

## Factors Associated with Symptoms of Depression among Injection Drug Users Receiving Antiretroviral Treatment in Indonesia

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### Abstract

**Objective:** Few studies have examined psychiatric comorbidity among HIV positive injection drug users (IDUs) in resource-limiting settings. We sought to identify key factors associated with symptoms of depression among IDUs receiving antiretroviral (ARV) treatment in Jakarta and Denpasar, Indonesia.

**Methods:** The cross-sectional study was conducted at five ARV delivery sites in Indonesia. Former IDUs aged 18 years or older having received ARV treatment for at least three months (n=117) were recruited and interviewed face-to-face. A 9-item version of the Center for Epidemiologic Studies Depression Scale was used to measure symptoms of depression. A structured questionnaire measured participants' demographic characteristics, social support and services received, current substance use, and treatment for drug dependency and HIV. Multiple logistic regression was used to calculate adjusted odds ratios (AOR) and 95% confidence intervals (CI).

**Results:** Of the 117 participants, 33% (39) exhibited symptoms of depression, 24% (28) reported using an illicit substance in the past month, and 29% (34) were in methadone treatment. Depressive symptoms were significantly associated with recent substance use in the last 30 days (AOR, 95% CI: 5.3, 1.9 to 15.4) and being on methadone (3.5, 1.2 to 10). Older age (per year 0.9, 0.8 to 1), full-time employment (0.2, 0.1 to 0.7), and living with parents (0.2, 0.1 to 0.6) appeared to be protective.

**Conclusion:** The results suggest that depression is common among Indonesian IDUs, even among patients enrolled in methadone treatment. HIV clinics and drug treatment programs need to recognize the risk/protective factors and also provide services to address this common comorbidity.

**Keywords:** Depression; HIV; Psychiatric comorbidity; Injection drug use; Antiretroviral treatment; Methadone; Indonesia

### Introduction

Antiretroviral therapy has transformed HIV into a chronic condition for those with access to treatment. Despite this clinical success, coping with the diagnosis and progression of the virus poses enormous psychiatric challenges that can exacerbate or lead to mental depression [1,2]. Studies show that people living with HIV experience depression at rates twice or more than that of uninfected individuals [3,4]. Major Depressive Disorder (MDD) is among the most commonly diagnosed comorbidities in people living with the virus [5] with prevalence rates in the U.S. ranging up to 50% [5,6].

Injection drug users (IDUs) are especially vulnerable to both HIV infection and MDD [7]. Physical, psychological and social dysfunctions resulting from drug addiction can add to the stress of living with HIV, accelerating the deterioration of mental health [8,9]. Depression, in turn, is associated with poorer biological responses, faster clinical progression and higher mortality among people living with the virus [5,10-15].

Although numerous studies examine the interplay between HIV, drug use, and mental depression, less than a handful have focused on such co-morbidity in developing countries. Yet, 78% of IDUs are estimated to reside within resource-poor regions [16]. In central Europe, Asia, the Middle East and southern Latin America, needle sharing is thought to account for 30-90% of all reported HIV infections. Given these high rates, and the likelihood that they also reflect a substantial number of people experiencing depression, the interactions between mental disorders, substance use, and HIV infection in a resource-poor context need to be understood and addressed.

This study utilizes cross-sectional data from a pilot study on adherence to ARVs among IDUs in Indonesia to identify factors associated with symptoms of depression in HIV-infected persons with a history of injection drug use. Along with countries throughout Asia including China, Viet Nam, Myanmar, and Iran, Indonesia is experiencing an HIV epidemic driven substantially by injection drug use [17]. Surveys in 2001 revealed an alarming high HIV infection rate of about 50% among IDUs in Jakarta [18]. More recent statistics show that about half of the nation's estimated 220,000 IDUs were infected

with HIV, comprising more than 40% of total HIV infections in the country [19].

In response to the challenge of the nation's growing subpopulation of IDUs who are highly vulnerable to HIV, Indonesia has instituted an array of harm reduction activities. Methadone maintenance was first established in Indonesia in 2003 at two pilot sites, one in Jakarta and another in Bali [17].

Indonesian clinics began offering anti-retroviral therapy in 2005, although the estimated coverage for the country by the end of 2008 was still below 40% [20]. Despite these efforts to successfully address the dual epidemics of drug addiction and HIV, services for IDUs who are infected remain modest, and little appears known about the mental health problems that can accompany these co-conditions.

In the following study, we examine the intersections of HIV, drug use, and mental depression among 117 IDUs receiving ARV treatment for HIV. Our analysis considers the possible relationship between the increased likelihood of reporting depressive symptoms and key personal and demographic characteristics. Ample evidence shows that methadone maintenance therapy (MMT) reduces drug use and its comorbidities [21], and our a priori hypothesis was that its use would reduce the likelihood of depressive symptoms.

Social support in the form of family involvement in treatment [22] and use of formal services [23-25] have been found to correlate with better mental health among people living with HIV. Thus, we have included measures of these key variables in our research. By helping to better understand the constellation of factors that are associated with depression among IDUs receiving ARV treatment, the results from the study have the potential to optimize intervention and increase the mental well-being of a highly vulnerable population.

## Methods

### Sample

This cross-sectional research focuses on depressive symptoms among patients with histories of injection drug use who were enrolled at five sites that deliver ARV services in Indonesia (three in Jakarta on the island of Java and two in Denpasar on the island of Bali). The Institutional Review Boards of the University of Illinois at Chicago and Atma Jaya Catholic University in Jakarta approved the study for the ethical protection of research participants.

To enroll in the study, prospective participants had to be 18 years of age or older, have a history of injection drug use, and have received antiretroviral medications for at least 3 months. During the study's recruitment period, clinic physicians briefly explained the research to eligible patients during their regular medical visits and obtained contact information from those who expressed interest in enrolling in the study. Research staff then contacted prospective participants to explain the research in greater detail and obtain informed consent.

A total of 142 patients agreed to participate. Of these, 25 cases were excluded from our analysis due to answers of "don't know" or "decline to answer" to one or more items about substance abuse or symptoms of depression. Comparison of these participants with those for whom there were no missing values showed no statistically significant differences. The following analysis is based on the 117 participants for whom there were complete data.

### Data Collection, Measures, and Coding

Trained research staff administered a structured questionnaire in Bhasa (Indonesia's official language) that asked participants to describe their demographic background, history of drug use, receipt of social support, use of HIV and methadone services, and symptoms of depression (if any). Each participant was assigned a unique study identification number to protect confidentiality. Participants received \$15 compensation for their travel expenses and time in being interviewed.

*Symptoms of depression* (SD) were assessed using a shortened 9-item version of the Center for Epidemiologic Studies Depression Scale (CES-D) [26,27]. CES-D has been validated and used widely across cultures, including in Indonesia [28,29]. The short version and the scoring scheme used here have been psychometrically assessed to improve the efficiency in identifying depressed individuals relative to the original CES-D [27]. Respondents were asked to rate how often over the past week they experienced the following nine situations: "I was bothered by things that usually do not bother me; I felt I could not shake off my blues even with help from my friends or family; I had trouble keeping my mind on what I was doing; I felt depressed; I felt that everything I did was an effort; my sleep was restless; I was happy; I enjoyed life; I felt sad." Response categories solicited for each item were, "less than 1 day, 1-2 days, 3-4 days, to 5-7 days in the past week."

Using methods suggested by Santor and Coyne [27], we dichotomously coded responses to each of the nine items. Responses of less than 1 or 1-2 days were scored as "0"; responses of 3 or more days were scored as "1." Next, scores were summed across all 9 items with a total score of 4 or more categorized as symptomatic of depression (SD) and 3 or less as non-symptomatic (NSD). Scale analysis yielded a Cronbach's  $\alpha$  value at 0.804, indicating that the scale performed with satisfactory internal consistency.

*Demographics Variables* were selected on either epidemiologic plausibility or previously demonstrated association with depression in HIV-positive drug using populations [30-32]. These covariates included age (continuous), self-reported current employment (employed full-time, employed part-time, working at informal jobs, a student, unemployed), and highest level of education (never attended school, elementary, junior high, high school, college).

*Recent Substance Use* in the last 30 days was measured based on participants' self-reports of how frequently they used one or more of the following drugs: alcohol, marijuana, heroin, cocaine, amphetamines or stimulants, tranquilizers or downers, other narcotics or opiates, and hallucinogens. Recent substance use for cocaine, heroin, Amphetamines/stimulants, tranquilizers/downers, other narcotics or opiates and hallucinogens was coded as "1" based on having used one or more of these substances in the last 30 days; lesser or no reported use was coded as "0." Alcohol and marijuana use, which formed a separate coding category, were coded as "1" if used at least once a week in the last 30 days and "0" for lesser or non-use.

Enrollment in *Methadone Maintenance Treatment (MMT)* was measured initially by asking participants if they currently received MMT, and then later confirmed through the patient's medical record. *Adherence* to ARVs was approximated by inquiring about the time frame of the last missing of the medications. Six options (never skipped medication, missed within the past week, within the past two weeks, within the past month, more than a month ago and more than three months ago) were given. Responses subsequently were coded into two categories for analysis: Never having missed a dose or not

having missed a dose for over a month was coded as “0;” Having missed at least one dose in the last month was coded as “1.”

*Family social support* was gauged by a series of questions regarding family involvement in HIV care, possible financial assistance from family members, and family living arrangements. The later was measured by asking participants if they currently lived with their mother/stepmother, father/stepfather or spouse. Multi-generational households are common in Indonesia. Anyone living with one or more parents, even if married, was coded as “living with parent.”

Three types of *formal social support* were assessed: 1) community outreach services, 2) HIV case management, and 3) HIV support group membership. In Indonesia, community outreach typically is delivered at the neighborhood level by former drug users who offer face-to-face HIV prevention education and assistance with getting into drug treatment to IDUs whether or not they are HIV-positive. HIV case management services most frequently are office-based but can include possible home visits. Services include assessing client needs, service planning and coordination, case monitoring, and crisis intervention. HIV support groups are composed of HIV positive people who meet periodically to provide peer support and discuss issues and problems they similarly confront. Participants were asked to report on which of these three services, if any, they received in the last 30 days.

### Statistical analysis

Demographic and socioeconomic characteristics were summarized using means with standard deviations (Stdv) for continuous variables and using proportions for categorical variables. Logistic regression models were used to determine factors independently associated with symptoms of depression and to adjust for the effects of potential confounders. Gender was not included in the analysis due to a small sample cell size [11] for women.

Univariate regression tested associations between individual candidate risk factors and SD. Multiple regression was used to examine the independent effect of each variable on depression while adjusted for the influence of all other variables. Based on the results of univariate analysis, each variable with a P value  $\leq 0.25$  was included in the starting multiple regression model [33], and the final model was refined through manual backward stepwise selection in addition to the hypothesis-driven testing of specific combinations of variables. Intercorrelations among the independent variables were examined and no substantial collinearity was present. All statistical tests were two-sided and considered significant at  $\alpha = 0.05$ . Ninety-five percent confidence intervals were estimated for calculated odds ratios.

### Results

Table 1 presents the demographic characteristics of the 117 participants. They are predominantly young (mean age about 31), male (93%) and high school educated (90%). Less than half have full-time jobs or are married. Median monthly income for this group equals approximately \$100 USD.

Univariate analyses comparing the socio-demographic characteristics of those with or without reported SD reveal no statistically significant differences by gender, education, income, marital status, or treatment site, whereas age and employment do correlate with the presence of SD (Table 1).

	<b>SD (n=39) No. (%*)</b>	<b>NSD (n=78) No. (%*)</b>	<b>Total (n=117) No. (%*)</b>	<b>p <sup>£</sup></b>
<b>Age, Mean (Stdv.)</b>	29.6 (3.5)	31.4 (5.0)	30.8 (4.6)	0.03
<b>Male</b>	36 (92.3)	70 (89.7)	106 (90.6)	0.9
<b>Education: high school or above</b>	34 (87.2)	71 (91.0)	105 (89.7)	0.5
<b>Employment: full-time</b>	12 (30.8)	39 (50.0)	51 (43.6)	0.05
<b>Last month's income above median</b>	15 (38.5)	42 (54.5)	57 (49.1)	0.1
<b>Married</b>	17 (43.6)	36 (46.2)	53 (45.3)	0.8
<b>Sites: Jakarta</b>	14 (35.9)	34 (43.3)	48 (41.0)	
<b>Bali</b>	25 (64.1)	44 (56.4)	69 (59)	0.4

\* Percentages over the column total n.  
<sup>£</sup> P-values were obtained from either t-tests (for continuous variables) or chi-square tests (for categorical variables), and were bolded and italicized when significant.

**Table 1:** Comparison of the socio-demographic characteristics of study participants exhibiting symptoms of depression (SD) versus non-symptomatic for depression (NSD).

Table 2 presents the frequencies and also the univariate analyses for social support, substance use, treatment effects and medication adherence regressed on SD. Informal support provided by family members was gauged by a series of questions regarding patients' living arrangement, family involvement in HIV care, and financial aid from family members. Of the 117 subjects, 56 (48%) lived with at least one parent in the household. In terms of formal support, less than 30% of the clients reported contact with an outreach worker or a HIV case manager in the last 30 days, while about 43% participated in a HIV support group. Neither family social support nor service use, however, were associated in univariate analysis with SD.

Meanwhile, over a quarter (28) of the study's participants reported substance use in the last 30 days. Tranquilizers and downers (n=22) were the most commonly cited substances, followed by heroin (n=8). Two participants reported recent use of amphetamines/stimulants, six participants reported use of other forms of narcotics or opiates. Cocaine use was not reported. Univariate analysis showed that being on methadone maintenance was associated with about three times greater odds of having SD.

Current substance use (heroin, amphetamines, tranquilizers/downers and other narcotics/opiates combined) was associated with about six times greater odds. The use of tranquilizers alone was associated with a five-fold increased risk for SD. The cell sizes for heroin and other forms of substance use were too small to allow independent statistical estimation (Table 2).

Of the 117 participants, 34 (29%) participants were concurrently in a MMT program and the treatment is associated with a 3-fold increase in the odds of SD. Fifty one (44%) reported full adherence to HIV medication in the last 30 days. Differences in adherence, however, were only shown through the univariate analysis to be marginally significant (p=0.055) when regressed on SD.

Family Social Support	SD (n=39) No. (%)	NSD (n=78) No. (%)	Total (n=117) No. (%)	OR <sup>€</sup> (95% CI)
Lives with at least one parent	17 (43.6)	39 (50)	56 (47.9)	0.8 (0.36, 1.67)
Family (spouse and/or parents) involved "a lot" with HIV care	18 (46.2)	43 (55.1)	61 (52.1)	0.7 (0.31, 1.47)
Received financial support from parents or relatives in the last 30 days	20 (51.3)	31 (39.7)	51 (43.6)	1.6(0.74, 3.46)
<b>Formal Social Support in the last 30 Days</b>				
Community outreach services	14 (35.9)	19 (24.4)	33 (28.2)	1.7 (0.76, 4.00)
HIV case management services	12 (30.8)	18 (23.1)	30 (25.6)	1.5(0.63, 3.50)
HIV support group membership	19 (48.7)	32 (41)	51 (43.6)	1.4 (0.63, 2.96)
<b>Substance Use in the last 30 days</b>				
Cocaine	0	0	0	--
Heroin *	5 (12.8)	3 (3.8)	8 (6.8)	--
Amphetamines/stimulants *	1 (2.6)	1 (1.3)	2 (1.7)	--
Tranquilizers/downers	14 (35.9)	8 (10.3)	22 (18.8)	4.9 (1.84, 13.07)
Other narcotics or opiates *	3 (7.7)	3 (3.8)	6 (5.1)	--
Combined substance use <sup>£</sup>	18 (46.2)	10 (12.8)	28 (23.9)	5.8 (2.3, 14.6)
Alcohol use once a week or more *	3 (7.7)	3 (3.8)	6 (5.1)	--
Marijuana use once a week or more *	1 (2.6)	5 (6.4)	6 (5.1)	--
<b>Treatment</b>				
Methodone Maintenance	18 (46.2)	16 (20.5)	34 (29.1)	3.3 (1.44, 7.66)
ARV Adherence	13 (33.3)	14 (17.9)	27 (23.1)	2.4 (0.98, 5.76)

<sup>€</sup> OR: odds ratio; CI: confidence interval. Significant estimates were bolded and italicized.  
<sup>\*</sup> Too few subjects for OR estimation.  
<sup>£</sup> Combined category of ever using in the last 30 days any of heroin, amphetamines/stimulants, tranquilizer/downers, and other narcotics or opiates.

**Table 2:** Univariate analyses for social support, substance use, and treatment effects in relation to symptoms of depression (SD) (N=117).

### Multivariate regression

Multivariate regression was used to identify factors associated with SD among the 117 participants. All variables shown in Table 2 were included in the calculation along with the demographic characteristics of age, employment, marital status, and income. After stepwise

removing non-significant effects, the analysis identified five factors independently associated with SD responses (Table 3). When adjusted together, the odds of being identified with SD are about 10% lower per year of age and about 80% less with full-time employment and living with parents. Methadone maintenance therapy and also recent substance were associated with more than a three-fold elevation in the odds of SD.

	Total n (%)	Odds Ratio * (95% CI)
Age (in years)	--	0.9 (0.79, 0.98)
Full-time job	51 (43.6)	0.2 (0.07, 0.69)
Living with parents	56 (47.9)	0.2 (0.07, 0.60)
Currently on methadone	34 (29.1)	3.5 (1.22, 10.00)
Current substance use <sup>£</sup>	28 (23.9)	5.3 (1.85, 15.42)

\*All the p-values < 0.05.

<sup>£</sup> Combined category of ever using in the last 30 days any of heroin, amphetamines/stimulants, tranquilizer/downers, and other narcotics or opiates.

**Table 3:** Multivariate regression for factor effects on the SD outcome (N=117).

### Discussion

Data on depressive disorder and other mental health problems in Indonesia are scarce, and only started to emerge in the past few years. Recent studies in Indonesia reported prevalence rates as high as 34% for depressive symptoms among elderly, 24% for self-rated depression among men and 28% for screening based depression among healthy people and CHD patients [34-36]. Our results suggest a comparably high prevalence of the problem among HIV-positive IDUs in Indonesia under ARV treatment, given that one-third of our sample reported having experienced symptoms of depression for at least three or more days in the past week.

Although only eight participants reported heroin use in the last 30 days, twenty-two in our sample reported using tranquilizers and downers including six who also reported heroin use. We don't know from our data if the tranquilizers were purchased as illicit street drugs or prescribed by a physician for mental health reasons that may or may not be related to living with HIV. In therapeutic use, these drugs are administered to relieve anxiety and produce a feeling of well-being by depressing the central nervous system. Individuals with SD sometimes buy them as street drugs in an attempt to self-medicate without knowing their possible side effects. In either instance, their use can be contraindicated for people with depressive symptoms in that they sometimes exacerbate such feelings [37]. While we can only speculate, the prevalent use of these substances among the subjects may have contributed to the elevated rate of developing SD.

The SD outcome is strongly linked to current substance use in both the univariate and multivariate analyses, consistent with the findings from different settings that also have found a link between mental challenges and ongoing use of substances among infected IDUs [38-40]. Our results suggest that psychiatric interventions are needed to help Indonesian patients to overcome the dual barriers to successful ARV treatment posed by dependency and depression. Such interventions might particularly benefit those Indonesian clients of younger age, without a full-time job and not living with parents

according to our data. Existing studies on mental health of HIV patients in a variety of settings have rarely identified age as a factor associated with depression [41,42], however younger age has been linked to higher risk of depression among other chronic disease patients [43,44] and the general population [45]. Consistent with our findings, employment has been shown in other studies as an important socioeconomic predictor of lower risk for depression [46,47]. Interestingly, many of our participants lived with their parents reflecting a general cultural condition in Indonesian society to maintain co-residence of adult children and parents [48]. Our results suggest that this living arrangement may exert some protective effect on the mental health status of this population since such co-residence was associated with an 80% reduction in the risk of SD. The actual efficacy of parental support in facilitating HIV care warrants further exploration with carefully devised family-centered interventions.

Given a number of studies reporting methadone's positive effects on patient socio-emotional wellbeing [21,49-51], our results showing a negative association between SD and MMT independent of ongoing substance use were unexpected. Possibly such contradiction may relate to where our study participants were in their overall treatment trajectory. Newly enrolled methadone patients often exhibit poor psychological health due to the negative correlates of recent drug dependency [52]. Mental depression and other adverse emotions, however, tend to improve with time, abstinence, and treatment [53,54]. Unfortunately for our analysis, we lack the data needed to determine if a substantial number of our participants were newly enrolled. A second possibility for a negative association could be that Indonesian substance users with symptoms of depression selectively seek methadone treatment more than those with better positive mental outlooks, as seen in previous studies [55]. Still another possibility is that the rigors of complying with methadone treatment (daily visits, geographic constraints) contribute to depression. Also, many studies of the treatment effects of MMT show that methadone alone is limited in its ability to counter the mental health problems that can accompany dependency [56-58]. When combined with depression management, however, drug treatment outcome may be greatly improved [52,59]. Since methadone programs often are directed by psychiatrists in Indonesia, the opportunity to integrate depression management into methadone treatment should not be overlooked. SD screening and counseling for newly enrolled patients may be particularly important.

Our study has several limitations that must be acknowledged. The original CES-D scale as well as the shortened version that we used is far from ideal in screening for depression due to low specificity [60,61]. Consequently as suggested by the scales' developers [27], we have carefully avoided referring to study participants identified with SD as being clinically depressed. Instead we limit our interpretations of study findings to over-threshold depressive symptoms, which is an important distinction. Nonetheless, we believe that evidence of SD in these patients indicates a need for further screening and care to more carefully diagnose and manage depression in this population. Such follow-up is especially important in view of the potential inter-correlation between SD and continuing substance use as suggested by our results.

Another limit of our study is that we are unable to examine gender effects as few women are enrolled in HIV care programs in Indonesia, and our sampling reflects their proportional representation at our four study sites. Data on female IDUs have always been scarce in the developing world even though 10% of IDUs in East and Southeast Asia

are thought to be women [62] and the percentage may be even higher for Indonesia [63]. Women with the co-conditions of drug dependency and HIV appear more vulnerable to depressive disorders than their male counterparts [64,65], and future research needs to reach more women in the target population for research and a parity of benefits.

Our study detected a strong linkage between severe depressive symptoms and ongoing substance use as well as involvement in methadone maintenance programs, highlighting the needs of co-management of dependency and depression for better treatment outcomes among HIV-infected IDUs in Indonesia. Elevated risk was suggested for those who are younger and unemployed, indicating that screening effort should be more focused on the characteristic subpopulation. The protective effect of co-residence with parents may indicate a unique opportunity for improving patient outcomes by enlisting family to facilitate and support HIV care, mental illness management, and drug treatment. Overall our investigation provides an unprecedented insight into the mental health status of HIV positive IDUs under treatment in Indonesia, and demonstrates the needs for more effective interventions to improve the care of this population.

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