QOL scale	Mean age (yrs)	Male (%)	Education (yrs)		Source of patients	Diagnostic criteria	Illness duration	PANSS or BPRS
1	Gomes	2016	Portugal	Case-control	64	32/32	WHOQOL-BREF	41.1	71.9	NA	Outpatients	DSM-IV	NA	NA	8
2	Sum	2015	Singapore	Case-control	178	122/56	WHOQOL-BREF	32.4	41.8	5.8	NA	DSM-IV	5.8	38.6	9
3	Afonso	2014	Portugal	Case-control	68	34/34	WHOQOL-BREF	33.8	64.7	11.8	Outpatients	DSM-IV	11.8	66.9	8
4	Kerfling	2013	Germany	Case-control	81	31/50	SF-36	38.4	58.1	NA	Outpatients	ICD-10	NA	47.7	7
5	Maat	2012	Netherland	Cohort	1584	1032/552	WHOQOL-BREF	27.3	77	4.3	NA	DSM-IV	4.3	5.5	5
6	Lucas	2012	Spain	Case-control	317	216/101	WHOQOL-BREF	38.5	60	NA	Mix	NA	NA	NA	4
7	Vancampfort	2011	Belgium	Case-control	100	60/40	SF-36	38.1	63.3	14.2	Inpatients	DSM-IV	14.2	NA	7
8	Woon	2010	Singapore	Case-control	130	83/47	WHOQOL-BREF	30.9	63.9	5.8	Outpatients	DSM-IV	5.8	39.9	9
9	Ulas	2010	Turkey	Case-control	173	88/85	WHOQOL-BREF	35.5	61.4	10.5	Mix	DSM-IV	10.5	65.1	7
10	Yen	2008	Taiwan	Case-control	202	96/106	WHOQOL-BREF	32.5	47.9	8.7	Outpatients	DSM-IV	8.7	NA	6
11	Ulas	2008	Turkey	Case-control	118	72/46	WHOQOL-BREF	35.7	61.1	10.6	NA	DSM-IV	10.6	58.2	6
12	Picardi	2006	Italy	Case-control	227	162/65	WHOQOL-BREF	36.8	69.1	NA	Outpatients	NA	NA	NA	5
13	Akvardar	2006	Turkey	Case-control	87	38/49	WHOQOL-BREF	37	60.5	NA	Outpatients	DSM-IV	NA	81.6	7
14	Awadalla	2005	Sudan	Case-control	310	99/211	WHOQOL-BREF	NA	NA	NA	Outpatients	ICD-10	NA	NA	7
15	Alptekin	2004	Turkey	Case-control	64	30/34	WHOQOL-BREF	39.7	46.7	16.3	Outpatients	DSM-IV	16.3	NA	8

BPRS, Brief Psychiatric Rating Scale; C, controls; DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD, International Statistical Classification of Diseases and Related Health Problems; NA, not applicable; NOS, Newcastle-Ottawa Scale; PANSS, Positive and Negative Syndrome Scale; S, schizophrenia; SF-36, Short Form-36 Health Survey; WHOQOL-BREF: World Health Organization Quality of Life- Brief Form; yrs, years

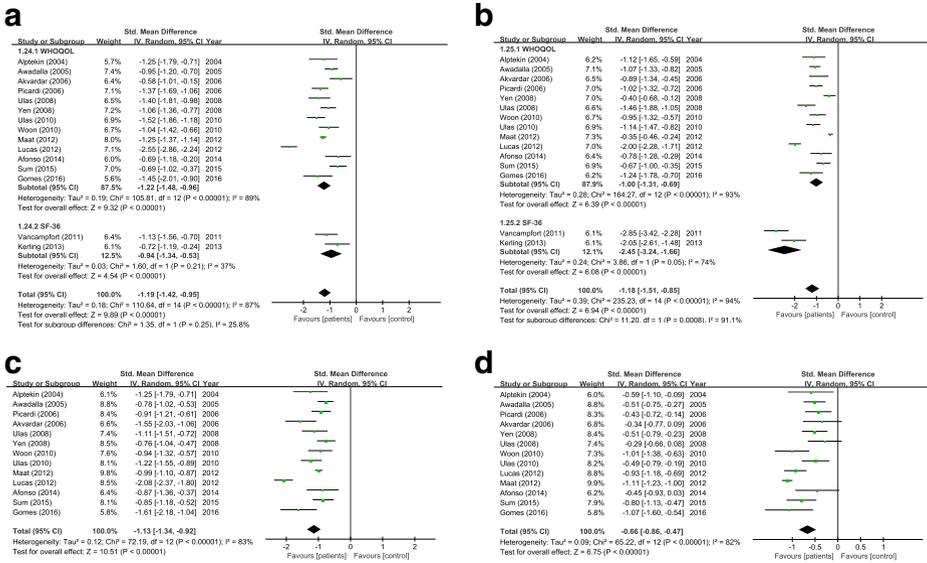


Fig. 2 Meta-analysis of QOL domains as assessed by WHOQOL and SF-36

In the meta-regression analyses, older age was negatively and significantly associated with higher QOL as assessed by the WHOQOL, including physical health ($B = -0.03$, $z = -3.22$, $P = 0.001$), psychological health ($B = -0.09$, $z = -10.86$, $P < 0.001$), and social relationships ($B = -0.04$, $z = -4.76$, $P < 0.001$) domains but not for the environment ($B = 0.04$, $z = 5.13$, $P < 0.001$) domain. Proportion of male subjects was positively associated with psychological health ($B = 0.02$, $z = 5.32$, $P < 0.001$) domain, and negatively associated with environment ($B = -0.02$, $z = -4.77$, $P < 0.001$) domain; it was not associated with physical health ($B = -0.005$, $z = -1.37$, $P = 0.17$) and social relationships ($B = 0.003$, $z = 0.72$, $P = 0.47$) domains.

Discussion

To the best of our knowledge, this was the first meta-analysis to compare QOL between schizophrenia subjects and healthy controls, with a focus on studies using two widely used QOL measures. Compared to healthy controls, schizophrenia subjects showed significantly lower QOL in physical, psychological, social and environmental domains. Several possible reasons could explain this finding. First, psychotic symptoms and comorbidities, such as depression and anxiety, medication-induced side effects could have an adverse impact on QOL [31, 32]. Second, poor nutrition [33], reduced physical activity [34, 35], and metabolic syndrome [7, 36] that are common in schizophrenia subjects, have been associated with lower QOL [37]. Third, social isolation, lack of access to environmental resources, stigmatization of the illness and discrimination, cognitive impairment and limited employment opportunities are factors commonly associated with schizophrenia, which could lead to poor life satisfaction and high psychological stress and low QOL [12, 38–40].

Our study found that older age was associated with lower QOL in most domains, which is consistent with previous findings [9, 41, 42]. Older subjects with schizophrenia are likely to

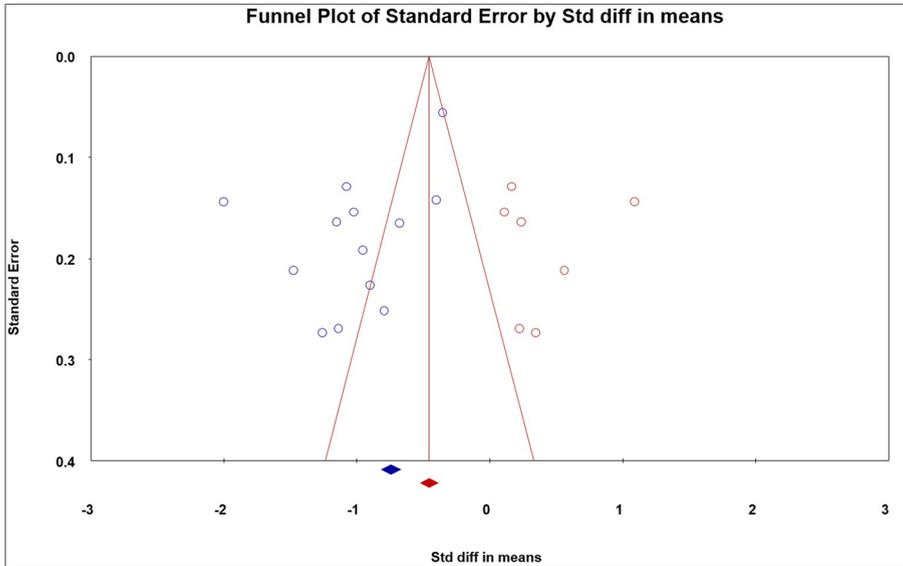
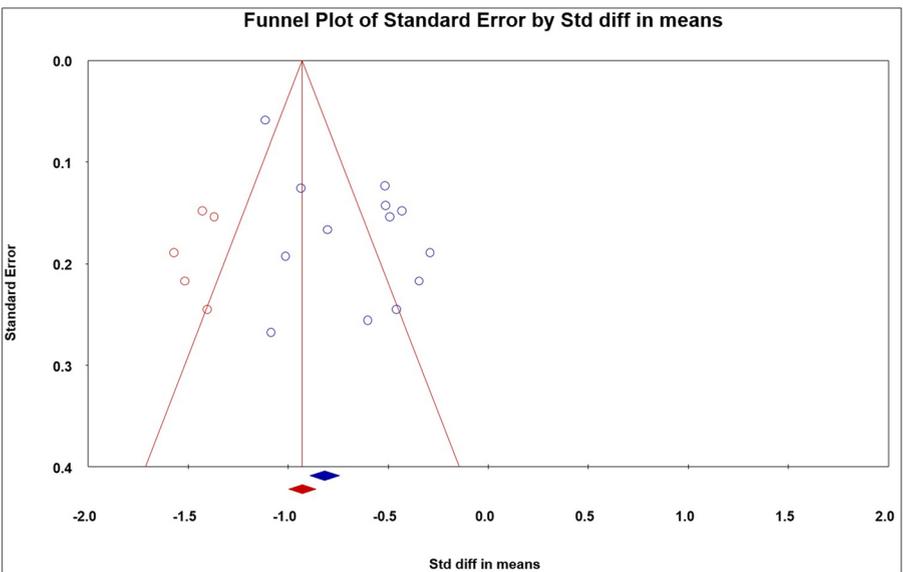
a**b**

Fig. 3 Filled funnel plots with Psychological and Environmental domain as assessed by WHOQOL

have more frequent physical comorbidities, poorer support and more severe cognitive and social functioning impairment [43–45], which could lead to poorer physical, psychological and social QOL compared to their younger counterparts. The association between gender and QOL in schizophrenia has been inconsistent; for example, some [9, 41] but not all [46] studies found that male patients had lower QOL. We found female subjects had lower psychological QOL, while males had lower environmental QOL. Gender differences in occupational and cognitive

Table 2 Subgroup analyses of WHOQOL scales

Subscale	Subgroup	Number of studies	Number of cases	Number of controls	SMD	95% CI	I ² (%)	P value	Q (P value)
Physical health	Overall	13	2006	1364	-1.22	-1.48, -0.96	89	<0.001	
	ID<9.6 (yrs)	4	1235	707	-1.04	-1.29, -0.78	73	0.01	0.84 (0.36)
	ID>9.6 (yrs)	4	224	199	-1.24	-1.59, -0.89	62	0.05	
	PANSS<61.7	3	277	149	-1.03	-1.43, -0.62	72	0.03	0.05 (0.83)
	PANSS>61.7	3	160	168	-0.94	-1.58, -0.31	86	<0.001	
	High income	8	1679	939	-1.27	-1.64, -0.90	92	<0.001	2.39 (0.30)
	Upper middle	4	228	214	-1.2	-1.62, -0.77	75	<0.007	
	Lower middle	1	99	211	-0.95	-1.20, -0.70			
	Overall	13	2006	1364	-1.00	-1.31, -0.69	93	<0.001	
	ID<9.6 (yrs)	4	1235	707	-0.55	-0.80, -0.30	74	0.01	10.81 (0.001)
Psychological health	ID>9.6 (yrs)	4	224	199	-1.15	-1.41, -0.89	30	0.23	
	PANSS<61.7	3	277	149	-1.01	-1.46, -0.57	77	0.01	0 (0.95)
	PANSS>61.7	3	160	168	-1	-1.23, -0.77	0	0.42	
	High income	8	1679	939	-0.92	-1.35, -0.49	95	<0.001	1.03 (0.60)
	Upper middle	4	228	214	-1.16	-1.39, -0.94	14	0.32	
	Lower middle	1	99	211	-1.07	-1.33, -0.82			
	Overall	13	2006	1364	-1.13	-1.34, -0.92	83	<0.001	
	ID<9.6 (yrs)	4	1235	707	-0.95	-1.04, -0.85	0	0.46	2.57 (0.11)
	ID>9.6 (yrs)	4	224	199	-1.13	-1.34, -0.93	0	0.67	
	PANSS<61.7	3	277	149	-0.95	-1.16, -0.74	0	0.60	1.69 (0.19)
Social Relationships	PANSS>61.7	3	160	168	-1.22	-1.55, -0.88	46	0.16	
	High income	8	1679	939	-1.12	-1.42, -0.81	89	<0.001	8.65 (0.01)
	Upper middle	4	228	214	-1.26	-1.46, -1.05	0	0.58	
	Lower middle	1	99	211	-0.78	-1.02, -0.53			
	Overall	13	2006	1364	-0.66	-0.86, -0.47	96	<0.001	
	ID<9.6 (yrs)	4	1235	707	-0.87	-1.17, -0.56	82	<0.001	5.24 (0.02)
	ID>9.6 (yrs)	4	224	199	-0.44	-0.64, -0.25	0	0.78	
	PANSS<61.7	3	277	149	-0.7	-1.10, -0.3	74	0.02	1.2 (0.27)
	PANSS>61.7	3	160	168	-0.44	-0.66, -0.22	0	0.86	
	High income	8	1679	939	-0.8	-1.02, -0.57	80	<0.001	6.46 (0.04)
Environment	Upper middle	4	228	214	-0.42	-0.61, -0.23	0	0.73	
	Lower middle	1	99	211	-0.51	-0.75, -0.27			
	Overall	13	2006	1364	-0.42	-0.61, -0.23	0	0.73	

Bolded values: *p* < 0.05; ID: illness duration; PANSS: Positive and Negative Syndrome Scale; SMD: standardized mean difference

impairment, psychopathology, response to treatment, employment rate and social support [47–50] could moderate the association between gender and QOL across studies.

Longer illness duration was associated with lower psychological but higher environmental QOL in this study, which is similar to previous findings [51, 52]. Subjects with longer illness duration may reduce their expectation over time and adapt to their situation, which may lead to increase life satisfaction in environmental domain [51, 53]. In addition, patients with longer illness duration could have a better relationship with their treating doctors; one study found that good therapeutic relationship could be a positive contributor to QOL in long-term patients [54]. In contrast, better insight is usually significantly associated with longer illness duration [55], which could lead to lower QOL [56–58]. Those living with schizophrenia with better insight could evaluate their life in a realistic way, and be aware of the extensive negative illness impact on their life conditions, thus leading to lower QOL [56].

Unexpectedly, we found higher income was associated with lower social and environmental QOL. According to the vulnerability-stress-coping QOL model [59], we assume that patients who had higher income are likely to have higher expectations regarding their social status and public acceptance. However, due to the extensive negative impact of schizophrenia on a wide range of life conditions, there is a great gap between their higher expectation and the reality, which then leads to lower social and environmental QOL. The relationship between QOL and severity of psychotic symptoms has been mixed; e.g., a study found that more severe positive symptoms were negatively associated with lower QOL [60], but another did not support this finding [61]. In this study there was no significant relationship between QOL and severity of psychotic symptoms.

The results of this meta-analysis should be interpreted with caution due to several limitations. First, in order to synthesize the data, only studies using the two mostly widely used QOL measures were included. Second, some factors related to QOL, such as use of antipsychotic medications, education level, family and social support, were not examined in this study due to incomplete data. Third, publication bias exists in psychological health and environmental domains.

In conclusion, this meta-analysis of studies confirmed that QOL in schizophrenia subjects is significantly lower than healthy controls, including in physical health, psychological health, social relationships and environmental domains. Clinicians and health authorities should develop effective interventions to address and improve QOL for this population.

Acknowledgements The study was supported by the University of Macau (MYRG2015-00230-FHS; MYRG2016-00005-FHS), the National Key Research & Development Program of China (No. 2016YFC1307200), the Beijing Municipal Administration of Hospitals Incubating Program (No. PX2016028) and the Beijing Municipal Administration of Hospitals' Ascent Plan (No. DFL20151801).

Compliance with Ethical Standards

Conflict of Interest All authors have no conflicts of interest to declare.

Human and Animal Rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent NA.

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Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

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