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Changes in drug use are associated with health-related quality of life improvements among methadone maintenance patients with HIV/AIDS

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Abstract
Purpose This longitudinal study assessed the changes in drug use patterns and health-related quality of life (HRQL) among HIV-positive drug users in the first methadone maintenance treatment (MMT) cohort in Vietnam.
Methods A secondary analysis was conducted on 370 HIV-positive drug users (age: mean ± SD: 29.5 ± 5.9 years; 95.7% men). Modified WHOQOL-BREF, self-report, and opioid confirmatory urine tests were used to assess HRQL and drug use behaviours at baseline, 3, 6, and 9 months. Generalized estimating equations (GEE) models were constructed to adjust for intra-individual correlations.
Results MMT response rate after 9 months was 89.9%. Rates of positive heroin urine tests rapidly decreased at the first trimester (18.1%) and then stabilized during the next 2 trimesters (11.8 and 14.4%). Among patients with continued drug use, frequency of use decreased from 3.4 to 0.7 time/day. Improvements in HRQL were large over the course of the study and highest in the psychological domain. Adjusting for propensity score in GEE models, ongoing heroin use during MMT resulted in large decrements in all HRQL domains.
Conclusions MMT improved the outcomes of treatment for drug users in ways that might facilitate success of antiretroviral therapy. Integrating MMT to HIV care and treatment services could be beneficial in injection-driven HIV epidemics in resource-scare settings.

Keywords Quality of life · HIV · Drug use · Methadone · Vietnam · WHOQOL-BREF

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Introduction

Antiretroviral treatment (ART) has dramatically reduced HIV-related mortality and morbidity and has improved quality of life of HIV/AIDS patients receiving treatment [1–3]. However, the effect of ART is less in injecting drug users (DUs) than in other patient groups [4]. Drug use is associated with severe comorbidities, delayed access to ART, and more importantly, adherence difficulties once ART is started [4, 5]. Treatment of opioid dependence has, therefore, become an important component of HIV care in injection-driven HIV epidemics.

Vietnam has one of the fastest growing HIV epidemics in Asia, largely driven by drug injection [5, 6]. According to the National Committee for AIDS, Drugs and Prostitution Prevention and Control, 146,731 DUs were recorded and managed in 90% of districts in the country [7]. Although HIV prevalence among DUs moderately decreased over the

last decade, from 29.4% in 2002 to 18.4% in 2009, DUs remained the largest HIV risk group accounting for 44% of prevalent HIV cases [7–9] and 50.6% of 15,713 newly detected HIV cases in 2009 [10]. Approximately 254,000 people are thought to be living with HIV/AIDS; among those, 25% are at WHO HIV stage III/IV or have a CD4 count $<$ 250 cells/μL and require ART [11]. Comprehensive HIV/AIDS care and treatment were prioritized as a cost-effective intervention in the National HIV/AIDS Strategic Plan [6, 12]. With substantial supports from international donors, free of charge HIV care and treatment services with antiretroviral drugs have rapidly scaled up in Vietnam [12–14]. However, the effectiveness of these interventions might be reduced as close to half of HIV patients were opioid dependent [4]. Since 2008, the Vietnam Ministry of Health created the first national methadone maintenance treatment (MMT) programme for DUs. Until then, the medical community had little experience with how opioid substitution benefits HIV care and antiretroviral treatment for HIV-positive DUs in the Vietnamese context [15–17].

The health-related quality of life (HRQL) indicators are widely applied in the sphere of HIV/AIDS. HRQL complements more objective outcomes that incorporate virologic and immunologic measures, comorbidities, and death [20–22]. HRQL is associated with physiological and biomedical status of HIV patients. In addition, HRQL has a good correlation with the patient's compliance with ART, particularly if adherence was sustained [18]. In MMT patients, Winklbaur et al. [19] observed that even short-term opioid maintenance was significantly related to higher HRQL scores. HRQL, therefore, could be used to predict the impact of MMT on care and treatment for HIV-positive DUs.

This study assessed the changes in drug use and HRQL during MMT, examined if these changes were different between DUs at early HIV stage and those at later HIV stages and receiving ART, and determined the impact of ongoing heroin use during MMT on HRQL among HIV-positive DUs in Vietnam.

Methods

Study setting

Two metropolitan areas with significant injection-driven HIV epidemics in Hai Phong and Ho Chi Minh City (Vietnam) were selected for the first national pilot MMT programme. These cities represent geographical areas with established HIV epidemics in large populations of injecting DUs, and settings where comprehensive HIV interventions have been implemented in the country. The first 6 pilot MMT clinics were organized as standalone sites. Participants were first informed about the availability of MMT services by the local authority of HIV/AIDS control and then selected on voluntary basis.

Hai Phong is a port city of about 1.8 millions citizens on the Red River Delta in northern Vietnam. It has a DU population of approximately 9,500, among whom 75% are injecting drugs and 40–50% are currently living with HIV/AIDS [14, 20]. The first 3 MMT pilot clinics in Hai Phong were established in 2008 in Le Chan, Ngo Quyen, and Thuy Nguyen Districts.

Ho Chi Minh City is the largest southern metropolitan centre in Vietnam with over 8 million residents. There are approximately 45,000 DUs in the city: 99% of whom are heroin users, mainly by injection [21]. Ho Chi Minh City has the largest HIV-positive population in Vietnam with 41,193 prevalent HIV-positive cases and had 23.1% of total newly detected HIV cases in the country in 2009 [7]. The MMT interventions in Ho Chi Minh City were piloted at District 4, District 6, and Binh Thanh District from May 2008.

Study design and participant recruitment

The Vietnam Administration of HIV/AIDS Control conducted a longitudinal cohort study of DUs recruited from January 2009 to October 2009. At baseline, patients were methadone-naïve, presented with drug use history, and did not have any severe health condition. After informed consent was obtained from volunteer participants, participants were tested for HIV at baseline. Repeated assessments were conducted at baseline, 3, 6, and 9 months. We used structured questionnaires in interviews with respondents to document self-reported drug use behaviours. Opioid (heroin) confirmation urine tests were done every 3 months. A self-administered questionnaire was used to measure HRQL.

In this pilot programme, DU individuals ($N = 968$) were recruited through 6 clinics. All participants received daily methadone free of charge under direct observation of health workers. Patients were not excluded from MMT if they continued opioid use as reported during interviews or confirmed by urine tests. The present study is a secondary analysis of the longitudinal assessments that included all participants who were HIV infected at baseline ($n = 370$).

This evaluation of the MMT programme for HIV-positive DUs is a component of an overall project by the Vietnam Administration of HIV/AIDS Control. Its focus is to develop a framework for economic evaluation of HIV/AIDS interventions in Vietnam [22]. A cost-benefit analysis of the overall project indicated significant societal benefits including cost savings from opioid abstinence, decrease in health care needs of DUs, and substantial

reduction in risk of HIV transmission [22]. These findings, among others, provided evidence to support the Government's decision to scale up MMT services for 80,000 DUs by 2020 in Vietnam.

Health-related quality of life instrument

The HRQL instrument used in this study was WHOQOL-BREF, an abbreviated version of the WHOQOL-100 [23]. This instrument has 26 items covering 4 domains (Physical, Psychological, Social, and Environment) and 2 general items (overall HRQL and General Health). The respondents answered each item using a five-point Likert scale ranging from 1 (Not at all) to 5 (Completely). For example, patients were asked to think about their life in the last 2 weeks in this question: 'Do you get the kind of support from others that you need?' Answering options would be: '1—Not at all; 2—Not much; 3—Moderately; 4—A great deal; and 5—Completely'. Most items were scaled in a positive direction, where a value of one indicates low or negative perception, and five indicates high or positive perception. Negative items were reverse scored. For example, 5 for 'Not at all' decreases to 1 for 'Completely'; this band score was reversed using the formula: New Score = 6−Original Score. Thus, the higher summary scores denote more favourable HRQL. In the morbidity domain, a higher score reflects a lower morbidity. Each item should contribute equally to the domain score; therefore, the ranges of raw domain scores are Physical (7–35), Psychological (6–30), Social (3–15), and Environment (8–40). To improve the comparability of the measurement, we converted the domain scores of the original and modified instruments into a 0–100 scale using the formula:

$$\text{Transformed scale} = \left(\frac{\text{Actual raw score} - \text{lowest possible raw score}}{\text{Possible raw score range}}\right) \times 100 \quad (1)$$

The Vietnamese version of the original WHOQOL-BREF instrument was developed following the protocol provided by the WHOQOL Group [24]. In the preparation phrase, a research group was formed and included health economists, infectious disease physicians, preventive medicine specialists, and linguistics expert. Another group of DUs with and without HIV/AIDS was also formed and included in the preparation phase. The Vietnamese version was created using forward–backward translation with subsequent reviews and discussions within and between the 2 groups. Patient cognitive debriefing forms were used to accelerate the process. In focus groups, participants were asked about additional socio-cultural or biomedical variables that should be included in the instrument. However, no new items emerged from these focus group interviews. Consequently, the Vietnamese version of 26 items was piloted in a conveniently selected small group of DUs for final amendments prior to data collection. Validation and psychometric properties of the measurement were tested following data collection. Methods are presented in the statistical analysis.

Statistical analysis

Descriptive statistics were used for health status, socio-demographic, and drug use-related characteristics of respondents. Chi-square and ANOVA tests were used to examine the differences between proportions and means.

Psychometric properties of WHOQOL-BREF

Confirmatory factor analysis was used to examine the construct validity of the Vietnamese version. Six factors were extracted by the principle component analysis at an eigenvalue of 1.0. Orthogonal Varimax rotation with Kaisers' normalization was used to increase the interpretability of these factors. Spearman's correlations between domain scores, overall quality of life, and general health status indicators were estimated for convergent validity. Internal consistency reliability of HRQL measurement, an average inter-item correlation, was estimated using Cronbach's alpha. In measuring groups' HRQL, a desirable Cronbach's alpha was 0.7.

Evaluating the changes in HRQL during MMT

Changes in the overall HRQL and domain scores were quantified using Cohen's effect size, which is defined as the magnitude of changes divided by standard deviations of the baseline measurements [28]. We also examined whether the changes in HRQL would distinguish early HIV-positive patients from later stage (ART) patients using the aetiological analysis described below.

Examining the association of ongoing drug use and HIV stages with HRQL

Propensity score In multivariate models, we examined the association of our exposures of interest, ongoing heroin use and HIV stages, and changes in HRQL. We assumed that the number of participants was disproportionate between exposure and non-exposure groups; thus, estimation would be biased. In addition, there might have been small numbers of patients with some certain characteristics

that influenced the estimability of the models. Because of this, *propensity scores* were employed to minimize the potential effect of pre-existing differences between different groups of exposure [25]. A propensity score is defined as the conditional probability of belonging to a particular exposure group given a vector of observed covariates, which summarizes information across potential confounders [26]. Propensity scores were estimated using logistic regression with exposures of interest as dependent variables. Predictors included socio-demographic characteristics, drug use history, and HIV stage and treatment status, adjusting for the longitudinal structure of data. A stepwise forward model building strategy [27] was applied where variables were selected based on the log-likelihood ratio test. We adopted a P value < 0.05 and excluded variables at P values > 0.3. The equations are expressed as follows:

$$\text{LOGIT}\,[P(\text{DrugUse}|\ \text{SES, HIST, ART})] = \alpha + \sum_i \beta_{1i}\text{SES}_i + \sum_i \beta_{2i}\text{HIST}_i + \sum_i \beta_{3i}\text{ART}_i \quad (2a)$$

$$\text{LOGIT}\,[P(\text{ART}|\ \text{SES, HIST, DrugUse})] = \alpha + \sum_i \beta_{1i}\text{SES}_i + \sum_i \beta_{2i}\text{HIST}_i + \sum_i \beta_{3i}\text{DrugUse}_i \quad (2b)$$

where

DrugUse: continued heroin use during MMT which was self-reported heroin use during the previous 3 months, self-reported heroin injection, or a positive opioid (heroin) confirmation urine test.
ART = 1 means that patients were at a more advanced stage of HIV infection and that they took both ART and MMT. ART = 0: early HIV stages.
SES represents socio-demographic characteristics of respondents.
HIST represents a drug use history.

Propensity score is calculated as follows:

$$\text{PROPENSITY} = \text{Predict}\,[P(\text{DrugUse}|\ \text{SES, HIST, ART})] \quad (3)$$

The generalized estimating equations (GEE) models were estimated for longitudinal data on the association of changes in HRQL with ongoing heroin use and HIV stages using autoregressive working correlations structure within clusters or subjects [28, 29, 30]. The models adjusted for *propensity scores* with these exposures of interest.

$$\text{QOL}_{ij}(\text{Exposure}|\ \text{PROPENSITY}_i) = \alpha + \sum_{k=1}^{6} \beta_{ijk}\text{PROPENSITY}_{ijk} + \lambda_{ij}(\text{Druguse})_{ij} + \varepsilon_{ij} \quad (4a)$$

$$\text{QOL}_{ij}(\text{Exposure}|\ \text{PROPENSITY}_i) = \alpha + \sum_{k=1}^{6} \beta_{ijk}\text{PROPENSITY}_{ijk} + \lambda_{ij}(\text{ART})_{ij} + \varepsilon_{ij} \quad (4b)$$

where

QOL: the overall HRQL or domain scores
PROPENSITY is the propensity score stratified into 6 categories.
Indices i, j represent the ith measurement of the jth subject.
The symbol λ_{ij} represents the differences in HRQL scores between patients with and without exposures of interest, adjusting for 6 strata of propensity scores and the longitudinal data structure.

Ethical consideration

The study protocol of the original cohort study was reviewed, and ethical approval was granted by Hanoi School of Public Health, Vietnam. Written informed consent was obtained from all participants. Respondents were able to withdraw from the cohort study at any time, and this did not affect their continuation of MMT. Our secondary data analysis was reviewed and approved by the Vietnam Ministry of Health, Administration of HIV/AIDS Control. Ethical approval was also granted by the Hanoi School of Public Health and the University of Alberta's Health Research Ethics Board.

Results

Socio-demographic characteristics of participants

All 370 patients diagnosed with HIV at baseline were selected for further analysis in this study. After 9 months, the number of patients decreased to 342 (92.4% of baseline). Three hundred and thirty-seven patients received 4 repeated measurements (89.9%). Most of these patients were men (95.7%) and completed high school or below (97%). Mean age was 29.5 years (Table 1). Respondents' employment changed over time with a decrement in the proportion of jobless from 39.7% at baseline to 31.3% in the third trimester ($\chi^2 = 6.24$, $P = 0.013$). The proportion of persons having a stable job, however, did not improve significantly ($\chi^2 = 0.01$, $P = 0.94$). Respondents living with other DUs accounted for 7.8% of the respondents at baseline and 4.2% during the follow-up.

Table 1 Socio-demographic characteristics of participants

	Baseline		3 months		6 months		9 months		χ^2/F statistic	*P*
	N	%	*N*	%	*N*	%	*N*	%		
Socio-demographics										
Age (years)										
Mean (SD)	29.5	(5.9)	29.5	(5.9)	29.5	(5.9)	29.5	(6.0)	0.01	0.99
Gender										
Male	354	(95.7)	353	(95.7)	348	(95.9)	328	(95.9)	0.04	0.99
Female	16	(4.3)	16	(4.3)	15	(4.1)	14	(4.1)		
Marital status										
Single	218	(58.9)	193	(53.9)	203	(58.5)	196	(58.3)	6.50	0.69
Married/live w partner	120	(32.4)	131	(36.6)	117	(33.7)	113	(33.6)		
Divorced	30	(8.1)	33	(9.2)	27	(7.8)	24	(7.1)		
Widow/widower	2	(0.5)	1	(0.3)	0	(0.0)	3	(0.9)		
Occupation										
Unemployed	147	(39.7)	142	(38.5)	128	(35.3)	107	(31.3)	11.00	0.28
Freelancer	95	(25.7)	105	(28.5)	113	(31.1)	105	(30.7)		
Stable jobs	43	(11.6)	36	(9.8)	45	(12.4)	36	(10.5)		
Others	85	(23.0)	86	(23.3)	77	(21.2)	94	(27.5)		
Religion										
Buddhism	157	(42.4)	156	(42.3)	153	(42.2)	143	(41.8)	0.27	0.99
Others	42	(11.4)	42	(11.4)	40	(11.0)	36	(10.5)		
None	171	(46.2)	171	(46.3)	170	(46.8)	163	(47.7)		
Education										
Illiterate	3	(0.8)	3	(0.8)	3	(0.8)	3	(0.9)	0.18	0.99
Primary (grade 1–5)	41	(11.1)	40	(10.9)	39	(10.8)	38	(11.1)		
Secondary (grade 6–9)	187	(50.7)	187	(50.8)	185	(51.1)	172	(50.4)		
High school (grade 10–12)	127	(34.4)	127	(34.5)	125	(34.5)	119	(34.9)		
Vocational/college/university	11	(3.0)	11	(3.0)	10	(2.8)	9	(2.6)		
History of drug use										
Age of 1st drug use	20.6	(5.3)	20.6	(5.3)	20.6	(5.4)	20.8	(5.5)	0.05	0.98
Length of drug use (years) mean (SD)	6.7	(3.6)	6.7	(3.6)	6.7	(3.7)	6.8	(3.7)	0.05	0.98
Living with other drug user	29	(7.8)	15	(4.2)	15	(4.3)	14	(4.2)	7.30	0.06

Psychometric properties of HRQL measures

Table 2 shows the construct validity, convergent validity, and reliability of the WHOQOL-BREF Vietnamese version for HIV-positive DUs. In factor analysis, six selected major factors accounted for 56.9% of the variance. The first factor, the Psychological dimension, accounted for 29.7% of the variance. All major factors had at least 3 items. Four original domain names were maintained in 4 parallel major factors. Two new domains ('Morbidity' and 'Performance', individual performance of functional and cognitive activities) were created based on factor loadings, the square root of domains' variance explained by factors. Consequently, these 6 modified domains were used for examining the associations between the changes in HRQL and drug use behaviours.

Convergent validity for overall HRQL and general health were moderate or good (Table 2). Cronbach's alpha of all domains was 0.81, indicating a good internal consistency reliability of the instrument. Cronbach's alpha was moderate for Performance, Social Relationship, and Performance domains, and acceptable for Morbidity, Physical, and Psychological Health domains.

Drug use patterns, changes, and magnitude of changes in HRQL over time

With their first opioid use at the age of 20.6 (95% CI = 20.1; 21.2), participants had used drugs for an average period of 6.7 years prior to entering the MMT programme (95% CI = 6.3; 7.1) (Table 1). The proportion of respondents with self-reported opioid use and positive

Table 2 Factor loading, convergent validity, and reliability of the WHOQOL-BREF in HIV+ drug users

	Items	Psychological	Physical health	Morbidity	Performance	Social relationships	Environment
Original domain							
Physical health	Sleep and rest		0.54				
	Activities of daily living		0.80				
	Work capacity		0.78				
	Pain and discomfort			0.85			
	Dependence on medicinal substances and medical aids			0.86			
	Energy and fatigue				0.61		
	Mobility				0.54		
Psychological	Thinking, learning, memory and concentration	0.43			0.46		
	Positive feelings	0.83					
	Spirituality/religion/personal beliefs	0.83					
	Bodily image and appearance				0.48		
	Self-esteem		0.65				
	Negative feelings			0.59			
Social relationships	Social support					0.69	
	Personal relationships					0.54	
	Sexual activity					0.60	
Environment	Freedom, physical safety and security	0.68					
	Physical environment (pollution/noise/traffic/climate)				0.50		
	Transport						0.51
	Financial resources		0.40				
	Opportunities for acquiring new information and skills				0.48		
	Participation in and opportunities for recreation/leisure activities					0.41	
	Home environment						0.61
	Health and social care: accessibility and quality						0.82
Convergent validity	Overall HRQL	0.57	0.47	0.25	0.42	0.42	0.31
	General health	0.46	0.49	0.36	0.44	0.43	0.25
Reliability	Cronbach's alpha	0.82	0.80	0.74	0.68	0.62	0.61
	% floor	1.4%	0.0%	0.0%	0.0%	0.0%	0.0%
	% ceiling	0.5%	0.9%	56.1%	0.2%	0.1%	1.2%
Eigen values		7.12	1.80	1.46	1.16	1.11	1.02
Explained variance (%)		11.1	10.9	9.9	8.8	8.6	7.7

heroin confirmation urine tests were initially 99.7 and 98.2%. This significantly decreased in the 2nd and 3rd trimesters of follow-up to 14.6 and 14.4%, respectively (Table 3). The kappa statistic (0.71) indicated a substantial agreement between reported heroin use and urine test.

Table 3 describes the changes in HRQL and subscale scores of HIV patients during MMT. The overall HRQL and domain scores rapidly increased over the first trimester, from 46.5 to 76.4, and then stabilized during the second and third trimesters. There were parallel variations in 6 domains' scores over the course of the study. Morbidity domain score was the highest (76.4–88.1), whereas the Social Relationships domain was the lowest (51.5–60.6). In the third trimester, scores slightly decreased, but this

Table 3 Changes in drug use patterns and HRQL in HIV+ patients over 9-month MMT

Drug use and HRQL	Baseline		3 months		6 months		9 months	
	N	(%)	*N*	(%)	*N*	(%)	*N*	(%)
Changes in drug use								
Drug use last 30 days	369.0	(99.7)	53	(14.4)	34.0	(9.4)	50	(14.6)
Frequency of use (times/day [SD])	3.4	(1.3)	1.0	(1.2)	0.5	(0.8)	0.7	(1.3)
Drug administration methods								
Drink	9	(2.3)	2	(3.6)	0	(0.0)	1	(2.0)
Smoked	44	(11.4)	19	(34.5)	11	(34.4)	11	(21.6)
Muscular injection	4	(1.0)	0	(0.0)	0	(0.0)	2	(3.9)
Intravenous injection	329	(85.2)	34	(61.8)	21	(65.6)	37	(72.5)
Type of drug								
Heroin	368	(95.1)	45	(84.9)	32	(94.1)	43	(82.7)
Others	19	(4.9)	8	(15.1)	2	(5.9)	9	(17.3)
Opioid urine test (+)	926	(98.2)	167	(18.1)	105	(11.8)	125	(14.4)
Changes in HRQL	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
Psychological health	46.5	(20.1)	63.9	(13.4)	65.0	(14.0)	63.2	(14.0)
Physical health	54.4	(14.8)	68.1	(12.1)	68.5	(12.4)	66.1	(13.0)
Morbidity	76.4	(23.5)	88.1	(17.7)	87.7	(18.2)	84.7	(20.1)
Performance	63.8	(13.3)	70.8	(12.7)	72.4	(12.4)	70.4	(12.7)
Social relationships	51.5	(12.3)	59.7	(11.5)	60.6	(11.8)	60.3	(12.2)
Environment	65.7	(12.8)	69.2	(11.8)	70.7	(10.8)	68.8	(11.5)
Overall composite score	59.7	(10.5)	70.0	(9.2)	70.8	(9.4)	68.9	(9.8)

change was not significant (paired *t* test, $P > 0.05$, data not shown).

Figure 1 illustrates the magnitude of changes in HRQL and subscales over time using Cohen's effect size. Compared to baseline, Physical and Psychological domains had large improvements over the course of study. Measures of individual performance and social relationships moderately increased, while the morbidity and environment measures demonstrated small increments within the sample group.

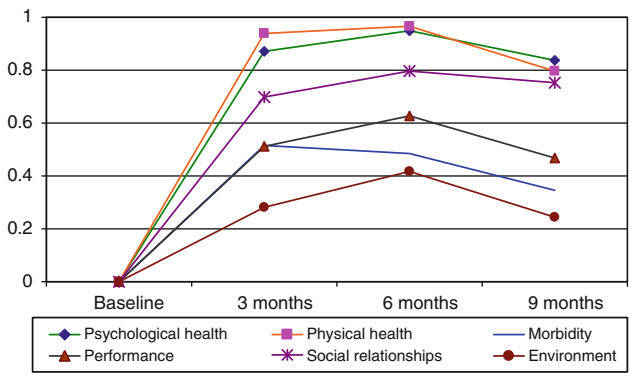

Fig. 1 Effect size of changes in overall HRQL and domains over time

Associations between drug use behaviours and HIV stages and HRQL

Results of the GEE models are shown in Table 4. Adjusting for propensity scores and intra-individual correlations, there were large decrements in overall HRQL, all subscales' scores, and especially in the psychological status among patients who continued to use heroin. During MMT, the overall HRQL of more advanced HIV patients who were also taking ART did not significantly differ from those not yet in need of ART. Across 6 domains, there was only a slight decrease in the morbidity domain among those patients who were taking ART (95% CI of difference = [−5.9; −1.2]).

Discussions

In this study, we observed a high retention rate in MMT among HIV-positive DUs over 9-month follow-up. The percentage of DUs continued to use and frequency of opioid use decreased along with significant improvements in HRQL of DUs at both advanced HIV stages with ART and earlier HIV stages. Except morbidity, ART patients benefited from MMT to the same degree as early

Table 4 Differences in HRQL with regard to ongoing drug use and HIV stages over 9-month MMT

	Coefficient[a]	Standard error	95% Confident interval	*P* value
Opioid confirmation test: positive versus negative ($n = 375$; 525 events ~37.6%)				
Psychological health	–12.9	0.9	–11.1 –14.7	<0.001
Physical health	–10.1	0.8	–8.6 –11.5	<0.001
Morbidity	–7.5	1.1	–5.3 –9.7	<0.001
Performance	–5.3	0.7	–3.9 –6.8	<0.001
Social relationships	–7.0	0.7	–5.7 –8.3	<0.001
Environment	–2.8	0.7	–1.5 –4.1	<0.001
Average	–7.6	0.6	–6.4 –8.7	<0.001
Reported drug use: yes versus no ($n = 375$; 506 events ~35.0%)				
Psychological health	–14.1	0.9	–12.4 –15.9	<0.001
Physical health	–10.8	0.8	–9.3 –12.3	<0.001
Morbidity	–8.8	1.1	–6.7 –11.0	<0.001
Performance	–6.2	0.7	–4.7 –7.6	<0.001
Social relationships	–7.3	0.7	–6.0 –8.6	<0.001
Environment	–3.5	0.7	–2.2 –4.8	<0.001
Average	–8.4	0.6	–7.3 –9.5	<0.001
Reported injecting drug: yes versus no ($n = 375$; 420 events ~29.1%)				
Psychological health	–14.9	1.0	–13.0 –16.8	<0.001
Physical health	–11.6	0.8	–10.0 –13.1	<0.001
Morbidity	–9.7	1.2	–7.4 –12.0	<0.001
Performance	–6.5	0.8	–5.0 –8.0	<0.001
Social relationships	–7.5	0.7	–6.1 –8.9	<0.001
Environment	–3.9	0.7	–2.6 –5.3	<0.001
Average	–8.9	0.6	–7.8 –10.1	<0.001
ART patients versus early HIV+ patients ($n = 375$; 638 events ~44.2%)				
Psychological health	0.7	1.0	2.7 –1.2	0.45
Physical health	–0.3	0.8	1.3 –1.9	0.72
Morbidity	–3.5	1.2	–1.2 –5.9	<0.001
Performance	–0.2	0.8	1.3 –1.8	0.77

Table 4 continued

	Coefficient[a]	Standard error	95% Confident interval	*P* value
Social relationships	–0.3	0.7	–1.7 1.1	0.68
Environment	0.9	0.7	–0.4 2.3	0.18
Average	–0.5	0.6	–1.7 0.7	0.40

[a] The coefficients show the differences in domain scores and overall average scores comparing those with and without exposures of interest over 9 months adjusting for propensity score and longitudinal data structure

HIV-positive DUs. During MMT, patients with ongoing heroin use reported substantially lower scores in overall HRQL and specific HRQL domains.

We developed and validated a Vietnamese version of the WHOQOL-BREF. This was then administered to a sample of HIV-positive DUs. Using factor analysis, items of the Vietnamese version were reclassified into 4 corresponding domains and 2 emerging domains ('Morbidity' and 'Performance'). This approach was applied in previous studies [31–34]. In practice, the reclassification of items using factor analysis helps create subsets of items that measure the same underlying factor. This increases the measures' reliability and construct validity [35, 36].

In many injection-driven HIV epidemics in Asia, drug use is illegal and characterized as 'a social evil' [37, 38]. Opioid users might be stressed by the financial burden of addiction, loss of their jobs, involvement in crime, and worrying about being arrested or having an overdose [38, 39]. In addition, they may have experienced stigma and discrimination by family and community against DUs. Some were ashamed, self-stigmatized, or lost their self-esteem [39, 40]. In the first trimester of the study, changes in psychological health were initially rapid and then maintained over time. This could be explained by the release from the economic and social burden of addiction, and by the fact that those patients who were opioid abstinent could continue to be economically productive. In addition, DUs had supports from health care workers and family members, which might reduce DUs' perceived stigma and improve their psychological status [19, 39, 41, 42].

Focusing on HIV-positive DUs, we established the potential effectiveness of MMT on HIV care and treatment outcomes. The traditional approach in Vietnam for treating opioid dependence, which is compulsory detention in rehabilitation centres, may prevent HIV/AIDS patient's access to ART in a timely manner or interrupt the treatment. HIV-positive DUs, who were opioid abstinent during MMT, might have better access and utilization of ART services [16, 43]. A previous study reported lower perceived HRQL, particularly in mental health, among DUs compared to other HIV-positive groups in Vietnam. In this study, HRQL was also related to poor access to health care and psychosocial support services [44]. In our current study, we observed the largest improvement in the Psychological domain. Scaling up MMT for DUs, therefore, could be an effective entry point for HIV testing and other HIV care and treatment services in Vietnam. Several studies have also shown the impact of MMT retention on adherence to ART, viral suppression, and treatment outcomes [17, 45–48]. Our findings confirmed that if the patients were in compliance with MMT and did not continue to use heroin to opioid abuse, their HRQL would significantly increase. Changes in HRQL domain scores were independent of ART, except for a minor decrement in 'Morbidity'. This supports the recommendation for injection-driven HIV epidemics: Integrating both MMT and ART services for drug abusers could improve the HIV care and treatment outcomes and HRQL in the Vietnamese setting.

Among 6 modified HRQL domains, Social Relationships had a modest improvement and lowest scores compared to other domains. We hypothesize that DUs could have complex social backgrounds [38]. Indeed, during the follow-up in the current study, very few of these DUs obtained stable jobs. This result highlights the need to provide vocational training services and livelihood supports for DUs to sustain the effectiveness of opioid substitution interventions. In contrast to the large early improvements in HRQOL, we observed slight decrements in the third trimester. Although these changes were not significant, they were consistent over all domains. It implies that efforts to maintain the initial achievements of this intervention are essential. Future studies that explore long-term impacts of MMT and identify predictors of ongoing heroin use would be helpful.

The strength of this study was the longitudinal assessments of a sufficient sample that supports the causal inference of changes in drug use and HRQL over time. In practice, the 9-month duration of follow-up might not be sufficient to assess the sustainability of this intervention. Another limitation of this design was that we did not have a

comparison group of those who were HIV-positive DUs without MMT. Continued opioid use during the previous month was self-reported by patients and might be biased; however, the Kappa statistics showed a good correlation of reported opioid use with urine tests during clinics visits. In addition, patients' report on their ongoing opioid use and positive urine test result were not disclosed, and patients were not treated differently. Notwithstanding these limitations, as the first national pilot MMT programme, the results of this maybe are useful towards developing future services and interventions for HIV-positive DUs in Vietnam, as well as other injection-driven HIV epidemics. This experience could prove useful to other programmes in resource-limited settings.

Conclusion

MMT improved the HRQL among HIV-positive DUs in Vietnam. Changes in drug use behaviours are significant predictors of HRQL. The study supports the recommendation that integrating MMT to HIV care and treatment services could be beneficial for comprehensive HIV care and treatment for DUs.

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