Quality of Life Research **11**: 753–762, 2002.

Validation of the World Health Organization quality of life instrument in patients with HIV infection☆

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Accepted in revised form 27 April 2002

Abstract

We studied the reliability and validity of the World Health Organization quality of life (WHOQOL) assessment instrument in patients with human immunodeficiency virus (HIV) infection. WHOQOL-BREF was used to assess 136 HIV-infected outpatients. The results were analyzed and compared with data from 213 healthy persons. The Cronbach's α for internal consistency ranged from 0.74 to 0.85 across domains in HIV-infected patients. The test–retest reliability ranged from 0.64 to 0.79 across domains at average 4-week retest interval. Factor analysis identified four major factors: social, psychological, environment, and physical, consistent with the four domains of the instrument. The scores of all four domains correlated positively with self-evaluated health status and happiness (r range: 0.52–0.60 and 0.55–0.73 across domains, respectively), and correlated negatively with the number and severity of symptoms (r range: -0.40 to -0.47 and -0.41 to -0.52, respectively). The scores of physical, psychological and social domains, but not the environment domain, discriminated between healthy persons and HIV-infected patients (all $p < 0.01$). We conclude that the WHOQOL-BREF can be a useful quality-of-life instrument in patients with HIV infection.

Key words: Human immunodeficiency virus infection, Quality of life, WHOQOL

Introduction

Improvements in life expectancy of patients with human immunodeficiency virus (HIV) infection in recent years [1], due to advances in highly active antiretroviral therapy, have led to greater emphasis of quality of life among these patients [2–10]. Measurement of quality of life is now an essential component in both clinical trials and cost-effectiveness analysis for HIV disease [11–15]. A wide variety of quality-of-life instruments have been applied in the evaluation of HIV-infected patients, including the multiple versions of the Medical Outcome Study (MOS) [16–19], the Quality of Well-Being Scale [19, 20], the HIV-QL31 [21], the HAT-QoL [22], the AIDS-HAQ [23], the HOPES [24], the MQoL-HIV [25], and the FAHI [26]. However, because these instruments were developed in the context of western culture, they may not be readily applicable to patients from societies with different cultural background, although several of these instruments have been used with success in some Asian countries [27].

In 1991, the World Health Organization (WHO) initiated a project to develop a generic quality-of-life instrument in 15 countries simultaneously, which led to the WHO quality of life (WHOQOL) assessment [28–31]. The WHOQOL has two

☆ The preliminary abstract of this paper was presented at Pan-Pacific Conference of the International Society for Quality of Life Research, Tokyo, April 2001.

unique features. First, it is based on a well-clarified definition of quality of life and encompasses physical, psychological, social and environment domains comprehensively [28], and is not just a functional assessment. Second, it is a cross-culture instrument developed for use across patient groups in various countries [29]. Despite these advantages, the reliability and validity of WHOQOL have not yet been well studied in HIV-infected patients. It is also unclear whether disease-specific modifications are needed. This study sought to determine the reliability and validity of the WHOQOL when used for the evaluation of patients with HIV infection.

Methods

Subjects

A total of 138 consecutive HIV-infected patients treated and followed up regularly at the outpatient clinics at the National Taiwan University Hospital (NTUH) (Taipei, Taiwan) and the Taipei Municipal Venereal Disease Control Institute (TMVDC) (Taipei, Taiwan) were enrolled. To evaluate the test–retest reliability, 44 of the 138 patients were retested after an average interval of 4.6 weeks (range: 1–8 weeks). NTUH and TMVDC have the largest cohort of patients with HIV infection in Taiwan. The two institutes cooperate closely to provide these patients the best integrative medical service in Taiwan, including pharmacological therapy, medical and surgical services, counseling for both patients and family, and social support network. Inpatients were not enrolled because most of them were too ill to respond adequately to the questionnaire. The diagnosis of HIV infection was confirmed by Western blot in all of the enrolled patients. Informed consent was obtained for all of the participants.

Version of WHOQOL

The WHOQOL-BREF (Taiwan version) [31, 32] was used. The WHOQOL-BREF [31] consists of 26 items, including one item (G1) for general quality of life, one item (G4) for health-related quality of life, and 24 items belonged to four domains (physical, psychological, social and environment). There are seven items in the physical domain, six items in the psychological domain, three items in the social domain, and eight items in the environment domain. The Taiwan version of the WHOQOL-BREF [32] contains the 26 original items, plus two national items of Taiwan; one item belonged to the social domain and another belonged to the environment domain. The method of application, reference time point, and the scoring of items were performed as described for the original WHOQOL-BREF [31]. In brief, the questionnaire was self-administrated. The participants were required to evaluate their quality of life in recent 2 weeks. The item scores ranged from 1 to 5, with a higher score indicating a better quality of life on the corresponding item. Because the number of items are different for each domain, the domain scores were calculated by multiplying the average of the scores of all items in the domain by the same factor of 4. Thus, the domain scores would have the same range from 4 to 20.

Qualitative research

The content validity of WHOQOL-BREF in patients with HIV infection was studied through qualitative research. Eleven HIV-infected patients, of different age, gender, social background and disease stage, were enrolled to focus groups. Four medical professionals, experienced in the care of HIV-infected patients, were also invited to form an expert committee. Focus groups and the expert committee were interviewed separately to identify the determinants and major concerns of quality of life in HIV-infected patients. With the permission of participants, the content of the interview was tape-recorded and then transcribed for analysis. Factors influencing quality of life were then identified and extracted. The results were compared with the content and definition of WHOQOL-BREF.

Health status measures

The convergent validity was studied through measuring the strength of correlation between WHOQOL-BREF domain scores and health status measures. The health status measures used in study included: (1) the self-evaluated health status

and self-evaluated happiness, both measured by a five-point response scales (Table 1); (2) the number and severity of symptoms, measured by the University of California at San Francisco (UCSF) symptoms and signs checklist for persons living with HIV disease (SSC-HIV) [33].

Table 1. Characteristics of 136 patients with HIV infection

Characteristics	% (N = 136)
Age (years)	
⩽30	34
31–40	42
>40	24
Male	96
Education of high school or more	82
HIV risk factor	
Men have sex with men	84
Heterosexual	15
Intravenous drug abuser	1
Presence of AIDS	35
Current antiretroviral therapy	
None[a]	10
PIs-based regimens[b]	80
NNRTIs-based regimens[c]	10
Self-evaluated health status	
Very poor	4
Poor	16
Fair	52
Good	25
Excellent	3
Self-evaluated happiness	
Very unhappy	2
Unhappy	19
Moderately happy	49
Happy	26
Very happy	4
Number of body symptoms	
None	4
1–10	34
11–20	40
21–30	22
Current CD4 cell count (/mm^3)	
⩽200	10
201–500	44
> 500	46
Current plasma HIV RNA (copies/ml)	
⩽5000	78
5001–20000	7
20001–100000	8
> 100001	7

[a] Including treatment-naive fresh cases and patients under structured treatment interruption.
[b] PIs – protease inhibitors.
[c] NNRTIs – non-nucleotide reverse transcriptase inhibitors.

We hypothesized that if WHOQOL-BREF accurately assessed quality of life in patients with HIV infection, then:

(1) WHOQOL-BREF domain scores should positively correlate with self-evaluated health status and happiness in these patients.
(2) WHOQOL-BREF domain scores should inversely correlate with number and severity of symptoms in these patients.

Severity of diseases

The discriminant validity was studied through comparing the WHOQOL-BREF domain scores between HIV-infected patients and healthy people, and between HIV-infected patients with different severity of diseases. The severity of HIV diseases were determined by (1) the number and severity of symptoms, measured by the UCSF symptoms and signs checklist for persons living with HIV disease (SSC-HIV) [33]; (2) the CD4 count, the plasma HIV RNA level, and the presence of acquired immunodeficiency syndrome (AIDS) assessed by the 1993 Centers for Disease Control and Prevention (CDC) criteria [34]. The data from 213 healthy persons, who were hospital volunteers or employees, or family members of non-HIV infected patients, were obtained for comparison.

We hypothesized that if WHOQOL-BREF accurately assessed quality of life in patients with HIV infection, then:

(1) Healthy persons should have better WHOQOL-BREF domain scores than HIV-infected patients.
(2) HIV-infected patients with milder disease should have better WHOQOL-BREF domain scores than HIV-infected patients with more severe disease.

Statistical analysis

The internal consistency reliability was evaluated using Cronbach's α. Test–retest reliability was evaluated using intraclass correlation coefficient (ICC). The construct validity was tested using exploratory factor analysis. The factor analysis was conducted through extracting factors by principal axis factoring, followed by Promax rotation with Kaiser normalization. Kaiser's 'eigenvalues greater than 1' rule was used to determine the number of

factors to rotate. Since this rule tends to include too many factors, solutions containing less numbers of factors were also sought. The significance of differences between domain scores was evaluated by Student's t test. All data was analyzed using SPSS for Windows Version 10.0. Two-tailed p values of <0.05 were considered to be statistically significant.

Results

Characteristics of subjects

Among the 138 enrolled patients, only two patients declined to participate. The response rate was 99% (136/138). The majority (114 of 136) of these patients were homosexual men. AIDS had been diagnosed in 47 patients (35%). Most (90%) of the patients were receiving highly active antiretroviral therapy, with current CD4 cell count $>200/mm^3$ and plasma HIV RNA <5000 copies/ml. A high percentage (62%) of patients reported more than 10 symptoms listed on SSC-HIV. The characteristics of the 136 HIV-infected patients are summarized in Table 1. The 213 healthy subjects included 97 men and 116 women, with age and education level distribution similar to that of 136 HIV-infected patients.

Descriptive statistics

Among the respondents (n = 136), the scores of items ranged from 1 to 5 in all but two items. The mean ± standard deviation (range) of the domain scores was 13.73 ± 2.24 (8.00–18.86) for the physical domain, 12.49 ± 2.75 (6.67–18.67) for the psychological domain, 12.85 ± 2.70 (6.00–20.00) for the social domain, and 13.14 ± 2.36 (7.50–19.11) for the environment domain.

Internal consistency and test–retest reliability

The Cronbach α values (n = 136) ranged from 0.74 to 0.85 across domains (Table 2). The α value of the entire questionnaire was as high as 0.93. All of the 44 patients tested twice were in apparently clinical stable condition, but there were variations in number of symptoms and SSC-HIV scores between the first and the second test ($r = 0.82$ and 0.78, respectively). Only eight patients showed no change in number of symptoms and signs on the checklist of SSC-HIV and only two patients showed no change in average SSC-HIV scores after an interval averaging 4 weeks (range 1–8 weeks). The majority of items had test–retest reliability ranging from 0.51 to 0.78 ($p < 0.01$, n = 44). In four of the items (pain, dependence on medical service, being respected by others, healthy environment), the response was less reproducible, probably because these items may not be stable during the 4 weeks. The test–retest reliability of domain scores was 0.72 (physical domain), 0.79 (psychological domain), 0.64 (social domain) and 0.71 (environment domain) (all $p < 0.01$, n = 44), respectively.

Table 2. Internal consistency of the WHOQOL-BREF in HIV-infected patients (n = 136)

	Cronbach's α
Physical domain	0.74
Psychological domain	0.81
Social domain	0.76
Environment domain	0.85
26 items	0.92
28 items (with two national items included)	0.93

Content validity

All of the focus groups and the expert committee gave the similar message. The early stage of HIV infection is often asymptomatic, but in the later stage, intractable fatigue and wasting syndrome can be disturbing. Loss of interpersonal relationships, particularly the relationship with family members, can be a painful experience. Potential discrimination in employment and medical service often forces patients to hide their HIV-positive status. A lot of varieties of symptoms, including nausea, vomiting, abdominal fullness, diarrhea, numbness, headache, insomnia, weakness, dry mouth, thirsty, shooting pain, flank pain, hematuria, skin rash, dizziness, insomnia, difficult to concentrate, loss of hair, and various kinds of lipodystrophy, etc. were experienced sooner or later under antiretroviral therapy. The types of symptoms were clearly associated with the types of medication prescribed. The complexity of some antiretroviral regimens was also troublesome. While fatigue, pain, body image, sleep, ability to

concentrate and personal relationships have been addressed in the WHOQOL-BREF, other symptoms due to adverse drug effects and the discrimination in workplace and medical service were not covered.

Construct validity

The scores of 26 items were all correlated with the scores of the corresponding domains (r range: 0.42–0.82 across items, all $p < 0.01$, n = 136). The scores of four domains were also all correlated with the scores for general quality of life (item G1) (r range: 0.49–0.64 across domains, all $p < 0.01$, n = 136) and the scores for health-related quality of life (item G4) (r range: 0.52–0.62 across domains, all $p < 0.01$, n = 136). Exploratory factor analysis of data from the 136 patients showed six factors with eigenvalues greater than 1, which explained 53% of total variance. However, the meanings of these six factors were fragmented, suggesting too many factors were used. Instead, a four-factor solution, which explained 47% of total variance, allowed meaningful interpretation for all four factors that were essentially corresponding to the four WHOQOL-BREF domains (Table 3).

Table 3. Exploratory factor analysis, principle axis factoring, Promax rotation with Kaiser normalization (n = 136)

Domains	Facets	Items	Factor 1 (Social)	Factor 2 (Psycho)	Factor 3 (Environ)	Factor 4 (Physical)
Physical	F1. Pain	3	−0.200	0.177	0.018	0.754
Physical	F11. Dependence on medical service	4	0.271	−0.202	−0.152	0.626
Physical	F2. Energy	10	0.128	0.239	0.399	0.153
Physical	F3. Sleep	16	−0.184	0.405	0.450	−0.082
Physical	F9. Ability to get around	15	0.674	0.147	−0.123	0.006
Physical	F12. Working ability	18	0.347	0.275	0.199	−0.047
Physical	F10. Daily activity	17	0.265	0.382	0.268	0.064
Psycho	F5. Ability to concentrate	7	0.002	0.585	0.175	0.078
Psycho	F6. Satisfied with oneself	19	0.171	0.743	−0.045	−0.103
Psycho	F8. Negative feelings	26	−0.107	0.533	0.092	0.070
Psycho	F24. Meaning of life	6	0.045	0.837	−0.118	−0.058
Psycho	F4. Enjoy life	5	0.353	0.113	0.022	0.055
Psycho	F7. Body image	11	0.470	0.444	−0.232	0.103
Social	F13. Personal relationship	20	0.547	0.010	0.082	−0.076
Social	F14. Social support	22	0.643	−0.051	−0.033	0.094
Social	F25. Respected by others	27	0.594	−0.052	0.228	0.065
Social	F15. Sexual life	21	0.021	0.148	0.387	0.193
Environment	F19. Accessibility to medical care	24	0.080	0.102	0.348	0.040
Environment	F22. Healthy environment	9	0.075	−0.176	0.732	−0.093
Environment	F23. Transportation	25	−0.069	0.099	0.688	−0.058
Environment	F17. Living condition	23	0.103	−0.075	0.602	−0.062
Environment	F16. Safety in daily life	8	0.389	0.378	0.030	0.045
Environment	F18. Enough money	12	0.512	0.116	0.145	−0.121
Environment	F20. Accessibility to daily information	13	0.580	0.320	−0.146	−0.157
Environment	F21. Leisure time	14	0.456	0.005	0.311	−0.083
Environment	F26. Get things like to eat	28	0.735	−0.274	0.185	0.091

Correlation between four factors

	Factor 1	Factor 2	Factor 3	Factor 4
Factor 1	1			
Factor 2	0.687	1		
Factor 3	0.624	0.604	1	
Factor 4	0.212	0.177	0.182	1

Table 4. Correlation between WHOQOL domain scores and health status measures (n = 136)

	Self-evaluated heath status	Self-evaluated happiness	Number of symptoms	Severity of symptoms
Domain scores				
Physical	0.53*	0.55*	−0.46*	−0.52*
Psychological	0.60*	0.73*	−0.47*	−0.49*
Social	0.52*	0.59*	−0.40*	−0.41*
Environment	0.57*	0.55*	−0.41*	−0.43*

* $p < 0.01$.

Convergent validity

The scores for the physical, psychological, social, and environment domains were all correlated positively with patients' self-evaluated health status and self-evaluated happiness (Spearman's r range: 0.52–0.60 and 0.55–0.73 across domains, respectively, all $p < 0.01$), and correlated negatively with the number and severity of symptoms (r range: −0.40 to −0.47 and −0.41 to −0.52 across domains, respectively, all $p < 0.01$) (Table 4).

Discriminant validity

The scores for the physical, psychological and social domains, but not the environment domain, discriminated between healthy persons and HIV-infected patients (all $p < 0.01$, Student's t test) (Table 5). This result remains valid if the 97 healthy men, rather than the total 213 healthy persons, were used as the healthy group for the comparison. The scores for all domains also discriminated between HIV-infected patients with more severe symptoms with an SSC-HIV score higher than the average (mean) and those with scores lower than the average (all $p < 0.01$, Student's t test), and between HIV-infected patients with a number of symptoms higher than the average (mean) and those with a number of symptoms lower than the average (all $p < 0.01$, Student's t test) (Table 5).

Under highly active antiretroviral therapy, the majority (72%) of the 47 patients initially with AIDS had a favorable clinical response, with a sustained rise in CD4 counts and durable suppression of plasma HIV RNA level, and remained free from opportunistic infections. With this im-

Table 5. Comparison of the WHOQOL domain scores (mean ± SD)

Domains	HIV-infected patients (N = 136)	Healthy persons (N = 213)	p-Value
(a) Between HIV-infected patients and healthy persons			
Physical	13.73 ± 2.24	15.39 ± 1.88	< 0.01
Psychological	12.49 ± 2.75	13.74 ± 2.11	< 0.01
Social	12.85 ± 2.70	14.00 ± 2.11	< 0.01
Environment	13.14 ± 2.36	13.11 ± 2.21	0.124
(b) Between HIV-infected patients with different number of symptoms			
	More[a] symptoms (N = 73)	Less[b] symptoms (N = 62)	
Physical	12.94 ± 1.99	14.69 ± 2.18	< 0.01
Psychological	11.54 ± 2.40	13.59 ± 2.75	< 0.01
Social	12.06 ± 2.35	13.76 ± 2.81	< 0.01
Environment	12.46 ± 2.20	13.92 ± 2.31	< 0.01
(c) Between HIV-infected patients with different severity of symptoms			
	High[c] SSC-HIV scores (N = 57)	Low[d] SSC-HIV scores (N = 78)	
Physical	12.56 ± 1.87	14.60 ± 2.13	< 0.01
Psychological	10.92 ± 2.15	13.58 ± 2.59	< 0.01
Social	11.70 ± 2.32	13.67 ± 2.68	< 0.01
Environment	12.08 ± 1.97	13.88 ± 2.34	< 0.01

[a] Number of symptoms more than the average (mean).
[b] Number of symptoms less than the average (mean).
[c] SSC-HIV scores higher than the average (mean).
[d] SSC-HIV scores lower than the average (mean).

provement of clinical status and none of our patients were currently hospitalized, although the scores for all domains were still consistently worse in patients initially with AIDS than in those initially without AIDS, the differences were not statistically significant (data not shown).

Discussion

In the present study, we demonstrated that the WHOQOL-BREF, in its Taiwan national version, can be a useful generic quality-of-life instrument in patients with HIV infection. The internal consistency was good. The domain scores were well correlated with self-evaluated health status and self-evaluated happiness, and inversely correlated with number and severity of symptoms. The scores of physical, psychological, and social domains also discriminated between HIV-infected patients and healthy persons, and between HIV-infected patients with different number and severity of symptoms. To provide further information about validity in this group of patients, a better design would have been to compare the generic WHOQOL to an existing, previously tested, leading disease-specific instrument, such as MOS-HIV [18]. However, because up to the beginning of this study there was still no Taiwan version for such instruments, we were unable to use this strategy to corroborate the validity of WHOQOL in the present study.

Although a reliability level of 0.90 was advocated by Nunnally [35] as a minimum standard for measurement that is designed for individual assessment, in practice it may be too stringent and many highly regarded quality-of-life instruments fail to meet this standard [36]. Even the test–retest reliability (24 hour) for physiological measurement of blood pressure, 0.87 for systolic pressure and 0.67 for diastolic pressure [36, 37], did not meet this standard, either. Furthermore, real changes of status may occur during the retest interval. To minimize the effect of real changes, the ideal interval between the first and the second test for quality of life would have been 2 weeks or less. However, most participants in this study found it difficult to make an extra visit to the clinic before the scheduled monthly follow-up. Although all 44 patients tested twice were in apparently clinical stable condition, there were variations in number of symptoms and SSC-HIV scores between the first and the second test ($r = 0.82$ and 0.78, respectively). Only eight patients showed no change in number of symptoms and signs on the checklist of SSC-HIV, and only two patients showed no change in average SSC-HIV scores. It indicated that minor but real changes of symptoms and subjective feelings might have occurred during the long interval (average 4.6 weeks) between the first and the second tests in our study. Thus, we obtained a test–retest reliability of 0.51–0.79 for items and domains, which was slightly less adequate compared with the reliability between 0.56 and 0.84 of the original WHOQOL-BREF [31].

The results of qualitative research suggested that the content of WHOQOL-BREF might not cover some important issues for HIV-infected patients who were under regular highly active antiviral treatment. For example, pain (or discomfort) and fatigue are the only body symptoms listed in the WHOQOL-BREF physical domain. Other disturbing symptoms, such as gastrointestinal upset, hematuria, dry mouth, thirsty, dizziness, and skin rash, are not specifically listed. Similarly, discrimination to HIV-infected persons in workplace and medical service are not particularly mentioned in the content of WHOQOL-BREF. It is interesting to note that, although the content of WHOQOL-BREF may not be comprehensive for HIV-infected patients, there was a consistently good correlation between domain scores and symptoms (inverse correlation), and between domain scores and self-evaluated health status measures. The strength of correlation with validation variables was comparable to that reported in previous WHOQOL literature [32]. During the initial validation of WHOQOL Taiwan version in general population, the magnitude of correlations between WHOQOL domain scores and the validation variables ranged from 0.33 to 0.63 [32]. In the present study, the correlation between WHOQOL domain scores and symptoms ranged from −0.40 to −0.47 (number of symptoms) and from −0.41 to −0.52 (SSC-HIV scores of symptoms severity). And the correlation between WHOQOL domain scores and self-evaluated health status measures ranged from 0.52 to 0.60 (self-evaluated health status) and from 0.55 to 0.73 (self-evaluated happiness).

The results of factor analysis in this study showed that some items were not best correlated with their related domains. This is most likely due to the overlapping of constructs between the domains, especially when perceived from the viewpoints of HIV-infected patients. For example, to persons without fixed sexual partners, sexual life may be more suitably classified in the environment domain rather than the social domain. The grouping of money, accessibility to daily information, leisure time, and getting thing one like to eat into factor 1 (social) may reflect the perception that economic security, information and leisure activity are an integral part of social life.

Previous studies have consistently shown that the presence, number, and severity of symptoms are the major determinants of quality of life in HIV-infected patients [3–6]. Clinical stage has only a weak association with quality of life after adjusting for the number of symptoms [3]. Using number and severity of symptoms as the disease severity markers, we found that the WHOQOL-BREF has good discriminant validity among patients with different severity of HIV disease. The magnitude of difference in domain scores was comparable to that reported between sick and healthy persons in the original validation of WHOQOL [29]. We did not use current CD4 count as the marker in the testing of discriminative validity because only a very small proportion ($<10\%$) of our patients had a low CD4 count ($\leqslant 200/mm^3$) when the questionnaire was applied (Table 1).

Although this study showed WHOQOL-BREF scores generally correlated well with validation variables in patients with HIV infection, it also showed some unique aspects of quality of life in HIV-infected patients were not covered. As a result, WHOQOL-BREF may be insensitive to the change of status in these aspects. It is thus worthwhile to formally develop a disease-specific module to enhance its sensitivity and responsiveness to clinical status [38]. This modular approach, initially proposed by Aaronson and coworker for cancer patients [39, 40], is a promising way to satisfy both the demand for cross-disease comparison for the purpose of resource allocation and the need for assessing the status of a particular disease in clinical trials. There are still no official guidelines for the development of a disease-specific module of the WHOQOL. To ensure cross-cultural validity, the official guidelines of The European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 instrument mandates that the development of disease-specific modules should involve a number of countries, each representing a broadly defined geographic and culture category [41]. We suggest that if an HIV-specific module of the WHOQOL is to be formally developed, both the general guidelines for disease-specific instruments [38] and the guidelines to ensure cross-cultural validity [39–41] should be followed.

We conclude that the WHOQOL-BREF, in its national version, can be a useful generic quality-of-life instrument in patients with HIV infection. To further enhance the sensitivity and responsiveness to clinical status, it is worthwhile to formally develop an HIV-specific module for WHOQOL.

Acknowledgements

This work was supported by grants NSC 89-2314-B-002-433-M56 and DOH91-DC-1056. We are indebted to Dr Kai-Ping Yao for constructive comments. We would like to thank Dr Shou-Chien Chen, Dr Shiow-Ing Wu, and the Taipei Municipal Venereal Disease Control Institute for allowing us to recruit their patients for participation in this study. We also thank Miss Yu-Yin Chang for her help in statistical analysis. Dr Mao-Yen Chen and Dr Jung-Der Wang contributed equally to this work.

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