

Psychological Distress and Quality of Life Among Opioid Substitution Therapy Participants with Histories of Injecting and Non-Injecting: A Cross-Sectional Study in Kathmandu, Nepal

Sagun Ballav Pant (✉ pants@uio.no)

University of Oslo

Suraj Bahadur Thapa

University of Oslo

John Howard

University of New South Wales Sydney

Saroj Prasad Ojha

Tribhuvan University

Lars Lien

Innlandet Hospital Trust

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Abstract

Background: Opioid use is a serious public health problem in Nepal. People who use opioids can experience severe psychological distress over time along with poor quality of life. Opioid substitution therapy (OST) is central in treating opioid dependence. This study aimed to examine factors associated with quality of life and severe psychological distress among OST therapy participants in the Kathmandu valley, Nepal and compare those who had injected opioids prior to OST and those who did not inject.

Methods: A cross-sectional study was conducted with 231 participants proportionately allocated across five OST sites in the Kathmandu Valley. They were administered a semi-structured questionnaire, the Nepalese versions of the Kessler 6 psychological distress scale and World Health Organization Quality of Life (WHOQOL-BREF). Univariate and multivariate analyses were used to elicit associations between severe psychological distress, quality of life, and independent variables.

Results: Of the participants 92% were male and about half were injecting drug users. Severe psychological distress was found in about one in four participants, and significantly more prevalent among participants with a history of injecting practices (32.2%) compared to non-injectors (15.9%). Higher mean psychological distress scores were observed among injecting drug users.

Those self-reporting a history of psychiatric illnesses were around seven times more likely to have severe psychological distress, and those with history of comorbidity around 1.6 times more likely. In the adjusted linear regression model, injecting drug users were likely to have lower physical quality of life compared to non-injectors. Age was positively associated with better social quality of life. Lower socioeconomic status and a history of self-reported mental illness and attempt to quit substance use, were found to have significantly lower quality of life on all four domains.

Conclusions:

This study demonstrated that OST participants with a history of injecting drug use were at higher risk of severe psychological distress and lower physical quality of life. In addition to OST, the complex and entangled needs of injecting drug users and non-injectors need to be addressed to improve quality of life and lessen psychological distress and a return to problematic substance use.

Background

Globally, an estimated 62 million people use opioids for non-medical reasons. This use of opioids accounted for 70 per cent of the 18 million healthy years of life lost due to disability and premature death (DALYs) attributed to drug use disorders in 2019. More than half of the estimated global number of opioid users reside in Asia [1]. In Nepal, opioids were the second most commonly used substance, according to the Drug Users survey-2020 [2]. Most people who use opioids in Nepal are either smoking/inhaling heroin, injecting opioids like buprenorphine and heroin, or using high doses of tramadol orally in combination with other substances [2, 3, 4]. People who inject drugs (PWID) in Nepal are usually injecting a

combination of opioids, benzodiazepines and antihistamines called the “South Asian Cocktail”, and this cocktail use behavior has increased health, social, economic and legal hazards in this population [5].

Opioid substitution therapy (OST), an evidence-based harm reduction initiative to people dependent on opioids, has been increasingly used in order to decrease the health, economic, and social consequences of substance use and to improve quality of life (QoL) [6]. OST programs are implemented by National Center for AIDS and STD Control (NCASC) in 12 sites across 10 districts of Nepal with the help of eight Government hospitals and four Non-government organizations (NGO) [7]. Even when improvement is observed for physical health, it has been noted that OST clients demonstrate more psychological distress and poorer QoL compared to general population [8]. Moreover, facets of mental health and quality of life are often overlooked, neglected or receive minimal attention in many harm reduction interventions [9].

Opioid use disorder (OUD) is mostly associated with medical and psychiatric co-morbidities which contribute to increased mortality and morbidity among those with OUD, with higher levels of depressive, anxiety, and antisocial personality disorders being the most common [10–12]. Drug dependence lowers the QoL with impact on all domains which are psychological, physical, social, and emotional domains [13]. Higher levels of perceived stigma and discrimination, especially in relation to injection drug use, are also associated with higher psychological distress, unhealthy behaviors and significantly poorer QoL [14, 15].

Injecting drug users (IDU), especially those using opioids, are at increased risk for harmful effects such as increased risk for thrombophlebitis, fatal, and non-fatal overdoses, tuberculosis, transmission of blood-borne infectious diseases (especially HIV, HCV) mainly associated with sharing injection equipment [3, 5, 16]. IDUs often have instability in many aspects of life including high prevalence of infectious disease, mental disorders, crime, violence, and lack of stable housing [17]. Several factors such as age, employment, duration of opioid dependence, psychiatric diagnosis and psychopharmacological medication have been associated with improved health related QoL amongst those receiving opioid substitution treatment [8].

The use of opiates, such as heroin, and synthetic opioids such as oxycodone, tramadol, fentanyl and buprenorphine have been of concern in many countries [1, 10, 15]. However, resource poor countries often face greater difficulties in addressing these diverse but entangled issues, especially where there is civil unrest, armed conflict, corruption, competing health needs, such as infant and maternal health, clean water, and pandemics.

Nepal, was one of the first South-Asian countries to introduce harm reduction interventions for PWID, with a needle and syringe program commencing in 1991, and OST in 1994 [18]. However, Nepal is still not able to provide sustainable, comprehensive health and psychosocial care for people who use drugs, especially in relation to psychological distress and QoL [3]. There are few studies in South-Asian settings exploring psychological distress and QoL among OST participants with histories of injecting and non-injecting opioid use, and its association with socio-demographic characteristics and other related variables [18]. Therefore, this study aims to detect any differences in QoL and SPD between OST participants with

histories of injecting and non-injecting drug use, examine the factors associated with them in terms of sociodemographic and OST characteristics, and identify implications for OST programs.

Methods

Study setting and design

A cross-sectional study among clients across five OST sites was conducted from January, 2021 to August, 2021 in three districts in the Kathmandu valley [Kathmandu and Lalitpur two each, and Bhaktapur one]. Among them, two were government hospital-based and three community based- Non-Governmental Organization run sites. The Kathmandu Valley has a population of about 2.5 million [19].

Sample size determination and sampling procedure

Sample size was calculated by using single population proportion formula for finite population and the selection of participants based on probability sampling using simple random sampling techniques. For the required sample size of 247 participants were proportionately allocated to five OST sites and were selected randomly through computer generated random numbers after listing potential participants in each OST site. With the response rate of 93.5%, there were 231 study participants (213 male and 18 female). Female clients were oversampled, as there were very few female clients across OST services.

Eligible participants were aged 18 to 60 years. Those in the first two weeks of initiation in OST or with any organic mental disorders such as dementia, delirium and amnesic syndromes were excluded due to likely difficulties in giving a reliable history.

Measures

A face-to-face structured interview was conducted by trained interviewers. Information regarding the study was explained to the participants by the core study team members, and written informed consent was obtained. The Nepalese version of the Kessler-6 psychological distresses scale (K-6) and the World Health Organization Quality of Life (WHOQOL-BREF) were used to assess psychological distress and quality of life across various domains respectively. A semi-structured questionnaire was developed to assess the sociodemographic variables and OST related information. Pretesting was done with 20 clients (about 10%) of the estimated sample size, and the questionnaires were reviewed and revised.

The internationally validated WHOQOL-BREF comprises 26 items in four domains: physical health (7 items), psychological health (6 items), social relationships (3 items) and environment (8 items). The two remaining WHOQOL-BREF items separately rate overall perception of quality of life and overall perception of the health of an individual [20]. The WHOQOL-BREF has been frequently used in research in Nepal and has been translated into Nepali [21,22], and has good discriminant validity, content validity, and test-retest reliability [20,23]. The physical health domain canvasses activities of daily living, energy and fatigue, mobility, pain and discomfort, sleep and rest, and work capacity. The psychological domain focuses on the ability to concentrate, self-esteem, body image, spirituality and the frequency of positive or negative

feelings. The social relationship domain includes personal relationship, social support, and sexual activity. The environment domain includes safety and security, home and physical environment satisfaction, financial security, health/social care availability, information and leisure activity accessibility and transportation satisfaction. The mean scores of items in each domain were used to calculate the domain score, and higher the domain score the higher the quality of life. QoL between 26-60 was categorized as mild, 61-95 moderate and 96-130 high [20].

The K-6 is a standardized, validated screening tool with 6 items that screen for a global measure of possible severe psychological distress over last 4 weeks which can be indicative of a serious mental illness [24]. Each of the following 6 questions are scored from 0 (none of the time) to 4 (all of the time): feeling nervous; hopeless; restless; that everything was an effort; was so sad that nothing could cheer him/her up; or felt worthless. Scores of 0-12 indicate not having a serious psychological distress and 13-24 as probably having psychological serious distress / mental illness [25]. This scale has been translated into Nepali language and used in Nepal [26,27].

Ethical approval

Ethical approval for this study was obtained from the ethical review board of the Nepal Health Research Council (Ref. no: 1698). Additional ethical approval was obtained from Regional Committees for Medical and Health Research Ethics in Norway (Ref. no: 154194). Permission was also obtained from each of the OST sites and written informed consent from the study participants.

Statistical analysis

Data was entered in SPSS version 27 for data analysis [28]. Rigorous checking of each questionnaire and cross verification of the errors was undertaken. Descriptive statistics from the data such as mean and standard deviations were calculated for the continuous variables and absolute numbers and percentages for the categorical variables. Chi square and independent sample T tests were computed for categorical and continuous variables, respectively. The Mann-Whitney U-test was used for not normally distributed continuous data. Multivariate analyses were performed to explore the association between severe psychological distress and QoL with independent socio-demographic and OST characteristics. Multivariate analyses were performed with linear and logistic regression models. The socio-demographic, clinical, and OST related variables were adjusted in both the models. Standardized Beta was reported for linear and adjusted odds ratio for logistic regression. Level of significance was set at 0.05.

Results

Table 1 summaries the socio-demographic characteristics of the OST participants. Among the 231 clients, 113 had never used opioids via injection (non-IDU) and 118 injected opioids before enrollment into OST. There was a significant difference for age, with mean age of non-IDU clients being 32.15 years and 35.3 years for the IDU ($p=0.001$). There were few women in either group; 9.7% for non-IDU and 5.9% for IDU. Non-IDU were significantly better educated with about one in three (30.1%) educated up to

university level and above but only 16.9% among the IDU ($p=0.028$). Significantly more IDU were separated or divorced 16.1% than non-IDU of 3.6% ($p=0.002$). About one in four (43.4%) non-IDU had attempted to quit substance use which was significantly less than the 74.6% IDU ($p<0.001$). The number of non-IDU with co-morbid medical conditions was significantly less (32.4%) than for IDU (67.6%) ($p<0.001$). More IDU belonged to upper middle socioeconomic class (61.9%) as compared to non IDU (45.8%) based on the modified Kuppuswami Scale for socio-economic status ($p=0.014$) [29].

Insert Table 1 about here

Table 2 outlines the difference in OST related characteristics between non-IDU and IDU clients. Methadone was the most used current OST modality in comparison to buprenorphine amid both non-IDU (80.5%) and IDU (69.5%). The duration of OST use was six or more months for most IDU clients (78.8%) and non-IDU clients (54%) ($p<0.001$). Significantly less non-IDU (8.8%) were arrested or taken into police custody after OST enrollment as compared to IDU (26.3%) ($p=0.001$). The mean duration of OST enrollment was higher in the IDU group (40.6 months) compared to the non-IDU (13.1 months) ($p<0.001$).

Insert Table 2 about here

Table 3 illustrates the differences in QoL and psychological distress between non-IDU and IDUs. Statistically significant differences were observed in all QoL domains and the overall QoL with lower mean scores for all domains in IDU compared to non-IDU; physical QoL ($p<0.001$), psychological QoL ($p=0.001$), social QoL ($p=0.004$), environmental QoL ($p=0.014$), overall QoL ($p<0.001$). The highest mean difference was observed in the environmental domain with 28.4 for non-IDU group and 27 for IDU. The mean for overall QoL in non-IDU was 94.4 and 86.7 for IDU. Likewise, the mean of Kessler-6 score was significantly lower for non-IDU clients; 4.5 versus 7 for IDU ($p=0.002$), and similarly for SPD among 15.9% for non-IDU and 32.2% for IDU ($p=0.004$).

Insert Table 3 about here

Table 4 shows the unadjusted and adjusted odds ratios for factors associated with severe psychological distress (SPD) using the logistic regression model. The model was adjusted for IDU status, sociodemographic characteristics, history of psychiatric illness, co-morbidities, substance abuse history, and being in custody.

In the adjusted model, IDU status did not show significant association with the SPD. Those having history of psychiatric illnesses were around 7 times more likely to have SPD (AOR=7.19, CI: 3, 17.22, $p<0.001$). Likewise, those with history of comorbidity also were around 1.6 times more like to have SPD than those who did not (AOR=1.58, CI: 1.11, 5.20, $p=0.025$).

Insert Table 4 about here

Table 5 presents the linear regression models for different domains of QoL adjusted for IDU status, sociodemographic characteristics, history of psychiatric illness, co-morbidities, substance abuse history,

and being in custody. IDU were likely to have lower physical QoL [standardized Beta (β)= -0.21; 95% CI: -3.27, -0.75, p-value<0.01] compared to non-IDU. Age was also positively associated with better social QoL (β = 0.16; 95% CI: 0.01, 0.12, p-value<0.05).

A history of self-reported mental illness was associated with lower QoL on all four domains of QoL [physical domain (β = -0.30; 95% CI: -5.56, -0.2.48, p-value<0.001); psychological domain (β = -0.25; 95% CI: -4.25, -1.41, p-value<0.001); social domain (β = -0.28; 95% CI: -3.03, -1.16, p-value<0.001); and environmental Domain (β = -0.22, 95% CI: -4.22, -1.18, p-value<0.001)].

Similarly, previous quit attempt was also associated with lower QoL across all four QoL domains [physical domain (β =-0.14; 95%, CI:-2.53,-0.13, p-value<0.05); psychological domain (β =-0.19; 95% CI:-2.78,-0.57, p-value<0.01); social relationships (β =-0.13; 95% CI:-1.48,-0.04, p-value<0.05); and environmental domain (β =-0.14 95% CI:-2.48,-0.11, p-value<0.05)].

Insert Table 5 about here

Likewise, those with upper middle or above socio economic status were more likely to have good quality of life compared to ones belonging to the lower middle class socio economic status with higher QoL score across all domains of QoL [physical domain (β =0.14; 95% CI:0.09,2.65, p-value<0.05); psychological domain (β =0.23; 95% CI:0.76,3.11, p-value<0.001); social relationships (β =0.29; CI:0.88,2.43, p-value<0.001); and environmental domain (β =0.31; 95% CI:1.55,4.07, p-value<0.001)].

Discussion

This study explored and compared psychological distress and QoL among OST participants with injecting and non-injecting histories. Given the importance of QoL and psychological distress among both injecting and non-injecting users, the findings demonstrate that QoL was lower in the IDU group compared to non-IDUs in the physical domain. Irrespective of IDU status, those who had history of self-reported mental illness, showed significant association with SPD and all domains of QoL. History of comorbidity also affected SPD, and past attempts to quit substance abuse and socioeconomic status were significantly associated with all domains of QoL.

Females in the study had higher odds of having SPD and lower QoL, consistent with other research [30]. The possible reasons for the gender differences in QoL and psychological distress may be due to household responsibilities, socio-cultural norms, limited income, higher level of perceived stigma, and barriers in access to health care facilities and treatment.

A history of mental illness was associated with lower QoL in all four domains in IDU (physical, psychological, social and environment). Studies in South Asia and the Middle East show high lifetime prevalence of psychiatric disorders, especially depression and anxiety, psychological distress and lower QoL among opioid users [13,33–40]. These are consistent with numerous studies from diverse sites in Europe, Nepal, Australia, the US, Slovakia, Taiwan and Vietnam [31,32,41–45]. Effectively addressing

mental health issues is crucial, and the studies reveal that QoL of people with opioid dependence improves with substitution therapies and provision of interventions addressing their individual and complex needs [46,47].

In the current study, upper middle or above SES participants had better quality of life than those with lower SES, highlighting well recognized health inequalities. The Scott et al. study demonstrated substantially lower personal well-being and related psychological stress and SES over time in a population of IDUs, but that housing and health services could make a difference [32]. Interestingly, while SES was associated with QoL and SPD, castes was not. Equitable, comprehensive opportunities for people on OST are required to meet their multiple and complex needs and reduce morbidity.

Implications:

It is well recognized that QoL and psychological distress are influenced by multiple and entangled factors which can exacerbate each other and produce further complexity. Some arise from genetic predispositions associated with physical and mental health outcomes, others are social and structural determinants of health [48] and include lack of positive nurturing, toxic relationships, social and environmental factors such as poverty and inadequate housing, disrupted education and employment, the substances used, and grief and loneliness from the loss of associates from various drug consumption settings who may have provided some support, validation and comfort. In addition, there is stigma and discrimination from the community in general, and even health and social service providers. [15,31,32].

This complexity is not new to OST services, but how to respond to build optimism, resilience, and agency in participants to improve QoL and reduce psychological distress is challenging, especially in resource poor settings. The application of principles of harm reduction for healthcare settings, such as humanism, pragmatism, individualism, autonomy, incrementalism, and accountability without termination can also provide guidance in redesign of OST settings to improve health outcomes, behaviors and relationships [49]. The co-development and regular, routine review of relapse prevention plans, and identifying current triggers and helpful responses is central to this.

Many OST programs want to be more than a 'clinic' where participants merely attend, get dosed, have minimal contact with staff, and depart. It is often possible to redesign the facility space(s) with participants to provide a welcoming, less drab and sterile physical appearance, positive spaces for socialization and acquisition of new skills, utilize the non-clinical various skills staff member possess (e.g., music, mechanics, sport, video), and develop free or affordable links to what cannot be provided, especially education, training, employment and safe housing.

Strengths And Limitations

This study provides novel evidence accentuating the distinct needs of people on OST who injected opioids. Reliability of data was assured as data were collected using standardized and validated

tools/instruments. However, there are some limitations. The cross-sectional study design limits establishing causation when considering the association between SPD and QoL and factors associated with them. The study might be subjected to recall bias as some of the questions depend on subjective memory. Another limitation can be that the study involves sampling bias, conveniently selecting OST sites from Kathmandu Valley, hence restricting possibilities to generalize findings to all clients in OST in Nepal or elsewhere. However, it can provide some guidance for further research to inform policy and guidelines for the development of evidence-informed interventions for OST programs.

Conclusion

OST participants in this study with a history of IDU reported higher levels of SPD with lower quality of life than the non IDUs. However, a history of self-reported mental illness affected both SPD and QoL irrespective of IDU status. It is well recognized that more than pharmacotherapy is required to better meet the multiple, entangled and complex needs of OST participants. To identify more clearly key and modifiable contributing factors, and which approaches and interventions are the most efficient and effective in buffering the onerous impacts of psychological distress and low quality of life particularly among IDUs in resource-poor settings, further research should include quantitative, qualitative, longitudinal, and intervention studies.

List Of Abbreviations

DALYs:	Disability-Adjusted Life Years
HIV:	Human Immunodeficiency Virus
IOM:	Institute of Medicine
IUD:	Injecting Drug User
K-6:	Kessler Psychological Distress Scale
NCASC:	National Center for AIDS and STD Control
NGO:	Non-government Organizations
OST:	Opioid Substitution Therapy
OUD:	Opioid Use Disorder
PWID:	People Who Inject Drugs
QoL:	Quality of Life
SES:	Socioeconomic Status

SPD: Severe Psychological Distress

TUTH: Tribhuvan University Teaching Hospital

WHO: World Health Organization

WHOQoL-BREF: World Health Organization Quality of Life short form instrument

Declarations

Ethics approval and consent to participate:

The ethical approval for this study was obtained from the ethical review board of the Nepal Health Research Council (Ref. no: 1698 and Regional Committees for Medical and Health Research Ethics (Ref. no: 154194). Permission was also taken from each of the OST sites and written informed consent from the participants.

Consent for publication:

Not applicable – no identifying data utilised.

Availability of data and material:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: None

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Author contributions:

SBP: research planning, design, data collection, analysis and drafting of the first manuscript

ST: research planning, design and co-supervision of the study from the beginning.

JH: research planning and manuscript preparation

SPO: research planning, design and manuscript preparation

LL: research planning, design and supervision of the study from the beginning.

All the authors critically revised the manuscript and gave final approval for publication.

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Tables

Table 1. Characteristics of non-injecting (Non IDU) and injecting drug users (IDU)

Characteristics	Non IDU		IDU		p-value
	n	%	n	%	
*Age in years, mean \pm SD	32.1 \pm 6.3		35.3 \pm 7.9		0.001
Gender					
Male	102	90.3	111	94.1	0.405
Female	11	9.7	7	5.9	
Education					
Primary and lower	7	6.2	16	13.6	0.099
Secondary	72	63.7	82	69.5	0.429
University and above	34	30.1	20	16.9	0.028
Caste					
Brahmin/Chhetri ^a	46	40.7	40	33.9	0.35
Janajati ^a	59	52.2	69	58.5	0.41
Dalit and others ^a	8	7.1	9	7.6	0.87
Employment status					
Employed	32	28.3	41	34.8	0.363
Unemployed	25	22.1	32	27.1	0.95
Self-employed	56	49.6	45	38.1	0.106
Marital status					
Married	64	56.6	64	54.2	0.714
Unmarried	45	39.8	35	29.7	0.138
Separated/ divorced	4	3.6	19	16.1	0.002
Types of family					
Nuclear	54	47.8	65	55.1	0.328
Extended	59	52.2	53	44.9	
Previous attempt to quit substance					
Yes	49	43.4	88	74.6	<0.001
No	64	56.6	30	25.4	

Presence of Co-morbid medical conditions					
Yes	35	32.4	73	67.6	<0.001
No	78	63.4	45	36.6	
Past history of mental illness					
Yes	15	13.3	23	19.5	0.273
No	98	86.7	95	80.5	
SES					
≥ Upper middle	70	61.9	54	45.8	0.014
≤ Lower middle	43	38.1	64	54.2	

*Independent sample t-tests for continuous variables and chi-square test for categorical variables

^a-Brahmin and Chhetri are the highest castes, Janajati are an indigenous caste, while Dalits are underprivileged, lowest caste in Nepal.

Table 2 Comparison of Opioid substitution therapy related characteristics between non-injectors and injectors.

Characteristics	Non-IDU		IDU		p-value
	n	%	n	%	
Current OST modality					
Methadone	91	80.5	82	69.5	0.053
Buprenorphine	22	19.5	36	30.5	
Duration of OST use					
Less than 6 months	52	46	25	21.2	<0.001
6 or more months	61	54	93	78.8	
Provision of 'take away' OST dose (Last month)					
Yes	21	18.6	22	18.6	0.0991
No	92	81.4	96	81.4	
Arrested or taken into Police custody after OST enrollment					
Yes	10	8.8	31	26.3	0.001
No	103	91.2	87	73.7	
	N	Mean±SD	n	Mean ±SD	
Duration since OST enrollment* (months)	113	13.1 ± 16.3	118	40.6 ±4.3	<0.001
Current Methadone daily doses*	91	22.6 ± 14.4	82	25.9 ± 20.2	0.211
Current Buprenorphine daily doses*	22	2.1± 1.06	36	2.2± 1.74	0.853

*Mann-Whitney U-test

Table 3. Difference in Quality of Life (QoL) and psychological distress among non IDU and IDUs

	Non IDU		IDU		p-value
	Mean	SD	Mean	SD	
Physical QoL	26.8	4.5	24	4.7	<0.001
Psychological QoL	22	3.6	20.1	4.8	0.001
Social QoL	10.4	2.6	9.3	2.9	0.004
Environmental QoL	28.4	3.9	27	5.1	0.014
Overall QoL	94.4	12.2	86.7	16.2	<0.001
Kessler-6 score	4.5	5.4	7	6.7	0.002
	n	%	n	%	
No serious psychological distress	95	84.1%	80	67.8%	0.004
Severe psychological distress	18	15.9%	38	32.2%	

Table 4. Factors associated with Severe psychological distress (SPD)

	Unadjusted OR	Adjusted OR
IDU (vs. Non-IDU)		
Yes	2.51 (1.32, 4.73)**	1.49 (0.49, 4.47)
Age		
	1.01 (0.97, 1.05)	0.98 (0.92, 1.04)
Gender (vs. Male)		
Female	1.63 (0.58, 4.66)	2.28 (0.59, 8.7)
Education (vs. Primary and lower)		
Secondary	0.87 (0.46, 1.64)	0.68 (0.21, 2.17)
University and above	0.99 (0.49, 2.01)	0.48 (0.12, 1.96)
Employment (vs. Employed)		
Unemployed	1.93 (0.45, 8.32)	2.44(0.38, 15.75)
Self-employed	1.40 (0.76, 2.60)	1.15 (0.54, 2.43)
Marital status (vs. Married)		
Unmarried	0.86 (0.46, 1.64)	0.68 (0.28, 1.64)
Separated/ divorced/ widowed	0.86 (0.30, 2.42)	0.49 (0.14, 1.79)
Family type (vs. Nuclear)		
Extended	0.92 (0.51, 1.69)	1.06 (0.51, 2.22)
Past history of mental illness (vs. No)		
Yes	6.43 (3.06, 13.52)***	7.19 (3.0, 17.22)***
Tried quitting substance use (vs. no)		
Yes	1.62 (0.86, 3.06)	0.95 (0.45, 2.02)
Been in custody after enrollment in OST (vs no)		
Yes	1.83 (0.88, 3.79)	1.18 (0.49, 2.86)
History of comorbidity (vs. no)		
Yes	2.85 (1.52, 5.36)***	2.40 (1.11, 5.20)*
Use of multiple substances (vs. no)		
Yes	2.53 (1.32, 4.85)**	1.58 (0.54, 4.58)
SES (vs. Lower middle and below)		
≥ Upper middle	1.35 (0.76, 2.43)	2.63 (0.51, 13.53)

*p-value <0.05

** p-value <0.01

*** p-value < 0.001

Table 5. Factors associated with Quality of life (QoL)

	Physical QOL	Psychological QOL	Social relationships QOL	Environmental QOL
	Beta (95% CI)	Beta (95% CI)	Beta (95% CI)	Beta (95% CI)
IDU (vs. Non-IDU)				
Yes	-0.21 (-3.27, -0.75)**	-0.12 (-2.18, 0.15)	-0.12 (-1.43, -0.09)	-0.05 (-1.70, 0.78)
Age	0.13 (-0.01, 0.17)	0.04 (-0.06, 0.11)	0.16 (0.01, 0.12)*	0.09 (-0.03, 0.14)
Gender (vs. Male)				
Female	-0.07 (-3.53, 0.89)	-0.09 (-3.47, 0.62)	-0.06 (-2.01, 0.67)	-0.05 (-3.06, 1.32)
Education (vs. Primary and lower)				
Secondary	0.18 (-0.24, 3.83)	0.16 (-0.45, 3.31)	0.06 (-0.89, 1.58)	0.21 (0.05, 4.06)
University and above	0.06 (-1.78, 3.12)	0.10 (-1.23, 3.29)	-0.05 (-1.79, 1.17)	0.2 (-0.25, 4.58)
Employment (vs. Employed)				
Unemployed	-0.08 (-5.28, 0.91)	-0.09 (-5.03, 0.67)	0.05 (-1.14, 2.60)	-0.09 (-5.27, 0.83)
Self-employed	-0.05 (-1.66, 0.73)	-0.05 (-1.51, 0.69)	-0.06 (-1.07, 0.38)	-0.67 (-1.58, 0.78)
Marital status (vs. Married)				
Unmarried	0.07 (-0.63, 2.10)	0.01 (0.01, 0.14)	0.01 (-0.76, 0.89)	0.04 (-0.97, 1.72)
Separated/ divorced/ widowed	0.04 (-1.31, 2.61)	0.07 (-0.80, 2.81)	-0.06 (-1.71, 0.66)	0.05 (-1.08, 2.78)
Family type (vs. Nuclear)				
Extended	0.06 (-0.59, 1.76)	0.08 (-0.38, 1.77)	0.01 (-0.65, 0.77)	0.09 (-0.27, 2.05)
Castes (vs. Brahmin and Chettri)				
Janajati	-0.10 (-2.17, 0.19)	-0.03 (-1.36, 0.81)	0.04 (-0.47, 0.95)	-0.06 (-1.69, 0.62)
Dalit and others	-0.01 (-2.53, 2.51)	0.08 (-0.75, 0.59)	0.08 (-0.49, 0.63)	-0.01 (-2.44, 2.42)

	2.01)	3.44)	2.23)	2.04)
Past history of mental illness (vs. No)				
Yes	-0.30 (-5.56, -2.48)***	-0.25 (-4.25, -1.41)***	-0.28 (-3.03, -1.16)***	-0.22 (-4.22, -1.18)***
Tried quitting substance use (vs. no)				
Yes	-0.14 (-2.53, -0.13)*	-0.19 (-2.78, -0.57)**	-0.13 (-1.48, -0.04)*	-0.14 (-2.48, -0.11)*
Been in custody after enrollment in OST (vs no)				
Yes	-0.07 (-2.43, 0.66)	-0.03 (-1.75, 1.09)	-0.04 (-1.19, 0.66)	-0.03 (-1.85, 1.17)
SES (vs. Lower middle and below)				
≥ Upper middle	0.14 (0.09 – 2.65)*	0.23 (0.76 – 3.11)***	0.29 (0.88, 2.43)***	0.31 (1.55, 4.07)***

*p-value <0.05

**p-value <0.01

***p-value <0.001