

Am J Addict. Author manuscript; available in PMC 2013 November 01.

Published in final edited form as:

Am J Addict. 2012 November; 21(0 1): S49–S55. doi:10.1111/j.1521-0391.2012.00300.x.

# Correlates of Depressive Symptoms among Alcohol-Using Methadone Maintained Adults

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# **Abstract**

**Background**—Alcohol-using clients are considered at great risk for hepatitis and ongoing liver damage. This study explores the correlates of depression among a sample of methadone maintained treatment (MMT) adults in the Los Angeles area, and is part of a larger study on hepatitis health promotion among MMT clients who use alcohol.

**Objectives**—We sought to determine correlates of depressive symptoms among moderate and heavy alcohol-using adults enrolled in methadone maintenance.

**Methods**—A cross-sectional correlation study was conducted of baseline data from a randomized control trial of adults (N = 189) receiving methadone maintenance treatment (MMT) in Los Angeles. Depressive symptoms were measured with the 10-item short-form CES-D.

**Results**—Multiple regression analysis revealed that pain and social support were key correlates of depressive symptoms. More pain was associated with higher levels of depressive symptoms (p=.001), while more social support was related to lower depressive symptom severity (p=.001). Having been in sufficiently poor health that a blood transfusion, clotting factors, or an organ transplant was necessary was associated with greater depressive symptomatology, as was having injected drugs in the past month (p=.024).

**Conclusions**—The findings from this investigation can aid clinicians in selecting clients to monitor for early signs of depression and encourage early treatment for opioid users with comorbidities.

**Scientific Significance**—The use of an interdisciplinary team to care for MMT clients, routinely screen for depressive symptoms, and emphasize adequate pain control is indicated.

# Introduction

Recent studies show the prevalence of depression among methadone maintained treatment (MMT) clients to be as high as 50%. In this population, physical health and function are likewise affected. For example, in a comparison of patients receiving MMT and matched controls, those receiving MMT reported significantly worse levels of depression, poor physical function and daytime sleepiness. Drug use was also high among persons who were enrolled in programs designed to substitute methadone for opiates and other drugs. In a study of 401 drug-dependent persons, major depression predicted using more substances and

#### **Declaration of Interest:**

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having increased symptoms of drug dependence.<sup>3</sup> Moreover, depression was also associated with poor opioid dependence treatment retention and outcomes.<sup>4</sup>

Among injection drug users (IDUs), depressive symptoms have been negatively correlated with perceived social support.<sup>5</sup> Low levels of family support have been associated with suicide attempts among MMT clients.<sup>6</sup> and MMT clients without a current partner are more likely than those with a partner to have depressive symptoms.<sup>7</sup> Additionally, any other Axis 1 psychiatric diagnosis, benzodiazepine use, and higher methadone dose (> 120 mg/day) have been associated with increased incidence of depression.<sup>1</sup>

Depression is likewise associated with chronic and severe pain, which is experienced by approximately 37% of patients enrolled in MMT.<sup>8</sup> When compared with MMT clients who reported no pain in the previous week, those reporting chronic moderate-to-severe pain had significantly higher levels of depression, anxiety, somatization, overall psychiatric distress and personality disorder criteria.<sup>9</sup>

In terms of physical health, it is well established in the literature that pain and depressive symptoms are synergistically linked. Particularly for clients with a history of IDU, self-medication with psychoactive drugs is problematic<sup>8</sup> and could lead to relapse, particularly for those in MMT. Providers must be cognizant of the alteration in pain perception of MMT clients who were former heroin users. <sup>10</sup> While limited research has been examined health status (apart from pain) and depression in MMT clients, Batki et al. <sup>11</sup> investigated the clinical factors that predict health-related quality of life (HRQOL) in MMT clients with untreated HCV infection, and found that depression scores significantly predicted HRQOL measures. These authors also found that HRQOL was not directly linked to the existence of chronic health conditions in their study population.

The present study adds to the literature on depressive symptoms experienced by adults on methadone maintenance by exploring the correlates of depression among a sample of MMT adults in the Los Angeles area. More uniquely, this study is part of a larger study on hepatitis health promotion among MMT clients who use alcohol. Alcohol-using clients in particular are considered at greatest risk for hepatitis risk and ongoing liver damage. In fact, it is estimated that between 67% and 96% of MMT clients have been exposed to Hepatitis C Virus (HCV). <sup>12,13</sup> Further, alcohol consumption is one of the most influential factors determining progression of disease in individuals with chronic HCV infection. <sup>14</sup> Yet, little is known about the correlates of depression among this unique sample who are in MMT. Understanding the correlates of depressive symptoms for adults enrolled in MMT programs is necessary for anticipating therapy complications and improving client outcomes.

## **Methods**

## Design

This study design was randomized controlled trial of hepatitis health promotion among moderate and heavy alcohol-using adults receiving MMT (*N*=189) based on the Addiction Severity Index. The study and associated materials were approved by the Human Subject Protection Committee.

#### **Theoretical Framework**

The framework used to guide our study on correlates of depression among alcohol-using MMT clients was the Comprehensive Health Seeking and Coping Paradigm (CHSCP). <sup>15</sup> This framework was originally adapted from the Lazarus and Folkman <sup>16</sup> stress and coping paradigm and the Schlotfeldt <sup>17</sup> health seeking and coping paradigm. This framework outlines the factors that may impact the lives of this vulnerable subgroup and include

selected sociodemographic, social, and psychological variables and personal resources. The latter dimension includes physical health and risks, history of abuse and victimization, as well as behavioral responses in relation to drug and alcohol use.

## Sample and Setting

Participants in the study were eligible if they: a) had received methadone for at least three months at their MMT site; b) were 18–55 years of age; and c) reported moderate-to-heavy alcohol use based on questions from the Augmented CAGE. Study participants attended one of five MMT sites located in Los Angeles and Santa Monica, California. These sites included: Bay Area Addiction and Research Treatment (BAART) clinics in the areas of Beverly, Southeast, and Lynwood, and non-BAART MMT sites in Santa Monica (Matrix) and Southeast Los Angeles (TriCity).

#### **Procedure**

MMT clients who were informed of the study by a posted flyer contacted the research staff. After more detailed information was provided about the study by the research staff, and all questions answered, informed consent was read, discussed and signed prior to undergoing a brief screening to determine if eligibility criteria were met. Immediately thereafter, the research staff administered a two-minute structured questionnaire composed of sociodemographic characteristics, a screener for alcohol use and severity of use, and a hepatitis-related health history.

For all eligible persons interested in participating in the study, detailed information was provided about the study. Final consent was obtained from clients who met eligibility criteria and wanted to continue. The baseline questionnaire was then administered to the clients by trained research staff.

#### Measures

Socioeconomic characteristics were measured by a structured instrument that assessed age, gender, race/ethnicity, years of education, partnership status, and number of children and current smoking.

Health was assessed in a number of ways in this study. General health was assessed by one item from the SF-36, <sup>19</sup> asking respondents to rate their overall physical health status on a 5-point scale from "excellent" to "poor." This single-item assessment has been used in a number of health surveys as an overall indicator of physical health. Since it was skewed toward worse health, health status was dichotomized as fair/poor versus better health in analyses. Level of pain in the past six months was also measured by a single item from the SF-36. Categories ranged from [1] "none" to [6] "very severe". Functional status was measured by four items from the SF-36. Respondents were asked whether they had "a lot of trouble," "little trouble," or "no trouble" with (1) lifting or carrying groceries; (2) climbing one flight of stairs; (3) walking one block; and (4) bathing and dressing. Reliability for the four items was 0.89 and a mean-item scale ranged from 1 to 3. Due to a highly skewed distribution, functional status was dichotomized at the mode of 3 (no trouble) for analysis. Finally, respondents were asked if they had ever received a blood transfusion, blood clotting factor or organ transplant.

Social support was measured by 9 items from the RAND Medical Outcomes Study Social Support Survey. <sup>21</sup> The items covered several dimensions of social support. Sample items included having someone to: help with daily chores when sick (tangible support), show love and affection (affectionate support), get together with for relaxation (positive social interaction), confide in (emotional support) and turn to for suggestions about how to deal

with personal problems (informational support). Chronbach's alpha for the 9 items was 0.94. A sum scale was formed with a range of 9–45. Since the scale was not approximately normally distributed, it was dichotomized at the median of 32 for analysis.

Drug use was measured by asking respondents how many years they had used selected drugs and how many days they had used selected drugs in the past month. Drugs assessed were: marijuana, cocaine and crack, heroin, methadone, other opiates/analgesics, barbiturates and other sedatives or tranquilizers, amphetamines, inhalants and hallucinogens. Respondents were also asked to report the administration routes, and if there was more than one for a given drug or class, the most severe route. Administration routes included oral, nasal, smoking, non-IV injection and IV injection. For this paper, we examined four categories of injection drugs: heroin, methadone, cocaine or amphetamines in the past month.

Alcohol use was measured by asking respondents how many drinks they had containing alcohol on a typical day when they were drinking in the past six months. Response options were (1) '1 or 2', (2) '3 or 4' ... (5) '10 or more.' This item is part of the Augmented CAGE. 18 For analytic purposes, responses were dichotomized at the median of 5 or 6 drinks a day. Heavy drinking was defined as five or more drinks per day on an average day, and moderate drinking was defined as less than five drinks per day on an average day. All eligible participants had to screen in as moderate-to-heavy alcohol drinkers.

Victimization was measured by two yes/no items asking about assault and rape in childhood and two comparable items asking about assault and rape after age 18.

The outcome, depressive symptoms, was measured with the 10-item short-form CES-D.<sup>22</sup> Like its parent, this scale measures depressive symptoms on a four-point continuum from 0 to 3. The 20-item CES-D has well-established reliability and validity.<sup>23</sup> In this sample, the internal consistency reliability for the 10-item scale was 0.79. After two positively-worded items were reversed, the 10-items were summed, yielding a scale score that ranged from 0 to 28.

# **Data Analysis**

Continuous variables were evaluated for normality and unadjusted associations of depressive symptoms with sociodemographic, health, social support, substance use, and victimization measures were examined with two-sample t tests, and analysis of variance. For simplicity of presentation, age and pain were dichotomized for these unadjusted tests. However, they were used as continuous measures in adjusted analyses. Because there were a large number of overlapping correlates of depressive symptoms, covariates that were significant at the 0.15 level in unadjusted analyses were entered into stepwise backward linear regression analysis. The 0.10 level was used for retention. Based on preliminary exploratory analyses, dummy variables representing an interaction between gender and health status (fair/poor versus better health) were included as set in the initial model. The reference group was men in better health. Findings were confirmed with stepwise forward analysis. Predictors in the final model were checked for multicollinearity. Analyses were conducted using SAS 9.1.3. The CHSCP model guided selection of potential correlates of depressive symptoms.

## Results

#### Sociodemographic Characteristics

Sociodemographic characteristics for the sample of 189 MMT participants are shown in Table 1. More than half the sample was male (57.4%) and nearly two- thirds were either African American or Hispanic; nearly one-quarter were white. The mean age of the sample

was 50.6 (SD = 9.0) and the average education reported was 11.5 years. Slightly over half (54%) reported having a significant other. Nearly two-thirds reported fair or poor health and moderate to very severe levels of pain. Social support primarily from substance users was reported by 16%.

In terms of substance use, approximately half reported heavy drinking (at least 5 drinks a day). IDU in the past month was reported by 40%. Childhood abuse was reported by nearly one-third of the sample, while slightly over one-third reported adult abuse and a quarter reported adult rape. The mean depressive symptom severity score was 14, and the overall rate of depression found in this sample was 64% (CES-D overall score > 16).

## **Associations with Depressive Symptoms**

As shown in Table 2, bivariate analysis revealed clients aged 50 or less experienced more severe depressive symptoms than older clients, as did Whites compared to non-Whites. Clients in fair or poor health, as well as those who experienced severe or very severe levels of pain, reported greater depressive symptom severity than their counterparts. Depressive symptomatology was also more prominent among clients with lower functional status, and those who previously received a blood transfusion. Severity of depressive symptoms was inversely related to more versus less support.

Substance use was also associated with depressive symptoms. Recent IDUs and heavy drinkers reported experiencing greater depressive symptom severity than their respective counterparts. Moreover, clients who reported childhood rape or adult abuse likewise experienced more depressive symptomatology than clients not reporting these events.

Finally, Spearman correlations revealed low but significant negative correlations for length of time in MMT and time on a stable methadone dose with depressive symptoms (both correlations -.16, p < .05; data not shown). [Insert table 2 here]

## **Multiple Regression Analysis**

Age, pain and social support were key correlates of depressive symptoms in the linear regression model (Table 3). Older age was associated with lower levels of depressive symptoms. More pain was associated with higher levels of depressive symptoms, while more social support was related to lower depressive symptom severity. Having been in sufficiently poor health that a blood transfusion, clotting factors, or an organ transplant was necessary was associated with greater depressive symptomatology, as was having injected drugs in the past month. White MMT clients had greater depressive symptomatology than MMT clients in good health. Women in fair/poor health had a higher level of depressive symptoms than men in good health; no difference was found for men in fair/poor health or women in good health. However, a significant interaction between gender and health was found in regression modeling, with women in fair/poor health having a relatively high mean for depressive symptoms. In particular, their mean depressive symptom score was 16.2 compared with 14.4, 12.1 and 11.8 for men in fair/poor health, women in good health and men in good health, respectively. The model had an overall F of 8.46 (p < .001). The model r-square was 0.30.

# **Discussion**

Our findings revealed that younger age, IDU in the last month, increased pain, having had a transfusion, white race/ethnicity, and a low level of social support were all correlated with depressive symptoms in a regression analysis for this sample of moderate and heavy alcohol users enrolled in MMT. Further, women in fair or poor health were particularly vulnerable to depressive symptoms.

We found that recent IDU was correlated with depressive symptoms. Indeed, substance use continued to be an issue for our many of our alcohol-using participants in this investigation. Many participants (40%) reported that they had injected drugs within the past month and half were heavy drinkers. While in bivariate analysis we found that heavy drinkers and recent injectors had greater depressive symptomatology than their respective counterparts, we did not find heavy drinking to be an independent correlate of depressive symptoms. These findings may have resulted from the fact that younger age was associated (r = .24) with heavy drinking and we included a number of covariates in the regression model. Brienza et al.<sup>7</sup> found that alcohol use disorder was a correlate of depression in MMT clients, controlling for age, race, education and HIV status. Nevertheless, our findings indicate the need for a holistic view of substance dependency. In light of the numerous studies highlighting the link between depression and alcohol and drug dependency,  $^{3,6,24-26}$  identification and treatment of depression is a tool in the prevention of continued drug and alcohol dependence.

The persistence of substance abuse, social and health-related physical factors associated with depression indicates the importance of addressing co-occurring disorders in a comprehensive manner. Pain predicted depressive symptoms in our study. The prevalence of chronic severe pain in MMT-enrolled clients was 37% in two previous studies. <sup>8,9</sup> Similar to the associations between chronic and severe pain and depression among MMT adults identified by Barry and colleagues, <sup>9</sup> higher levels of pain were significantly associated with greater levels of depressive symptoms in this sample.

In bivariate analyses, lower functional status and having had severe enough health problems to merit blood transfusions were significantly associated with greater depressive symptomatology in this sample of alcohol-using MMT clients. Blood transfusions continued to be a correlate of depressive symptoms in regression analysis. These findings are novel to the current work published about MMT clients. Given that the majority of the participants reported only fair or poor health, and over one-third reported severe or very severe pain, linkage to health care services may be a strategy to mitigate both depressive symptoms and substance abuse. As MMT clinics are often the portal between the inconsistent or crisis-based health care received by active users and referrals to appropriate medical services, these clinics are well positioned to make needed linkages to health care.

The large majority of participants in this study received social support from non-drug users or from non-drug users and drug users equally. Moreover, a lower level of social support was correlated with greater depressive symptoms. These findings further advance the literature on the relationship of social support and depressive symptoms among moderate-to-heavy alcohol users in MMT. Although a significant portion of the sample had recently used injection drugs at the time of assessment, those who received social support exclusively from other drug users represented a small minority. This may indicate a harm reduction effect of MMT programs in improving current and former drug users' ability to form and maintain relationships with non-users. Perhaps the structure introduced by participation in MMT programs into the lives of users is responsible for the high prevalence of social support from non-substance users. Further investigation of this finding is certainly merited.

Likewise, we found significant correlations between depressive symptoms and length of time in MMT and length of time on a stable dose of methadone. Prior literature has reported that patients enrolled in long-term methadone treatment experience improvement in psychiatric status. <sup>27,28</sup> In fact, higher rates of depression were found among attendees of a needle exchange program compared to a MMT program, highlighting the fact that drug addicted persons who enter MMT do so with psychiatric co-morbidities. <sup>29</sup> While no prior research was found linking methadone dose with depressive symptoms, there is a long

history of research which links a stable dose of methadone of 80–100mg/day with better treatment retention<sup>30,31</sup> More research is likewise needed on the relationship between depressive levels of MMT clients and those who drop out.

Another novel finding was gender-related. Our study is the first to report that women who were in fair/poor health were particularly vulnerable to depressive symptoms. Other studies have found gender 1,7,24,32 to be related to depression in MMT clients. Specifically, those who were female were more likely to suffer from depressive symptomatology. Our study partially confirms these findings in that a trend for an overall gender difference was found in unadjusted analyses; however, in this sample, it was women in fair/poor health who had a relatively high level of depressive symptoms.

# Implications for Practice

We found depressive symptoms to be high among this group of alcohol-using MMT clients. The findings from this investigation can aid clinicians in selecting clients to monitor for early signs of depression and encourage early treatment for opioid users with comorbidities. The findings of this study have implications for clinical prevention and recognition of depressive symptoms in this population. The use of an interdisciplinary team to care for MMT clients, routinely screen for depressive symptoms, and emphasize adequate pain control is indicated.

Blood transfusions, pain, and the interaction of gender with physical health in the regression model suggest that a multidisciplinary treatment team will best be able to care for MMT clients, who are at risk for depression. Health professionals, including physicians, nurses, and social workers, are needed to assist in providing symptom management support, adjust doses of methadone, manage other medications, and provide counseling regarding social needs and support. Mental health specialists are needed given the degree of depression in the overall sample (64%) and the fact that recent IDU was associated with more intense depressive symptoms.

MMT clinic staff also have the opportunity to connect a population with numerous and often severe health problems to appropriate health services, including mental health services. Whereas depression has been associated with more substance use<sup>3</sup> and more symptoms of withdrawal, <sup>33</sup> when identified it can also represent an opportunity for clinicians to offer MMT clients the mental health care they need. Increased involvement with clinical providers can lead to better opioid dependence treatment outcomes. <sup>1</sup> As this cross-sectional study cannot provide information on causality, future studies should assess the efficacy of linking social services and health resources in improving MMT clients' satisfaction with their treatment providers and adherence to MMT. <sup>34</sup>

Additionally, clinics could provide improved mental health care for clients if a screening questionnaire or interview included: age, gender, a general health status question, a pain question, a transfusion or blood product question and social support assessment in their intake and case management protocols. This could help to identify clients who may be at high risk for depressive symptoms, and monitor them closely for signs of depression.

Clients in MMT have hyperalgesic responses and may require more analgesia than non-MMT clients. <sup>35</sup> However, Berg et al. <sup>36</sup> found widespread ambiguity amongst MMT providers regarding the management of chronic pain. Requests for more pain medications can be interpreted as a craving for drugs. <sup>35</sup> Providers must acknowledge these ambiguities and seek to provide adequate pain control, with the knowledge that uncontrolled chronic severe pain can contribute heavily to depression.

#### Limitations

Our findings are limited due to the cross-sectional nature of this study and causation is not implied. Because of the cross-sectional design, the causes of depressive symptoms cannot be determined; moreover we were not able to examine whether depression was secondary to alcohol use. Instead, associations are reported. In addition, because the measure of drinks per day was categorical in nature, we were unable to assess whether women had four drinks or more at a time and we defined binge drinking as five or more drinks per day for everyone. This study is also limited to the specific demographics of the sample, urban MMT-seeking clients in the Los Angeles area. However, our findings confirm results from studies in other geographic areas. Some characteristics that were associated with depression in preceding studies with MMT adults, such as psychiatric diagnosis, benzodiazepine use and higher methadone dose were not investigated in this study. Findings are also limited by self-report data, leaving a possibility for reporting bias. However, participants did report a high rate of recent injection drug use.

## Implications for Research

Further research is needed to investigate the circumstances under which participants of MMT continue to use drugs and alcohol and the prevalence of depression among those who do and do not continue to use. Given that 40% of this sample had injected within the previous month and 50% were heavy drinkers, longitudinal research is needed to determine why for some opioid-dependent individuals substance use declines only with continued participation in MMT and why some never stop using illicit drugs. Similarly, more studies are needed to identify factors, including psychiatric comorbidities that influence long-term retention in MMT programs. The body of literature on the effectiveness of MMT would also benefit from a detailed quantitative analysis of the influence and dosage of ancillary services offered by methadone clinics, such as providing or linking to mental and general health care, and hepatitis and HIV testing, in terms of retention and health outcomes.

# Acknowledgments

This study was funded by Grant AA015759 from the National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD (Dr. Nyamathi).

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Table 1

# Sample characteristics

Measure	Mean	(SD)
Age	50.6	(9.0)
Education	11.5	(2.1)
Pain	3.6	1.6
Functional Status	2.4	(0.7)
Depressive Symptoms	14.0	(6.0)
	N	%
Male Gender	109	57.4
Race/Ethnicity:		
African American	67	35.3
White	45	23.7
Hispanic	57	30.0
Other	21	11.1
Partnered	102	54.0
Any Children	142	75.1
Fair/Poor Health	117	61.6
Transfusion, ever	53	27.9
Social Support	30.1	(11)
Primary Social Support Source:		
Substance Users	29	16.0
Non-Substance Users	82	45.3
Equally Divided	70	38.7
Heavy Drinker*	94	49.5
Injection Drug User past month	76	40.0
Childhood Abuse	55	29.0
Childhood Rape	31	16.3
Adult Abuse	65	34.2
Adult Rape	50	26.3

<sup>\* 5</sup> or more drinks daily

Table 2

Associations with depressive symptoms (N=189)

Measure	Mean	SD	P Value*
Age:			.004
<= 50	15.2	6.2	
> 51	12.7	5.7	
Gender:			.073
Male	13.3	6.2	
Female	14.9	5.7	
Race/Ethnicity:			.037
African-American	12.6	6.0	
White	16.2	6.0	
Hispanic	14.1	5.7	
Other	12.6	12.0	
Partnered:			.445
Yes	13.6	5.9	
No	14.3	6.2	
Fair/Poor Health:			.001
Yes	15.2	5.6	
No	11.9	6.1	
Severe/Very severe Pain:			.003
Yes	15.9	5.8	
No	13.0	5.9	
Functional Status:			.017
Highest	12.7	5.9	
Other	14.8	6.0	
Transfusion, ever:			.001
Yes	16.3	5.7	
No	13.0	5.9	
Social Support:			.001
Upper Median	12.4	5.7	
Lower Median	15.6	6.0	
Heavy Drinker †:			.006
Yes	15.2	5.9	
No	12.8	6.0	
Injection Drug Use Past Month:			.024
Yes	15.2	5.8	.02.
No	13.2	6.1	
Childhood Abuse:	10.2	0.1	.486
Yes	14.4	5.9	
No	13.8	6.1	
Childhood Rape:	15.0	0.1	.015
Chiranoou Rape.			.013

Measure	Mean	SD	P Value*
Yes	16.4	4.9	
No	13.5	6.1	
Adult Abuse:			.043
Yes	15.2	5.8	
No	13.3	6.1	

<sup>\*</sup> p value based on t-test or analysis of variance

 $<sup>^{\</sup>dagger}_{5}$  or more drinks daily

 $\label{eq:Table 3} \begin{tabular}{ll} \textbf{Table 3} \\ Linear regression model for depressive symptoms (N=188) \\ \end{tabular}$ 

Measure	Coefficient	Std Err	P Value
Age	-0.10	0.04	.009
White (vs non-white)	1.87	.091	.042
Women Excellent/Good Health *	-1.17	1.31	.373
Women in Fair/Poor Health*	2.81	1.11	.012
Men in Fair/Poor Health*	0.88	1.05	.406
$Pain^{ \! \! \! \! \! \! \! \! \! \! \! \! \! \! \! \! \! \! \!$	0.74	0.26	.006
Transfusion, Ever	2.00	0.88	.024
More Social Support <sup>‡</sup>	-2.88	0.77	.001
Injection Drug Use Past Month	1.97	0.80	0.015

<sup>\*</sup> reference group is men in good, very good or excellent health

higher scores indicate more pain

 $<sup>\</sup>frac{1}{2}$  versus social support below the median level