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## ORIGINAL ARTICLE

# Quality of life and its determinants for heroin addicts receiving a methadone maintenance program: Comparison with matched referents from the general population



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**Background/Purpose:** Quality of life (QoL) is found to be lower in heroin addicts; however, few studies examine detailed QoL performance and related factors in heroin patients attending a methadone maintenance treatment program (MMTP). The study thus aimed to explore QoL and its determinants for publicly-funded and self-paid patients attending an MMTP.

**Methods:** Participants were recruited in Jianan Psychiatric Center, Tainan, Taiwan, during their first clinic visit for the MMTP. Age-, sex-, education-, and municipality-matched referents were collected from the 2001 Taiwan National Health Interview Survey database. The participants had a mean age of 38.29 years [standard deviation (SD) = 7.65 years] for publicly-funded ( $n = 129$ ) and 37.97 years (SD = 7.16 years) for self-paid ( $n = 105$ ) MMTP patients. Matched referents ( $n = 217$ ) were 37.74 years (SD = 7.44 years). All participants were measured with the brief version of the World Health Organization's Quality of Life

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(WHOQOL-BREF) assessment. MMTP patients additionally went through tests for the hepatitis B virus, hepatitis C virus, and human immunodeficiency virus (HIV).

**Results:** Both publicly-funded and self-paid MMTP patients had lower QoL scores than their matched counterparts in the physical and psychological domains ( $p < 0.05$ ) after control for confounding by age, sex, education, and municipality. Detailed individual item analyses showed that publicly-funded MMTP patients had lower scores for almost all items related to the physical, psychological, and social domains as compared to the referents because of HIV infection ( $p < 0.05$ ).

**Conclusion:** To improve the QoL of heroin users coming for MMTP, we recommend that clinicians pay attention to the comorbidity of HIV infection and individual items/facets.

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## Introduction

Habitual opioid use has been studied in many countries,<sup>1–3</sup> and the findings indicate that dependent opioid users, including heroin users, continue to use opioids despite their substantially impaired health. Moreover, many researchers<sup>4,5</sup> report that even dependent heroin users who have sought treatment may continuously use heroin for decades. Degenhardt et al<sup>4</sup> performed a meta-analysis of 58 prospective studies on mortality rates for opioid users, and found that the crude mortality rate was 2.09 per 100 person-years. In addition, opioid users who are out of treatment have a higher mortality risk<sup>4</sup> and are more depressed<sup>6</sup> than those who are in treatment. A number of studies have thus examined the importance and effects of methadone maintenance treatment (MMT), a primary treatment option for heroin users.<sup>7–10</sup>

MMT, which provides patients with a daily dosage of methadone over a long, continuous period, has been documented to inhibit illicit opiate abuse, human immunodeficiency virus (HIV) risk behavior, criminality, and mortality.<sup>11–13</sup> However, the cost directly related to such programs (MMTPs) is not covered by the National Health Insurance (NHI) system in Taiwan, even though this program covers as much as 99% of the population and includes a broad coverage of services (e.g., outpatient service, inpatient care, traditional Chinese medicine, dental care, childbirth, occupational therapy, and physical therapy).<sup>14,15</sup> However, because of the rapid spread and high prevalence of HIV among drug users,<sup>16,17</sup> the Taiwan Center for Disease Control (CDC) has permitted MMTP since 2006 to control the spread of this disease.<sup>18</sup> Moreover, two kinds of MMTPs (publicly-funded and self-paid) are administered, with publicly-funded MMTP being free for patients for up to 1 year, while the fee for the self-paid MMTP is about US\$100 per month for each patient. Patients who receive publicly-funded MMTP are required to meet one of the following criteria: (1) being HIV seropositive; (2) applying for deferred prosecution; or (3) having been incarcerated because of violating the Drug Control Act. Because of these criteria, we suspect that the health conditions of such patients, including the quality of life (QoL), would be different compared to those seeking self-paid MMTP, and thus the current study examines this issue.

Due to the health burden of heroin users, in recent years there has been increasing interest in measuring their QoL.

QoL, based on multidimensional underlying concepts (physical, psychological, social, and environment), provides clinicians with a holistic view of an individual's health condition,<sup>19,20</sup> and has been suggested as an important tool for evaluating drug programs.<sup>21</sup> Obtaining a better understanding of QoL among heroin users or those receiving MMTP is thus crucial, with studies finding that such individuals tend to have impaired QoL, which may be due to their comorbid infectious diseases, such as hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV.<sup>22–24</sup> For example, Astals et al<sup>22</sup> applied the Short Form-12 to compare QoL between heroin users and the European general population, and found that the former group had significantly lower scores for both the physical and psychological components of the instrument compared to the general population. Other researchers<sup>25,26</sup> have used the World Health Organization's Quality of Life, Brief Version (WHOQOL-BREF) to examine the QoL of heroin users. Lin et al<sup>25</sup> and Yen et al<sup>26</sup> compared scores on four domains of the WHOQOL-BREF between heroin users and healthy controls, and while both found significant differences for the Physical, Psychological, and Social domains, there was no consistent finding for the Environment domain.

Although many studies have explored the QoL of heroin users,<sup>22,23,25,26</sup> few have analyzed changes in their scores and determinants of individual items. There is thus still a need to understand which facets/items should be paid more attention to improve the QoL of such patients, and provide guidance to the clinicians and stakeholders who take care of them. As such, the purposes of this study were: (1) to examine the QoL differences between heroin users coming for MMTPs and their matched referents after stratification according to whether they were publicly-funded or self-paid; and (2) to determine the QoL domain and item scores and their determinants in order to be able to suggest possible improvements in the care of these patients.

## Methods

### Participants

The study was approved by the Hospital Ethics Committee of the Jianan Psychiatric Center, Tainan, Taiwan (Institutional Review Board number: JMH9601) before commencement.

All patients who were diagnosed with opioid dependence by qualified psychiatrists from the Jianan Psychiatric Center, based on the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)*,<sup>27</sup> and who were willing to join the MMTP were invited to participate from March 2006 to July 2008. All participants were required to meet the following criteria to be recruited for this study: (1) to be older than 20 years, (2) to have sufficient mental competence to answer questionnaires, and (3) to be a first time participant in an MMTP. After signing an informed consent form, each participant completed a demographic sheet and the WHOQOL-BREF questionnaire; all participants also underwent HBV, HCV, and HIV tests.

Participants were classified as publicly-funded MMTP ( $n = 129$ ) if they met one of the following criteria: (1) being HIV seropositive; (2) applying for deferred prosecution; or (3) having been incarcerated because of violating the Drug Control Act. Otherwise, the participant was classified as a self-paid MMTP ( $n = 105$ ) participant.

A matched reference group was randomly sampled from the 2001 National Health Interview Survey (NHIS) database constructed by the National Health Research Institutes and the Bureau of Health Promotion, Department of Health, Taiwan. They were matched with the MMTP participants based on age ( $\pm 5$  years), sex, years in education ( $< 6$  years,  $7-12$  years, and  $\geq 13$  years), and municipality. The purpose of the 2001 NHIS is to provide nationwide health-related estimates, including health conditions, health behavior, and usage of medical resources, for the population of Taiwan. Using multi-stage sampling proportioned to household population size, a total of 27,160 eligible people living in 7357 households were identified, and thus the sample was representative of the Taiwanese population with regard to age, sex, and the urbanization index.<sup>28</sup> Subsequently, the 2001 NHIS collected 25,464 people living in 6271 households (response rate: 93.8% by person and 91.4% by household) from August 2001 to January 2002.<sup>29</sup> In addition, 13,048 people aged from 20 years to 89 years filled out the WHOQOL-BREF, which was one of the tools used to measure various health-related factors such as healthy behaviors.<sup>30</sup>

The healthy control participants were matched using a simple random method with the following steps: (1) each healthy control was assigned a random number; (2) all the controls were grouped according to age, sex, municipality, and years in education; (3) the controls were put into sequence in their groups based on the random number that had been assigned to them; (4) the healthy controls were matched to the heroin-dependent patients using a 1:1 ratio; (5) all selected controls were moved out of the pool; (6) 1 year was added or subtracted to the age of the controls when no more controls can be matched with the patients; and (7) Step 6 was carried out repeatedly, for a total addition or subtraction of up to 5 years. We decided to use a 1:1 ratio for selecting healthy controls based on the following power calculations: using a small effect size (Cohen's  $d = 0.2$ ) on a two-sided paired  $t$  test with an alpha error of 0.05 and power of 0.8; the suggested total sample size, as obtained by G\*Power 3.1.5,<sup>31</sup> was 199. Each group thus needed 100 individuals, giving a total sample size of 200 for the comparison. Because our heroin-dependent sample was 234 (publicly-funded, 129 and self-paid, 105),

the 1:1 ratio would be sufficient for each comparison of heroin users and healthy controls. However, we finally matched only 217 healthy controls (113 matched with publicly-funded and 104 with self-paid) for the following reason: our heroin-dependent sample was generally young people with low educational levels. In fact,  $> 95\%$  of them have been educated for  $< 12$  years (Table 1), in contrast to the majority of young people in Taiwan, who have been to junior college or higher. Nevertheless, we obtained  $> 100$  pairs of matched healthy controls and heroin users for both publicly-funded and self-paid MMTP, thus giving sufficient power for data analyses.

## WHOQOL-BREF

The WHOQOL-BREF Taiwan version is a generic QoL questionnaire that contains two general items (viz., "overall QoL" and "general health") and 26 items within four domains (viz., Physical: 7 items, Psychological: 6 items, Social: 4 items, and Environment: 9 items). The WHOQOL-BREF Taiwan version was developed in 1999 under the WHO guidelines,<sup>32</sup> for which strong psychometric properties have been found, including reliability (internal consistency and test-retest reliability) and validity (content validity, criterion-related validity, known-group validity, and construct validity).<sup>32,33</sup> In addition, satisfactory psychometric properties were also established in a sample with psychiatric disorders,<sup>19</sup> as well as in one with heroin addiction.<sup>34</sup> Each item scored from 1 (representing the worst condition) to 5 (representing the best), except for three items ("Pain and discomfort" and "Medication" in the Physical domain, and "Negative feelings" in the Psychological domain) that were reversely coded. In addition, domain scores were calculated according to a 4–20 scale, where a higher score represented better QoL.

In addition to the domain scores, we also applied the item scores for in-depth analyses, and this was done for the following reasons. First, the item score could provide us with more detailed information than the total score.<sup>35</sup> For example, if someone has a low score in the Physical domain, clinicians may have difficulties defining which physical problems they suffer from. By contrast, if someone has a low score in the item of activities of daily living, then clinicians would be able to focus on this major functional problem. Second, the item properties of the WHOQOL-BREF have been found to be satisfactory.<sup>34</sup>

## Data analysis

All data were analyzed using SPSS software, version 15.0 (SPSS Inc., Chicago, IL, USA). Descriptive analyses were applied to show participant characteristics for each group (publicly-funded MMTP, self-paid MMTP, and matched referents). Differences in the WHOQOL-BREF domain scores between publicly-funded MMTP and matched referents, and those between self-paid MMTP and matched referents, were analyzed using paired  $t$  tests. In addition, Cohen's  $d$  (aka effect size) was used to detect the magnitude of the differences, and values of 0.2, 0.5, and 0.8 indicated small, moderate, and large effects, respectively. The Cohen's  $d$  was calculated as: (WHOQOL-BREF

**Table 1** Demographics and WHOQOL-BREF scores for patients coming for a methadone maintenance treatment program (MMTP) and matched referents from the general Taiwanese population.

	Publicly-funded ( <i>n</i> = 129)	Matched referents <sup>a</sup> ( <i>n</i> = 113)	Cohen's <i>d</i>	Self-paid ( <i>n</i> = 105)	Matched referents <sup>a</sup> ( <i>n</i> = 104)	Cohen's <i>d</i>
Age (y)	38.29 ± 7.65	37.53 ± 7.75		37.97 ± 7.16	37.97 ± 7.13	
Sex						
Female	11 (8.5)	11 (9.7)		13 (12.4)	13 (12.5)	
Male	118 (91.5)	102 (90.3)		92 (87.6)	91 (87.5)	
Educational years						
< 6 y	4 (3.1)	4 (3.5)		1 (0.9)	1 (1.0)	
7–12 y	119 (92.2)	103 (91.2)		103 (98.2)	102 (98.0)	
≥ 13 y	6 (4.7)	6 (5.3)		1 (0.9)	1 (1.0)	
Living status <sup>b</sup>						
With others	118 (91.5)			98 (96.1)		
Alone	11 (8.5)			4 (3.9)		
Age of first heroin use (y)	25.59 ± 5.89			26.92 ± 6.80		
Employment status <sup>b</sup>						
Fixed	68 (53.1)			56 (53.3)		
Nonfixed	60 (46.9)			49 (46.7)		
HIV carrier						
Seronegative	84 (65.1)			105 (100.0)		
Seropositive	45 (34.9)			0 (0.0)		
HBV carrier						
Seronegative	106 (82.2)			89 (84.8)		
Seropositive	23 (17.8)			16 (15.2)		
HCV carrier						
Seronegative	4 (3.1)			9 (9.4)		
Seropositive	125 (96.9)			96 (90.6)		
WHOQOL-BREF						
Physical	11.93 ± 1.86	15.01 ± 1.93	−1.12***	12.53 ± 1.90	15.44 ± 2.15	−1.07***
Psychological	12.01 ± 2.66	13.51 ± 2.34	−0.41***	12.88 ± 2.07	13.58 ± 2.44	−0.24*
Social	12.73 ± 3.13	13.95 ± 1.98	−0.31**	13.50 ± 2.76	14.03 ± 2.34	−0.15
Environment	12.47 ± 2.80	12.86 ± 1.88	−0.12	13.48 ± 2.24	12.88 ± 2.18	0.20*

Data are presented as *n* (%) or mean ± SD.

\* *p* < 0.05.

\*\* *p* < 0.01.

\*\*\* *p* < 0.001.

Cohen's *d* = mean difference divided by pooled SD; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; SD = standard deviation; WHOQOL-BREF = Taiwanese brief version of the World Health Organization's quality of life.

<sup>a</sup> Matched referents were paired with MMTP patients according to age (± 5 years), sex, years of education, and municipality.

<sup>b</sup> With missing values.

domain scores for the publicly-funded MMTP or self-paid MMTP group minus WHOQOL-BREF domain scores for matched referents) divided by the pooled standard deviation (SD).<sup>35,36</sup> A negative *d* value indicated that the MMTP groups had a QoL lower than those of their matched counterparts, and a positive *d* value indicated that the MMTP groups rated their QoL as being higher than their matched counterparts did.

Regression models in univariate and multivariate levels were constructed to determine the impacts of MMTP. Specifically, the regression models constructed healthy controls as the reference group to compare their QoL scores with publicly-funded and self-paid MMTP patients. Moreover, additional hierarchical multiple linear regression models were used to determine the effect of publicly-

funded MMTP and self-paid MMTP on QoL scores (including the WHOQOL-BREF domain scores and item scores) with adjustment for demographic and/or clinical characteristics (Model 0: without any adjustment; Model 1: age, sex, educational years, living status, and fixed employment; Model 2: age, sex, educational years, living status, fixed employment, HIV-positive, HBV-positive, and HCV-positive infections). However, because we did two sets of regression models (i.e., 1 set of healthy controls vs. MMTP patients and another set of publicly-funded vs. self-paid MMTP patients), we adopted Bonferroni adjustment to control the second set of regression models, with *p* = 0.025 being significant. In addition, sensitivity analyses were performed for males only in all the above analyses, including paired *t* tests, Cohen's *d*, and regression models.

## Results

In total, 234 patients coming for an MMTP together with 217 age-, sex-, municipal- and education-matched healthy referents were successfully recruited, and their demographics were comparable, as summarized in Table 1. In addition, few MMTP participants lived alone (8.5% in publicly-funded MMTP and 3.9% in self-paid MMTP), and slightly more than half of them had fixed employment among both the publicly-funded and self-paid MMTPs. HIV carriers were mainly in the publicly-funded MMTP group (65.1%), while the self-paid MMTP group had no HIV carriers. Less than one fifth of the MMTP participants were HBV carriers, and > 90% were infected with HCV. Moreover, the mean ages of first heroin use were  $25.59 \pm 5.89$  years for those in the publicly-funded MMTP group, and  $26.92 \pm 6.80$  years for those in the self-paid MMTP group (Table 1).

Publicly-funded MMTP participants had significantly lower scores in the physical, psychological and social domains as compared with their matched referents, of which the magnitude of difference for the Physical domain was found to be the largest ( $d = -1.12$ ), followed by the Psychological ( $d = -0.41$ ), and Social ( $d = -0.31$ ) domains, as summarized in Table 2. By contrast, the self-paid MMTP participants showed significantly lower scores in the Physical and Psychological domains, but the scores in the Environment domain were higher in comparison to those of their matched referents. In addition, the magnitude of difference for scores was large for the Physical domain ( $d = -1.07$ ) and small for the Psychological domain (Table 1).

After adjustment for demographic characteristics (age, sex, and years in education), publicly-funded MMTP participants showed significantly lower scores for all items in the Physical, Psychological, and Social domains, and for four of nine items in the Environment domain, in comparison with the matched referents, as summarized in Table 3. By contrast, significantly lower scores were found for five of seven items in the Physical domain, one of six items in the Psychological domain, and one of four items in the Social domain among the self-paid participants as compared with their matched referents. The self-paid participants also showed significantly higher scores for three out of nine items in the Environment domain (Table 2).

We constructed linear models to compare QoL scores between publicly-funded and self-paid MMTP participants, with the results showing that the former had significantly lower scores in eight out of 26 items, as summarized in Table 3. However, all these differences disappeared after incorporating clinical data and controlling for confounding. In other words, differences in the payment scheme were not associated with any significant QoL score difference in Model 2. Instead, the significant differences for six out of eight items were explained by HIV infection (Model 2), for which there was no significant difference in any item or domain score in the Physical domain. Similar trends can be also found in only male heroin users, based on our sensitivities analyses (Appendix 1).

## Discussion

In general, our results indicating that heroin users tend to have a poorer QoL than healthy controls are corroborated

by previous reports,<sup>22,37</sup> including studies conducted in Taiwan.<sup>25,26</sup> The two Taiwanese studies<sup>25,26</sup> documented lower scores in the Physical, Psychological, and Social domains in MMTP patients compared with those for healthy referents after controlling for age, sex, and education. Because some studies<sup>38,39</sup> have reported that people living in rural areas tend to exhibit lower QoL scores as compared with those living in urban areas, we controlled for municipality and corroborated the findings of poorer scores in patients coming for MMTPs (Table 1). Moreover, we examined the scores for individual items to obtain more detailed results, and derived some new information that should be of interest to stakeholders (Table 2). Because publicly-funded MMTP patients had generally poorer scores in all items and domains in comparison with those that were self-paid, we controlled clinical factors for potential confounding and found that HIV infection explains the major differences between these two groups (Table 3). However, because we simultaneously controlled HIV, HBV, and HCV infections, their effects were adjusted. The results showed that HIV infection had a significant effect on many item scores, while those of HBV and HCV infections did not. In addition, we used another set of regression models that omitted HBV and HCV infections (Appendix 2), and the results were almost identical to those for Model 2 in Table 3. Therefore, we are confident in our results of the full model (i.e., Model 2) on Table 3.

According to the current government regulations in Taiwan, enacted to control the spread of HIV and heroin abuse, a patient is only eligible for publicly-funded MMTP if he/she is either HIV seropositive or has a criminal record (e.g., for a violation of the Drug Control Act). These patients may have more difficulties related to social interaction in the community than self-paid MMTP patients, because there is a stigma related to carrying HIV<sup>40</sup> and being a criminal,<sup>41</sup> thus they may not live in a friendly environment. The results of our multiple linear regressions show that the group effect (publicly-funded vs. self-paid) diminished after we included HIV infection in the model (Table 3), and that the effects of most items/facets shifted toward individuals being HIV-positive. We thus tentatively concluded that the QoL differences between the two groups were at least partially due to the impact of being HIV-positive. This result provides clinicians with an important direction for treating MMTP patients, as HIV should be simultaneously diagnosed and treated during such programs. Because we did not have access to the criminal records of our participants, we were unable to explore the effects of these on QoL for the patients undergoing MMTP. However, we could see that the score differences for self-esteem (Psychological domain), personal relationship, social support, being respected (Social domain), health service, and transportation (Environment domain) were not explained by HIV infection, and thus they might be attributed to the criminal records of the MMTP patients. However, further research is needed to examine this hypothesis.

Our finding of impaired QoL for the heroin users examined in this study generally agreed with previous studies.<sup>22,25,26</sup> However, some differences were found when we carefully compared our results with those of two other studies<sup>25,26</sup> using the same instrument, i.e., the

**Table 2** Regression coefficients of model construction for publicly-funded and self-paid methadone maintenance treatment program (MMTP) patients versus matched referents<sup>a</sup> on the WHOQOL-BREF.

Domain Item #	Item description	Univariate <sup>b</sup>				Multivariate <sup>c</sup>			
		Publicly-funded		Self-paid		Publicly-funded		Self-paid	
		B(SE)	p	B (SE)	p	B(SE)	p	B(SE)	p
Physical		-3.26 (0.22)	< 0.001*	-2.73 (0.24)	< 0.001*	-3.27 (0.22)	<0.001*	-2.72 (0.24)	<0.001*
Q3	Pain & discomfort	-1.52 (0.11)	< 0.001*	-1.49 (0.12)	< 0.001*	-1.52 (0.11)	<0.001*	-1.48 (0.12)	<0.001*
Q4	Medication	-2.06 (0.11)	< 0.001*	-2.23 (0.11)	< 0.001*	-2.04 (0.11)	<0.001*	-2.25 (0.11)	<0.001*
Q10	Energy & fatigue	-0.39 (0.09)	< 0.001*	-0.14 (0.10)	0.14	-0.40 (0.09)	<0.001*	-0.14 (0.10)	0.16
Q15	Mobility	-0.44 (0.09)	< 0.001*	-0.25 (0.10)	0.008*	-0.44 (0.09)	<0.001*	-0.25 (0.10)	0.01*
Q16	Sleep & rest	-0.62 (0.10)	< 0.001*	-0.38 (0.11)	0.001*	-0.63 (0.10)	<0.001*	-0.37 (0.11)	0.001*
Q17	Activities of daily living	-0.36 (0.08)	< 0.001*	-0.21 (0.09)	0.02*	-0.36 (0.08)	<0.001*	-0.21 (0.09)	0.02*
Q18	Work capacity	-0.35 (0.10)	< 0.001*	-0.12 (0.10)	0.24	-0.35 (0.10)	<0.001*	-0.13 (0.10)	0.22
Psychological		-1.59 (0.27)	< 0.001*	-0.71 (0.29)	0.014*	-1.61 (0.27)	<0.001*	-0.68 (0.29)	0.019*
Q5	Positive feelings	-0.24 (0.11)	0.03*	0.04 (0.12)	0.73	-0.25 (0.11)	0.02*	0.06 (0.12)	0.62
Q6	Spirit/religion/beliefs	-0.38 (0.12)	0.001*	-0.15 (0.13)	0.24	-0.40 (0.12)	0.001*	-0.13 (0.13)	0.30
Q7	Concentration	-0.48 (0.10)	< 0.001*	-0.01 (0.11)	0.90	-0.48 (0.10)	<0.001*	-0.003 (0.11)	0.98
Q11	Body image	-0.24 (0.10)	0.02*	-0.02 (0.11)	0.85	-0.24 (0.10)	0.02*	-0.02 (0.11)	0.86
Q19	Self-esteem	-0.45 (0.09)	< 0.001*	-0.19 (0.10)	0.06	-0.45 (0.09)	<0.001*	-0.19 (0.10)	0.06
Q26	Negative feelings	-0.60 (0.10)	< 0.001*	-0.73 (0.11)	< 0.001*	-0.60 (0.10)	<0.001*	-0.73 (0.11)	<0.001*
Social		-1.37 (0.29)	< 0.001*	-0.55 (0.31)	0.08	-1.37 (0.29)	<0.001*	-0.54 (0.31)	0.09
Q20	Personal relationship	-0.20 (0.08)	0.02*	-0.06 (0.09)	0.48	-0.20 (0.09)	0.02*	-0.06 (0.09)	0.48
Q21	Sexual activity	-0.70 (0.10)	< 0.001*	-0.35 (0.11)	0.001*	-0.70 (0.10)	<0.001*	-0.35 (0.11)	0.001*
Q22	Social support	-0.25 (0.09)	0.007*	-0.15 (0.10)	0.12	-0.25 (0.09)	0.008*	-0.15 (0.10)	0.12
Q27	Being respected	-0.22 (0.09)	0.016*	0.01 (0.10)	0.92	-0.23 (0.09)	0.015*	0.01 (0.10)	0.90
Environment		-0.40 (0.26)	0.13	0.56 (0.28)	0.048*	-0.42 (0.26)	0.11	0.58 (0.28)	0.04*
Q8	Safety & security	-0.23 (0.11)	0.03*	0.10 (0.11)	0.40	-0.24 (0.11)	0.025*	0.11 (0.12)	0.35
Q9	Physical environment	0.02 (0.10)	0.87	0.41 (0.11)	< 0.001*	0.02 (0.10)	0.88	0.42 (0.11)	<0.001*
Q12	Financial resources	-0.31 (0.12)	0.007*	-0.06 (0.12)	0.64	-0.33 (0.12)	0.004*	-0.04 (0.12)	0.75
Q13	Information acquisition	-0.27 (0.10)	0.007*	-0.01 (0.11)	0.97	-0.28 (0.10)	0.006*	-0.002 (0.11)	0.98
Q14	Leisure activities	0.05 (0.11)	0.65	0.45 (0.11)	< 0.001*	0.04 (0.11)	0.70	0.47 (0.11)	<0.001*
Q23	Home environment	-0.05 (0.09)	0.56	0.07 (0.10)	0.46	-0.06 (0.09)	0.52	0.08 (0.10)	0.42
Q24	Health service	0.16 (0.09)	0.08	0.22 (0.10)	0.02*	0.16 (0.09)	0.075	0.21 (0.10)	0.03*
Q25	Transportation	-0.17 (0.09)	0.047*	-0.02 (0.09)	0.85	-0.18 (0.09)	0.046*	-0.02 (0.09)	0.82
Q28	Eating	-0.08 (0.09)	0.40	0.08 (0.10)	0.43	-0.08 (0.10)	0.38	0.08 (0.10)	0.42

\* Statistically significant ( $p < 0.05$ ).

B = regression coefficient; MMTP = methadone maintenance treatment program; SE = standard error; WHOQOL-BREF = Taiwanese brief version of World Health Organization's quality of life.

<sup>a</sup> Referents were selected from the general population and matched according to age, sex, education, and municipality with MMTP patients.

<sup>b</sup> Without any adjustment.

<sup>c</sup> Adjusted for age, sex, and educational years.

**Table 3** Regression coefficients of model construction for WHOQOL-BREF scores comparing self-paid and publicly-funded methadone maintenance treatment program (MMTP) patients.

Domain Item #	Model 0 <sup>a</sup>		Model 1 <sup>b</sup>		Model 2 <sup>c</sup>			
	Self-paid vs. publicly-funded		Self-paid vs. publicly-funded		Self-paid vs. publicly-funded		HIV positive vs. HIV-negative	
	B (SE)	p <sup>d</sup>						
Physical	0.53 (0.25)	0.036	0.64 (0.25)	0.012*	0.50 (0.28)	0.08	-0.37 (0.36)	0.30
Q3: Pain & discomfort	0.03 (0.13)	0.83	0.03 (0.14)	0.81	0.06 (0.15)	0.68	0.11 (0.19)	0.55
Q4: Medication	-0.18 (0.13)	0.18	-0.18 (0.13)	0.19	-0.05 (0.15)	0.72	0.29 (0.19)	0.12
Q10: Energy & fatigue	0.25 (0.11)	0.027	0.29 (0.11)	0.012*	0.17 (0.13)	0.18	-0.31 (0.16)	0.057
Q15: Mobility	0.19 (0.11)	0.09	0.20 (0.11)	0.07	0.19 (0.13)	0.77	-0.03 (0.16)	0.87
Q16: Sleep & rest	0.23 (0.13)	0.08	0.30 (0.13)	0.026	0.21 (0.15)	0.17	-0.23 (0.19)	0.21
Q17: Activities of daily living	0.14 (0.10)	0.17	0.17 (0.10)	0.10	0.07 (0.12)	0.55	-0.28 (0.15)	0.055
Q18: Work capacity	0.23 (0.12)	0.07	0.27 (0.12)	0.028	0.17 (0.14)	0.21	-0.23 (0.17)	0.19
Psychological	0.89 (0.32)	0.006*	0.89 (0.32)	0.006*	0.45 (0.35)	0.20	-1.23 (0.44)	0.006*
Q5: Positive feelings	0.28 (0.13)	0.035	0.30 (0.13)	0.025*	0.15 (0.15)	0.32	-0.46 (0.18)	0.013*
Q6: Spirit/religion/beliefs	0.23 (0.15)	0.12	0.23 (0.15)	0.15	0.05 (0.16)	0.78	-0.52 (0.21)	0.013*
Q7: Think	0.47 (0.13)	< 0.001*	0.45 (0.13)	0.001*	0.24 (0.14)	0.09	-0.60 (0.18)	0.001*
Q11: Body image	0.22 (0.12)	0.08	0.23 (0.13)	0.07	0.18 (0.14)	0.22	-0.16 (0.18)	0.38
Q19: Self-esteem	0.26 (0.12)	0.025*	0.30 (0.12)	0.012*	0.18 (0.13)	0.17	-0.32 (0.17)	0.055
Q26: Negative feelings	-0.13 (0.13)	0.33	-0.17 (0.13)	0.20	-0.11 (0.14)	0.45	0.20 (0.18)	0.27
Social	0.82 (0.39)	0.038	0.79 (0.40)	0.051	0.14 (0.44)	0.76	-1.93 (0.55)	0.001*
Q20: Personal relationship	0.13 (0.11)	0.21	0.14 (0.11)	0.20	0.07 (0.12)	0.54	-0.20 (0.15)	0.20
Q21: Sexual activity	0.34 (0.13)	0.009*	0.33 (0.14)	0.015*	0.10 (0.15)	0.49	-0.66 (0.19)	0.001*
Q22: Social support	0.10 (0.12)	0.43	0.07 (0.13)	0.59	-0.08 (0.14)	0.58	-0.43 (0.18)	0.015*
Q27: Being respected	0.23 (0.12)	0.052	0.24 (0.12)	0.055	0.02 (0.13)	0.87	-0.64 (0.17)	<0.001*
Environment	0.95 (0.35)	0.006*	0.93 (0.35)	0.001*	0.42 (0.39)	0.27	-1.48 (0.49)	0.003*
Q8: Safety and security	0.33 (0.13)	0.014*	0.31 (0.13)	0.02*	0.18 (0.15)	0.22	-0.46 (0.19)	0.015*
Q9: Physical environment	0.40 (0.12)	0.001*	0.34 (0.12)	0.006*	0.18 (0.13)	0.17	-0.40 (0.17)	0.02*
Q12: Financial resources	0.25 (0.14)	0.07	0.28 (0.14)	0.05	0.12 (0.16)	0.43	-0.44 (0.20)	0.027
Q13: Information acquiring	0.27 (0.13)	0.037	0.25 (0.13)	0.048	0.12 (0.14)	0.41	-0.43 (0.18)	0.018*
Q14: Leisure activities	0.41 (0.13)	0.002*	0.41 (0.13)	0.003*	0.20 (0.15)	0.18	-0.59 (0.18)	0.001*
Q23: Home environment	0.12 (0.11)	0.24	0.09 (0.11)	0.41	-0.02 (0.12)	0.89	-0.29 (0.15)	0.051
Q24: Health service	0.06 (0.11)	0.61	0.09 (0.12)	0.46	0.02 (0.13)	0.85	-0.19 (0.16)	0.25
Q25: Transportation	0.16 (0.11)	0.15	0.18 (0.11)	0.09	0.07 (0.12)	0.73	-0.33 (0.15)	0.03
Q28: Eating	0.16 (0.11)	0.16	0.14 (0.11)	0.22	0.07 (0.13)	0.59	-0.20 (0.16)	0.22

\* Statistically significant ( $p < 0.025$ ).

B = regression coefficient; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; MMTP = methadone maintenance treatment program; SE = standard error; WHOQOL-BREF = Taiwanese brief version of the World Health Organization's quality of life.

<sup>a</sup> Without any adjusted variable.

<sup>b</sup> Age, sex, educational years, living status, and fixed employment were adjusted.

<sup>c</sup> Age, sex, educational years, living status, fixed employment, HIV-positive, HBV-positive, and HCV-positive infections were adjusted.

<sup>d</sup> Bonferroni adjustment for multiple comparisons was used, and the significant  $p$  value was set at 0.025 because we compared healthy controls versus MMTP patients (Table 2) and publicly-funded MMTP versus self-paid MMTP patients (Table 3).

WHOQOL-BREF. Because different scales of the WHOQOL-BREF were adopted, we first converted all WHOQOL-BREF domain scores in the two earlier studies<sup>25,26</sup> into a 4–20 scale, and calculated the Cohen's *d*. We found that Lin et al<sup>25</sup> reported a significant and large difference in Environment domain scores between heroin users and healthy controls, as summarized in Appendix 3. However, this trend was not found in our results and those of Yen et al<sup>26</sup>. The differences among these studies were thus mainly due to the different WHOQOL-BREF scores among healthy controls (Lin et al<sup>25</sup>  $14.08 \pm 2.08$ ; Yen et al<sup>26</sup>  $12.26 \pm 2.58$ ; referents of our publicly-funded participants,  $12.86 \pm 1.88$ ; referents of our self-paid participants,  $12.88 \pm 2.18$ ), as the WHOQOL-BREF domain scores were similar for heroin users in previous studies<sup>25,26</sup> and the current one. A potential explanation for this is that the healthy controls were recruited from different areas and might have expressed different subjective feelings about their environments.

Although previous studies<sup>22,25,26</sup> reported low QoL domain scores among heroin users, they did not delineate the detailed difficulties and suffering related to clinical care.<sup>35</sup> A layer by layer analysis of QoL difficulties from domain scores to item scores is thus critical. Taking our results as examples, both publicly-funded MMTP and self-paid MMTP patients (or we may say HIV-positive and negative MMTP patients, respectively) were found to have physical and psychological QoL problems. However, using item scores we found that publicly-funded MMTP (HIV-positive) patients had worse scores for all of the items in the Physical and Psychological domains compared to their matched counterparts. As for self-paid MMTP (HIV-negative) patients, they seemed to have no problems related to "Energy and fatigue" and "Work capacity" in the Physical domain, and seemed to only have one problem ("Negative feelings") in the Psychological domain. Based on the information obtained from a detailed analysis of individual item scores, clinicians will be able to address the different physical and psychological needs of publicly-funded MMTP (HIV-positive) and self-paid MMTP (HIV-negative) patients. Another interesting finding from the item-level analyses was that the self-paid MMTP patients had three item scores (Q9: Physical environment; Q14: Leisure activities; Q24: Health service) that were significantly higher than their counterparts. A possible explanation for this is that the self-paid MMTP patients may have a higher socioeconomic status, and thus they were more likely to live in a healthier physical environment, have enough resources for leisure activities, and receive adequate health services. An alternative explanation would be that they felt better able to master their environmental conditions, and thus tended to report high scores for these three items. However, as we did not have any additional data to corroborate these hypotheses, future studies on this issue are needed.

The strength of this study was that it collected representative referents and conducted a comprehensive control of confounding factors for comparison, and thus it is able to provide clinicians with valuable knowledge related to managing MMTP patients. However, this study also has the following limitations. First, the participants were recruited from patients who were coming for their first clinic visit for

MMTP, and thus generalizing our results to those who have already been receiving MMTP treatment may not be appropriate. However, the results of this study of fresh patients could be used as a guide for clinicians in order to make improvements to various items and domains, as highlighted by the QoL findings. Second, because all individuals participated in MMTP, the findings of this study may not be applicable to heroin users who are receiving no treatment. Third, because the WHOQOL-BREF is a self-rated measurement, heroin users with impaired cognitive abilities may rate their QoL scores inaccurately. However, the WHOQOL-BREF has been validated using item response theory in patients who were heroin-dependent,<sup>34</sup> and so any such bias may not be significant. Fourth, the matched referents were collected in 2001, and the heroin users coming for MMTP were recruited from 2006 to 2008, and thus there was a time gap between when the two groups' data was collected, and this may have impacted the WHOQOL scores, especially for the Social and Environment domains. Finally, because the NHIS data did not include living status and specific chronic viral infections in the survey, such as HBV, HCV, HIV, and so on, we were unable to adjust for these factors in the QoL analysis. However, both HBV and HCV are chronic infections, and patients usually appear to be healthy unless cirrhosis and/or liver cancer develops, and before this they may not significantly affect the patients' QoL. By contrast, HIV infection, although also chronic, generally affects patient's QoL in many aspects, especially since it is still seen as a stigma in Taiwan. Therefore, the impairment of QoL among heroin users may at least be partially attributed to their HIV status, and possibly also to HBV and HCV infections. Future studies collecting a sample of controls with the same conditions would be useful to clarify the magnitudes to which these infections confounded our results.

In conclusion, heroin users in MMTP, especially those with HIV infection, suffer from poorer QoL in the Physical, Psychological, and Social domains as compared with age-, sex-, education-, and municipality-matched referents. Further analyses of individual items sheds some light on possible improvements to treatment practices. HBV and HCV infection, which currently have effective treatments that are available, appear to impact QoL less in the case of MMTP patients. By contrast, HIV infection is a major factor that should be diagnosed and addressed, while the stigma of heroin use and HIV infection is another factor that should be examined in future studies.

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## Appendix 1. Sensitivity analyses for males only.

**Table S1** Demographics and WHOQOL-BREF scores between patients coming for a methadone maintenance treatment program (MMTP) and matched referents from the general Taiwanese population.

	Publicly-funded ( <i>n</i> = 118)	Matched referents <sup>a</sup> ( <i>n</i> = 102)	Cohen's <i>d</i>	Self-paid ( <i>n</i> = 92)	Matched referents <sup>a</sup> ( <i>n</i> = 91)	Cohen's <i>d</i>
Age (y)	39.04 ± 7.36	38.28 ± 7.54		38.88 ± 7.08	38.87 ± 7.08	
Educational years						
< 6 y	4 (3.4)	4 (3.9)		1 (1.1)	1 (1.1)	
7–12 y	108 (91.5)	92 (90.2)		90 (97.8)	89 (97.8)	
≥ 13 y	6 (5.1)	6 (5.9)		1 (1.1)	1 (1.1)	
Living status <sup>b</sup>						
With others	107 (90.7)			85 (95.5)		
Alone	11 (9.3)			4 (4.5)		
Age of 1 <sup>st</sup> heroin use (y)	25.55 ± 5.86			27.59 ± 6.89		
Employment status <sup>b</sup>						
Fixed	65 (55.6)			53 (57.6)		
Nonfixed	52 (44.4)			39 (42.4)		
HIV carrier						
Seronegative	78 (66.1)			92 (100.0)		
Seropositive	40 (33.9)			0 (0.0)		
HBV carrier						
Seronegative	95 (80.5)			79 (85.9)		
Seropositive	23 (19.5)			13 (14.1)		
HCV carrier						
Seronegative	4 (3.4)			7 (7.6)		
Seropositive	114 (96.6)			85 (92.4)		
WHOQOL-BREF						
Physical	11.97 ± 1.82	15.06 ± 1.93	−1.11***	12.62 ± 1.95	15.38 ± 2.17	−0.98***
Psychological	12.03 ± 2.61	13.57 ± 2.32	−0.42***	13.00 ± 2.16	13.58 ± 2.49	−0.19
Social	12.60 ± 3.13	13.98 ± 2.01	−0.35**	13.60 ± 2.75	14.03 ± 2.39	−0.12
Environment	12.52 ± 2.71	12.90 ± 1.82	−0.12	13.53 ± 2.31	12.88 ± 2.18	0.21*

Data are presented as *n* (%) or mean ± SD.

\* *p* < 0.05.

\*\* *p* < 0.01.

\*\*\* *p* < 0.001.

Cohen's *d* = mean difference divided by pooled SD; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; SD = standard deviation; WHOQOL-BREF = Taiwanese brief version of the World Health Organization's quality of life.

<sup>a</sup> Matched referents were paired with MMTP patients according to age (± 5 years), sex, years of education, and municipality.

<sup>b</sup> With missing values.

**Table S2** Regression coefficients of model construction for publicly-funded and self-paid methadone maintenance treatment program (MMTP) patients versus matched referents<sup>a</sup> on the WHOQOL-BREF.

Domain Item #	Item description	Univariate <sup>b</sup>				Multivariate <sup>c</sup>			
		Publicly-funded		Self-paid		Publicly-funded		Self-paid	
		B(SE)	p	B (SE)	p	B(SE)	p	B(SE)	p
Physical		-3.23 (0.23)	< 0.001*	-2.65 (0.25)	< 0.001*	-3.23 (0.23)	< 0.001*	-2.64 (0.25)	<0.001*
Q3	Pain & discomfort	-1.51 (0.11)	< 0.001*	-1.49 (0.12)	< 0.001*	-1.51 (0.11)	< 0.001*	-1.48 (0.12)	<0.001*
Q4	Medication	-2.05 (0.11)	< 0.001*	-2.25 (0.12)	< 0.001*	-2.03 (0.11)	< 0.001*	-2.27 (0.12)	<0.001*
Q10	Energy & fatigue	-0.38 (0.10)	< 0.001*	-0.12 (0.10)	0.24	-0.38 (0.10)	< 0.001*	-0.12 (0.11)	0.25
Q15	Mobility	-0.42 (0.09)	< 0.001*	-0.22 (0.10)	0.031*	-0.42 (0.09)	< 0.001*	-0.21 (0.10)	0.037*
Q16	Sleep & rest	-0.62 (0.11)	< 0.001*	-0.36 (0.12)	0.002*	-0.63 (0.11)	< 0.001*	-0.36 (0.12)	0.002*
Q17	Activities of daily living	-0.35 (0.09)	< 0.001*	-0.18 (0.09)	0.06	-0.35 (0.09)	< 0.001*	-0.17 (0.09)	0.07
Q18	Work capacity	-0.36 (0.10)	< 0.001*	-0.06 (0.11)	0.60	-0.36 (0.10)	< 0.001*	-0.06 (0.11)	0.56
Psychological		-1.62 (0.28)	< 0.001*	-0.63 (0.31)	0.043*	-1.62 (0.28)	< 0.001*	-0.60 (0.31)	0.054
Q5	Positive feelings	-0.21 (0.11)	0.07	0.05 (0.12)	0.70	-0.21 (0.11)	0.06	0.07 (0.12)	0.59
Q6	Spirit/religion/beliefs	-0.38 (0.12)	0.003*	-0.12 (0.13)	0.36	-0.38 (0.12)	0.002*	-0.10 (0.13)	0.44
Q7	Concentration	-0.47 (0.11)	< 0.001*	0.02 (0.12)	0.89	-0.46 (0.11)	< 0.001*	0.03 (0.12)	0.82
Q11	Body image	-0.23 (0.11)	0.032*	0.03 (0.12)	0.78	-0.24 (0.11)	0.03*	0.03 (0.12)	0.77
Q19	Self-esteem	-0.46 (0.10)	< 0.001*	-0.15 (0.11)	0.15	-0.46 (0.10)	< 0.001*	-0.16 (0.11)	0.15
Q26	Negative feelings	-0.68 (0.11)	< 0.001*	-0.76 (0.12)	< 0.001*	-0.68 (0.11)	< 0.001*	-0.76 (0.12)	<0.001*
Social		-1.51 (0.31)	< 0.001*	-0.46 (0.33)	0.17	-1.52 (0.31)	< 0.001*	-0.45 (0.34)	0.18
Q20	Personal relationship	-0.20 (0.09)	0.026*	-0.07 (0.10)	0.94	-0.20 (0.09)	0.027*	-0.01 (0.10)	0.95
Q21	Sexual activity	-0.74 (0.10)	< 0.001*	-0.37 (0.11)	0.001*	-0.75 (0.10)	< 0.001*	-0.36 (0.11)	0.001*
Q22	Social support	-0.29 (0.10)	0.003*	-0.11 (0.11)	0.30	-0.29 (0.10)	0.003*	-0.11 (0.11)	0.30
Q27	Being respected	-0.28 (0.10)	0.005*	0.02 (0.11)	0.83	-0.28 (0.10)	0.004*	0.03 (0.11)	0.81
Environment		-0.37 (0.27)	0.18	0.58 (0.30)	0.052	-0.38 (0.27)	0.16	0.60 (0.30)	0.04*
Q8	Safety & security	-0.20 (0.11)	0.07	0.13 (0.12)	0.28	-0.21 (0.11)	0.06	0.14 (0.12)	0.24
Q9	Physical environment	0.02 (0.11)	0.87	0.43 (0.12)	< 0.001*	0.02 (0.11)	0.88	0.43 (0.12)	<0.001*
Q12	Financial resources	-0.31 (0.12)	0.011*	-0.09 (0.13)	0.50	-0.32 (0.12)	0.008*	-0.07 (0.13)	0.62
Q13	Information acquisition	-0.28 (0.11)	0.008*	-0.05 (0.11)	0.69	-0.28 (0.11)	0.008*	-0.04 (0.11)	0.70
Q14	Leisure activities	0.07 (0.11)	0.51	0.46 (0.12)	< 0.001*	0.07 (0.11)	0.52	0.47 (0.12)	<0.001*
Q23	Home environment	-0.05 (0.09)	0.56	0.05 (0.10)	0.59	-0.06 (0.09)	0.53	0.06 (0.10)	0.55
Q24	Health service	0.18 (0.10)	0.06	0.28 (0.10)	0.008*	0.17 (0.10)	0.065	0.26 (0.10)	0.011*
Q25	Transportation	-0.14 (0.09)	0.12	-0.01 (0.10)	0.94	-0.15 (0.09)	0.12	-0.01 (0.10)	0.92
Q28	Eating	-0.12 (0.10)	0.24	0.10 (0.11)	0.33	-0.12 (0.10)	0.23	0.11 (0.11)	0.31

\* Statistically significant ( $p < 0.05$ ).

B = regression coefficient; MMTP = methadone maintenance treatment program; SE = standard error; WHOQOL-BREF = Taiwanese brief version of World Health Organization's quality of life.

<sup>a</sup> Referents were selected from the general population and matched according to age, sex, education, and municipality with MMTP patients.<sup>b</sup> Without any adjustment.<sup>c</sup> Adjusted for age, sex, and educational years.

**Table S3** Regression coefficients of model construction for WHOQOL-BREF scores comparing self-paid versus publicly-funded methadone maintenance treatment program (MMTP) patients.

Domain Item #	Model 0 <sup>a</sup>		Model 1 <sup>b</sup>		Model 2 <sup>c</sup>			
	Self-paid vs. publicly-funded		Self-paid vs. publicly-funded		Self-paid vs. publicly-funded		HIV positive vs. HIV-negative	
	B (SE)	<i>p</i> <sup>d</sup>						
Physical	0.59 (0.27)	0.03	0.69 (0.27)	0.011*	0.49 (0.30)	0.10	-0.53 (0.38)	0.17
Q3: Pain & discomfort	0.02 (0.14)	0.91	0.02 (0.14)	0.88	0.05 (0.16)	0.75	0.10 (0.20)	0.61
Q4: Medication	-0.21 (0.14)	0.14	-0.20 (0.14)	0.16	-0.10 (0.16)	0.54	0.24 (0.20)	0.23
Q10: Energy & fatigue	0.26 (0.12)	0.035	0.28 (0.12)	0.022*	0.14 (0.13)	0.29	-0.37 (0.17)	0.033
Q15: Mobility	0.20 (0.12)	0.09	0.21 (0.12)	0.08	0.20 (0.13)	0.13	-0.002 (0.17)	0.99
Q16: Sleep & rest	0.26 (0.14)	0.07	0.32 (0.14)	0.025*	0.19 (0.16)	0.22	-0.36 (0.20)	0.07
Q17: Activities of daily living	0.17 (0.11)	0.11	0.20 (0.11)	0.08	0.08 (0.12)	0.50	-0.33 (0.15)	0.03
Q18: Work capacity	0.30 (0.13)	0.019*	0.34 (0.13)	0.008*	0.24 (0.14)	0.09	-0.24 (0.18)	0.19
Psychological	0.99 (0.34)	0.004*	0.96 (0.34)	0.005*	0.50 (0.37)	0.18	-1.33 (0.47)	0.006*
Q5: Positive feelings	0.26 (0.14)	0.07	0.26 (0.14)	0.06	0.10 (0.15)	0.53	-0.50 (0.19)	0.012*
Q6: Spirit/religion/beliefs	0.25 (0.16)	0.11	0.23 (0.16)	0.14	0.02 (0.17)	0.89	-0.59 (0.22)	0.007*
Q7: Think	0.48 (0.14)	0.001*	0.44 (0.14)	0.002*	0.24 (0.15)	0.12	-0.60 (0.19)	0.002*
Q11: Body image	0.27 (0.13)	0.046	0.27 (0.14)	0.047	0.23 (0.15)	0.13	-0.13 (0.19)	0.51
Q19: Self-esteem	0.31 (0.12)	0.015*	0.33 (0.13)	0.008*	0.22 (0.14)	0.11	-0.30 (0.18)	0.09
Q26: Negative feelings	-0.08 (0.13)	0.57	-0.11 (0.14)	0.44	-0.06 (0.15)	0.68	0.13 (0.19)	0.51
Social	1.05 (0.42)	0.012*	1.02 (0.42)	0.017*	0.26 (0.46)	0.57	-2.25 (0.58)	<0.001*
Q20: Personal relationship	0.19 (0.11)	0.09	0.19 (0.11)	0.10	0.11 (0.13)	0.37	-0.25 (0.16)	0.12
Q21: Sexual activity	0.38 (0.14)	0.007*	0.37 (0.14)	0.01*	0.14 (0.16)	0.38	-0.70 (0.20)	<0.001*
Q22: Social support	0.18 (0.13)	0.16	0.15 (0.13)	0.26	-0.03 (0.14)	0.86	-0.50 (0.18)	0.007*
Q27: Being respected	0.30 (0.13)	0.019*	0.31 (0.13)	0.02*	0.04 (0.14)	0.80	-0.80 (0.18)	<0.001*
Environment	0.95 (0.37)	0.01*	0.89 (0.37)	0.017*	0.29 (0.40)	0.48	-1.78 (0.51)	0.001*
Q8: Safety & security	0.33 (0.14)	0.015*	0.30 (0.14)	0.033	0.13 (0.15)	0.40	-0.55 (0.19)	0.005*
Q9: Physical environment	0.41 (0.13)	0.002*	0.34 (0.13)	0.009*	0.15 (0.14)	0.28	-0.51 (0.18)	0.005*
Q12: Financial resources	0.22 (0.14)	0.13	0.24 (0.15)	0.11	0.03 (0.16)	0.84	-0.58 (0.20)	0.005*
Q13: Information acquiring	0.24 (0.13)	0.08	0.22 (0.14)	0.11	0.07 (0.15)	0.62	-0.45 (0.19)	0.018*
Q14: Leisure activities	0.39 (0.14)	0.006*	0.37 (0.14)	0.01*	0.13 (0.15)	0.40	-0.67 (0.20)	0.001*
Q23: Home environment	0.11 (0.11)	0.33	0.07 (0.11)	0.55	-0.07 (0.12)	0.57	-0.38 (0.16)	0.016*
Q24: Health service	0.10 (0.12)	0.41	0.12 (0.12)	0.30	0.04 (0.13)	0.75	-0.25 (0.17)	0.13
Q25: Transportation	0.14 (0.12)	0.24	0.16 (0.12)	0.16	0.04 (0.13)	0.75	-0.37 (0.16)	0.023*
Q28: Eating	0.22 (0.12)	0.07	0.20 (0.12)	0.11	0.11 (0.13)	0.41	-0.24 (0.17)	0.17

\* Statistically significant ( $p < 0.025$ ).

B = regression coefficient; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; MMTP = methadone maintenance treatment program; SE = standard error; WHOQOL-BREF = Taiwanese brief version of the World Health Organization's quality of life.

<sup>a</sup> Without any adjusted variable.

<sup>b</sup> Age, sex, educational years, living status, and fixed employment were adjusted.

<sup>c</sup> Age, sex, educational years, living status, fixed employment, HIV-positive, HBV-positive, and HCV-positive infections were adjusted.

<sup>d</sup> Bonferroni adjustment for multiple comparisons was used, and the significant  $p$  value was set at 0.025 because we compared healthy controls versus MMTP patients (Table 2) and publicly-funded MMTP versus self-paid MMTP patients (Table 3).

## Appendix 2. Examining the effects of HIV-positive infection without HBV- and HCV-positive infections.

Domain Item #	Model 2 <sup>a</sup>				Model 2 <sup>b</sup>			
	Self-paid vs. publicly-funded		HIV-positive vs. HIV-negative		Self-paid vs. publicly-funded		HIV-positive vs. HIV-negative	
	B (SE)	<i>p</i> <sup>c</sup>						
Physical	0.51 (0.28)	0.07	-0.37 (0.35)	0.29	0.50 (0.28)	0.08	-0.37 (0.36)	0.30
Q3: Pain & discomfort	0.07 (0.15)	0.64	0.11 (0.19)	0.57	0.06 (0.15)	0.68	0.11 (0.19)	0.55
Q4: Medication	-0.07 (0.15)	0.62	0.29 (0.19)	0.12	-0.05 (0.15)	0.72	0.29 (0.19)	0.12
Q10: Energy & fatigue	0.18 (0.13)	0.15	-0.31 (0.16)	0.06	0.17 (0.13)	0.18	-0.31 (0.16)	0.057
Q15: Mobility	0.19 (0.12)	0.12	-0.03 (0.16)	0.85	0.19 (0.13)	0.77	-0.03 (0.16)	0.87
Q16: Sleep & rest	0.21 (0.15)	0.15	-0.24 (0.19)	0.20	0.21 (0.15)	0.17	-0.23 (0.19)	0.21
Q17: Activities of daily living	0.07 (0.12)	0.53	-0.29 (0.15)	0.049	0.07 (0.12)	0.55	-0.28 (0.15)	0.055
Q18: Work capacity	0.19 (0.14)	0.16	-0.23 (0.17)	0.19	0.17 (0.14)	0.21	-0.23 (0.17)	0.19
Psychological	0.46 (0.35)	0.19	-1.23 (0.44)	0.006*	0.45 (0.35)	0.20	-1.23 (0.44)	0.006*
Q5: Positive feelings	0.14 (0.15)	0.35	-0.46 (0.18)	0.012*	0.15 (0.15)	0.32	-0.46 (0.18)	0.013*
Q6: Spirit/religion/beliefs	0.06 (0.16)	0.73	-0.51 (0.20)	0.013*	0.05 (0.16)	0.78	-0.52 (0.21)	0.013*
Q7: Think	0.24 (0.14)	0.09	-0.60 (0.18)	0.001*	0.24 (0.14)	0.09	-0.60 (0.18)	0.001*
Q11: Body image	0.18 (0.14)	0.22	-0.16 (0.18)	0.39	0.18 (0.14)	0.22	-0.16 (0.18)	0.38
Q19: Self-esteem	0.19 (0.13)	0.15	-0.31 (0.16)	0.059	0.18 (0.13)	0.17	-0.32 (0.17)	0.055
Q26: Negative feelings	-0.10 (0.14)	0.48	0.19 (0.18)	0.30	-0.11 (0.14)	0.45	0.20 (0.18)	0.27
Social	0.13 (0.43)	0.77	-1.90 (0.55)	0.001*	0.14 (0.44)	0.76	-1.93 (0.55)	0.001*
Q20: Personal relationship	0.07 (0.12)	0.57	-0.20 (0.15)	0.19	0.07 (0.12)	0.54	-0.20 (0.15)	0.20
Q21: Sexual activity	0.11 (0.15)	0.47	-0.65 (0.19)	0.001*	0.10 (0.15)	0.49	-0.66 (0.19)	0.001*
Q22: Social support	-0.08 (0.14)	0.57	-0.42 (0.17)	0.017*	-0.08 (0.14)	0.58	-0.43 (0.18)	0.015*
Q27: Being respected	0.02 (0.13)	0.89	-0.63 (0.17)	< 0.001*	0.02 (0.13)	0.87	-0.64 (0.17)	< 0.001*
Environment	0.42 (0.38)	0.28*	-1.47 (0.48)	0.003*	0.42 (0.39)	0.27	-1.48 (0.49)	0.003*
Q8: Safety & security	0.16 (0.15)	0.28	-0.45 (0.19)	0.017*	0.18 (0.15)	0.22	-0.46 (0.19)	0.015*
Q9: Physical environment	0.20 (0.13)	0.14	-0.40 (0.17)	0.017*	0.18 (0.13)	0.17	-0.40 (0.17)	0.02*
Q12: Financial resources	0.13 (0.16)	0.41	-0.43 (0.20)	0.028	0.12 (0.16)	0.43	-0.44 (0.20)	0.027
Q13: Information acquiring	0.11 (0.14)	0.46	-0.44 (0.18)	0.016*	0.12 (0.14)	0.41	-0.43 (0.18)	0.018*
Q14: Leisure activities	0.20 (0.15)	0.16	-0.58 (0.18)	0.002*	0.20 (0.15)	0.18	-0.59 (0.18)	0.001*
Q23: Home environment	-0.02 (0.12)	0.90	-0.29 (0.15)	0.047	-0.02 (0.12)	0.89	-0.29 (0.15)	0.051
Q24: Health service	0.02 (0.13)	0.89	-0.19 (0.16)	0.23	0.02 (0.13)	0.85	-0.19 (0.16)	0.25
Q25: Transportation	0.07 (0.12)	0.55	-0.33 (0.15)	0.031	0.07 (0.12)	0.73	-0.33 (0.15)	0.03
Q28: Eating	0.08 (0.13)	0.56	-0.19 (0.16)	0.24	0.07 (0.13)	0.59	-0.20 (0.16)	0.22

\* Statistically significant ( $p < 0.025$ ).

B = regression coefficient; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; MMTP = methadone maintenance treatment program; SE = standard error; WHOQOL-BREF = Taiwanese brief version of the World Health Organization's quality of life.

<sup>a</sup> Age, sex, educational years, living status, fixed employment, and HIV-positive infection were adjusted.

<sup>b</sup> Age, sex, educational years, living status, fixed employment, HIV-positive, HBV-positive, and HCV-positive infections were adjusted.

<sup>c</sup> Bonferroni adjustment for multiple comparisons was used, and the significant  $p$  value was set at 0.025 because we compared healthy controls versus MMTP patients (Table 2) and publicly-funded MMTP versus self-paid MMTP patients (Table 3).

### Appendix 3. Comparing WHOQOL-BREF domains with those of Lin et al<sup>25</sup> and Yen et al<sup>26</sup>.

Study	Heroin user		Healthy control		Cohen's <i>d</i>
	Mean	SD	Mean	SD	
Lin et al <sup>25</sup>	(n = 121)		(n = 157)		
Physical	12.51	1.86	13.57	1.82	-0.57
Psychological	12.18	2.01	13.07	1.96	-0.45
Social	12.59	2.78	13.80	2.02	-0.51
Environment	12.71	2.24	14.08	2.08	-0.64
Yen et al <sup>26</sup>	(n = 123)		(n = 106)		
Physical	12.48	2.42	15.28	1.90	-1.28
Psychological	11.50	2.69	12.66	1.97	-0.49
Social	12.21	2.53	13.87	2.14	-0.71
Environment	11.92	2.11	12.26	2.58	-0.14
Current study	(n = 129)		(n = 113)		
Publicly-funded					
Physical	11.93	1.86	15.01	1.93	-1.12
Psychological	12.01	2.66	13.51	2.34	-0.41
Social	12.73	3.13	13.95	1.98	-0.31
Environment	12.47	2.80	12.86	1.88	-0.12
Current study	(n = 105)		(n = 104)		
Self-paid					
Physical	12.53	1.90	15.44	2.15	-1.07
Psychological	12.88	2.07	13.58	2.44	-0.24
Social	13.50	2.76	14.03	2.34	-0.15
Environment	13.48	2.24	12.88	2.18	0.20

Cohen's *d* = mean difference divided by pooled SD; SD = standard deviation; WHOQOL-BREF = Taiwanese brief version of the World Health Organization's quality of life.

### References

- Chang KC, Lin CY. Effects of publicly-funded and quality of life on attendance rate among methadone maintenance treatment patients in Taiwan: an 18-month follow-up study. *Harm Reduct J* 2015. Accepted.
- Hser YI. Predicting long-term stable recovery from heroin addiction: findings from a 33-year follow-up study. *J Addict Dis* 2007;26:51–60.
- Degenhardt L, Charlson F, Mathers B, Hall WD, Flaxman AD, Johns N, et al. The global epidemiology and burden of opioid dependence: results from the global burden of disease 2010 study. *Addiction* 2014;109:1320–33.
- Degenhardt L, Bucello C, Mathers B, Briegleb C, Ali H, Hickman M, et al. Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies. *Addiction* 2010;106:32–51.
- Oppenheimer E, Tobutt C, Taylor C, Andrew T. Death and survival in a cohort of heroin addicts from London clinics: a 22-year follow-up study. *Addiction* 1994;89:1299–308.
- Wang PW, Wu HC, Yen CN, Yeh YC, Chung KS, Chang HC, et al. Predictors of the severity of depressive symptoms among intravenous heroin users receiving methadone maintenance treatment in Taiwan: an 18-month follow-up study. *Psychol Addict Behav* 2012;26:145–50.

- Che Y, Assanangkornchai S, McNeil E, Li J, You J, Chongsuvivatwong V. Patterns of attendance in methadone maintenance treatment program in Yunnan Province, China. *Am J Drug Alcohol Abuse* 2011;37:148–54.
- Hubbard RL, Craddock SG, Flynn PM, Anderson J, Etheridge RM. Overview of 1-year follow-up outcomes in the Drug Abuse Treatment Outcome Study (DATOS). *Psychol Addict Behav* 1997;11:261–78.
- Puigdollers E, Domingo-Salvany A, Brugal MT, Torrens M, Alvarós J, Castillo C, et al. Characteristics of heroin addicts entering methadone maintenance treatment: quality of life and gender. *Subst Use Misuse* 2004;39:1353–68.
- Yang F, Lin P, Li Y, He Q, Long Q, Fu X, et al. Predictors of retention in community-based methadone maintenance treatment program in Pearl River Delta, China. *Harm Reduct J* 2013;10:3.
- Clausen T, Anchersen K, Waal H. Mortality prior to, during and after opioid maintenance treatment (OMT): a national prospective cross-registry study. *Drug Alcohol Depend* 2008;94:151–7.
- Farré M, Mas A, Torrens M, Moreno V, Camí J. Retention rate and illicit opioid use during methadone maintenance interventions: a meta-analysis. *Drug Alcohol Depend* 2002;65:283–90.
- Marsch LA. The efficacy of methadone maintenance interventions in reducing illicit opiate use, HIV risk behavior and criminality: a meta-analysis. *Addiction* 1998;93:515–32.
- Chien IC, Chang KC, Lin CH, Chou YJ, Chou P. Prevalence of diabetes in patients with bipolar disorder in Taiwan: a population-based national health insurance study. *Gen Hosp Psychiatry* 2010;32:138–41.
- Chien IC, Chou YJ, Lin CH. Prevalence of psychiatric disorders among national health insurance enrollees in Taiwan. *Psychiatr Serv* 2004;55:691–7.
- Ko NY, Wang PW, Wu HC, Yen CN, Hsu ST, Yeh YC, et al. Self-efficacy and HIV risk behaviors among heroin users in Taiwan. *J Stud Alcohol Drugs* 2012;73:469–76.
- Rhodes T, Lowndes C, Judd A, Mikhailova LA, Sarang A, Rylkov A, et al. Explosive spread and high prevalence of HIV infection among injecting drug users in Togliatti City, Russia. *AIDS* 2002;16:F25–31.
- Chen YM, Kuo SH. HIV-1 in Taiwan. *Lancet* 2007;369:623–5.
- Su CT, Ng HS, Yang AL, Lin CY. Psychometric evaluation of the Short Form 36 Health Survey (SF-36) and the World Health Organization Quality of Life Scale Brief Version (WHOQOL-BREF) for patients with schizophrenia. *Psychol Assess* 2014;26:980–9.
- Bobes J, García-Portilla P, Sáiz PA, Bascarán T, Bousoño M. Quality of life measures in schizophrenia. *Eur Psychiatry* 2005;20:S313–7.
- Torrens M, San L, Martinez A, Castillo C, Domingo-Salvany A, Alonso J. Use of the Nottingham Health Profile for measuring health status of patients in methadone maintenance treatment. *Addiction* 1997;92:707–16.
- Astals M, Domingo-Salvany A, Buenaventura CC, Tato J, Vazquez JM, Martin-Santos R, et al. Impact of substance dependence and dual diagnosis on the quality of life of heroin users seeking treatment. *Subst Use Misuse* 2008;43:612–32.
- Deng CF, Ma X, Zhou H, Liu QL, Yang Y, Song Z, et al. Quality of life of heroin dependent patients with methadone maintenance therapy. *Sichuan Da Xue Xue Bao Yi Xue Ban* 2009;40:539–43.
- Korthuis PT, Zephyrin LC, Fleishman JA, Saha S, Josephs JS, McGrath MM, et al. Health-related quality of life in HIV-infected patients: the role of substance use. *AIDS Patient Care STDs* 2008;22:859–67.

25. Lin SH, Chen KC, Lee SY, Hsiao CY, Lee IH, Yeh TL, et al. The economic cost of heroin dependency and quality of life among heroin users in Taiwan. *Psychiatry Res* 2013;209:512–7.
26. Yen CN, Wang CSM, Wang TY, Chen HF, Chang HC. Quality of life and its correlates among heroin users in Taiwan. *Kaohsiung J Med Sci* 2011;27:177–83.
27. American Psychiatric Association, Diagnostic and statistical manual of mental disorders, 4th ed., Author; Washington, DC.
28. Hung YT. *Sampling design of the National Health Interview Survey. NHIS Brief Communication No. 2.* Taipei, Taiwan: National Health Interview Survey; 2002.
29. Lin SH. *Field collection and completeness of data in the National Health Interview Survey. NHIS Brief Communication No. 4.* Taipei, Taiwan: National Health Interview Survey; 2002.
30. Lee LJH, Chung CW, Chang YY, Lee YC, Yang CH, Liou SH, et al. Comparison of the quality of life between patients with non-small-cell lung cancer and healthy controls. *Qual Life Res* 2011;20:415–23.
31. Faul F, Erdfelder E, Lang AG, Buchner A. G\*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 2007;39:175–91.
32. Yao G, Chung CW, Yu CF, Wang JD. Development and verification of validity and reliability of the WHOQOL-BREF Taiwan version. *J Formos Med Assoc* 2002;101:342–51.
33. The WHOQOL-Taiwan Group. *Development of the World Health Organization Quality of Life Scale Brief Version, Taiwan, version, and using manual.* 2nd ed. Taipei, Taiwan: The WHOQOL-Taiwan Group; 2005.
34. Chang KC, Wang JD, Tang CP, Cheng CM, Lin CY. Psychometric evaluation, using Rasch analysis, of the WHOQOL-BREF in heroin-dependent people undergoing methadone maintenance treatment: further item validation. *Health Qual Life Outcomes* 2014;12:148.
35. Su CT, Wang JD, Lin CY. Child-rated versus parent-rated quality of life of community-based obese children across gender and grade. *Health Qual Life Outcomes* 2013;11:206.
36. Portney LG, Watkins MP. *Foundations of clinical research: Applications to practice.* 2nd ed. Upper Saddle River, New Jersey: Prentice Hall Health; 2000.
37. De Maeyer J, Vanderplasschen W, Broekaert E. Quality of life among opiate-dependent individuals: a review of the literature. *Int J Drug Policy* 2001;21:364–80.
38. Wallace AE, Weeks WB, Wang S, Lee AF, Kazis LE. Rural and urban disparities in health-related quality of life among veterans with psychiatric disorders. *Psychiatr Serv* 2006;57:851–6.
39. Weeks WB, Kazis LE, Shen Y, Cong Z, Ren XS, Miller D, et al. Differences in health-related quality of life in rural and urban veterans. *Am J Public Health* 2004;94:1762–7.
40. Parker R, Aggleton P. HIV and AIDS-related stigma and discrimination: a conceptual framework and implications for action. *Soc Sci Med* 2003;57:13–24.
41. Rasmusen E. Stigma and self-fulfilling expectations of criminality. *Journal of Law and Economics* 1996;39:519–44.