

Anxiety and Its Influencing Factors in Methadone Maintenance Treatment Users

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Research

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Abstract

Background: Anxiety, a major factor that affects the therapeutic effect and dropout rate of methadone maintenance treatment, has a high prevalence among MMT users. This study aims to investigate the prevalence of anxiety in MMT users and explore the main influencing factors of anxiety of methadone maintenance treatment users.

Methods: 177 methadone maintenance treatment users in Guangzhou, China were evaluated. The socio-demographic, duration and MMT-related characteristics were documented. Anxiety, quality of life and sleep quality were evaluated by Beck Anxiety inventory (BAI), the Quality of Life-Drug Addiction (QOL-DA) and Pittsburgh Sleep Quality Index (PSQI) respectively. The correlation between different factors and BAI score was also analyzed.

Results: The BAI total score, QOL-DA score, PSQI score were 7.1 ± 8.2 , 163.5 ± 21.4 , 6.0 ± 4.0 respectively. 30.5% of the subjects showed mild to severe anxiety. Treatment interruption, QOL-DA score and PSQI score had strong correlations with the score of BAI, with correlation coefficients of 0.17, -0.08 and 0.50 respectively.

Conclusions: Anxiety symptoms were commonly presented in MMT users. Treatment interruption, quality of life and sleep quality are the major factors affecting anxiety of MMT users.

Background

Opioid abuse remains a global problem, with implications for social security and the spread of diseases such as AIDS. There were around 53 million people worldwide had used opioids in 2018, and around 29 million people of them had used opiates such as heroin and opium¹. Methadone is a synthetic μ -opioid receptor agonist that has similar effect to heroin². Methadone maintenance treatment (MMT), a substitutive therapy, has been proved helpful in reducing opioid abuse, drug-related risk behaviors, the infection rate of AIDS and crimes³⁻⁵, as well as improving patient's overall wellbeing⁶. China started methadone maintenance treatment programs in 2004 and gradually promoted it across the country. By 2013 there were 763 clinics providing service to about 0.2 million heroin users⁷.

Anxiety, is one of the major factor⁸ that affects the treatment compliance of methadone maintenance treatment and the preservation rate of methadone therapy⁹. It was reported that over 18% among MMT users has anxiety symptom¹⁰⁻¹³. The treatment compliance and the preservation rate of MMT are two key points to reducing the risk of withdrawal symptoms, drug relapse and overdose due to decreased tolerance^{14,15}. Moreover, anxiety increase the rate of dropout while methadone maintenance treatment and then the risk of injection practices, HIV infection and criminal behaviors among MMT users might increase.¹⁰. In addition, the high suicide rate of MMT users has a strong correlation with anxiety¹⁶. Exploring anxiety and its influencing factors in MMT users would be conducive to reducing a series of adverse risks such as dropout rate, relapse rate and suicide rate.

Previous studies indicated that education level, employment status¹⁰, coincident drug use¹⁷ and benzodiazepine use¹⁸ are the factors that influence the anxiety in MMT users. Low education, unemployment and positive urine drug test results and benzodiazepine use were the risks for anxiety among MMT users^{10,17,18}. However, there is still a lack of studies to comprehensively analyze the effects of MMT users' personal status, opioid abuse, methadone treatment and life status on their anxiety. This study explored the anxiety in MMT users and mainly focuses on exploring the influence of personal status, previous opioid use duration, methadone treatment and life quality on anxiety of MMT users. In addition, sleep quality, which was considered as a factor affecting anxiety¹⁹, would be further explored in relation to anxiety of MMT users.

Methods

Sample and data collection

A cross-sectional study was conducted from May to December 2019 in the MMT clinic of the Affiliated Brain Hospital of Guangzhou Medical University in Guangzhou, Guangdong Province. This clinic have provided treatment services for over 200 registered MMT users in Guangzhou.

MMT users were conveniently recruited if they were: (1) aged at least 18 years old; (2) received methadone treatment for at least 12 months; (3) accepted to participate and signed informed consent; (4) did not have severe cognitive impairments that might affect the communication between subjects and researchers. Among 210 MMT users interviewed, 177 of them accepted to participate (response rate of 84.3%). All participants signed informed consent. All participants were involved in face-to-face interviews with researchers. Measures

Socio-demographic, cumulative duration of heroin use and MMT-related characteristics

Background data of each participant were recorded, including gender, age, years of education, living situation, marital status, drinking status and smoking status. Cumulative duration of heroin use was measured in months. Characteristics related to Methadone maintenance treatment was also recorded, including cumulative duration of MMT, current therapeutic does, changes in therapeutic dose (current therapeutic dose minus initial therapeutic dose), and whether treatment had ever been interrupted.

Standardized scales

The Beck Anxiety Inventory, a brief measure of anxiety with a focus on somatic symptoms of anxiety, was used to assess anxiety in MMT users. The total score ranges from 0–63.0–9, normal/minimal level; 10–18, mild anxiety; 19–29, moderate anxiety; and 30–63, severe anxiety^{20,21}.

The Quality of Life-Drug Addiction (QOL-DA) was used in this study to assess participants' life quality. QOL-DA is a valid, reliable and responsive instrument for measuring the quality of life of opioid dependent individuals²². The QOL-DA was developed by Chong-hua Wan in 1997 for drug-dependent patients in China. The QOL-DA consists of 40 items that measure four dimensions include physiology, psychology, society and symptoms²². The reliability of the overall items, physiology, psychology, symptoms and society was 0.866, 0.795, 0.826, 0.914 and 0.714^{22,23}.

The Pittsburgh Sleep Quality Index (PSQI), a standardized self-administered questionnaire that is used for evaluating sleep quality and disturbances in the past month, was used to assess the sleep quality of MMT users. The total score of PSQI is ranging from 0 to 21. Responses with a total score of more than 5 are classified as people with poor sleep quality, while those with a score of less than 5 are classified as people with good sleep quality²⁴.

Statistical Analysis

SPSS version 19.0 was used to analyze data. T-test (for data with normal distribution), Chi-square test were used to detect the differences of variables between two durations of anxiety: no anxiety and anxiety. A p-value < 0.05 (two-tails) was used to identify statistical significance. Pearson correlation (for data with normal distribution) and Spearman rank correlation were used to describe the association between factors and BAI score. Further multiple linear regression analysis were done on variables which had strong correlation with BAI score.

Results

Characteristics of MMT users

Socio-demographic characteristics, cumulative duration of heroin use, MMT-related characteristics, BAI score, QOL-DA score and PSQI score are presented in Table 1. Altogether there were 177 methadone maintenance treatment users enrolled in the study of which 155 were male (87.6%) and 22 were female (7.5%). The average age was 51.8 ± 5.7 (Mean \pm SD). The average cumulative duration of heroin use was 261.4 ± 82.6 months (Mean \pm SD) and the cumulative duration of MMT was 100.9 ± 60.7 months (Mean \pm SD). The average dose of current methadone treatment was 37.3 ± 22.1 mg (Mean \pm SD). There were 72 subjects (40.7%) had ever interrupted methadone treatment. The average BAI score, QOL-DA score and PSQI score were 7.1 ± 8.2 , 163.5 ± 21.4 and 6.0 ± 4.0 respectively.

The percentages of subjects clarified by BAI scale are presented in Fig. 1. For the measure of anxiety, 123(69.5%) subjects showed minimal level of anxiety (score 0–9), 37(20.9%) subjects showed mild anxiety (score 10–18), 14(7.9%) subjects showed moderate anxiety (score 19–29), 3(1.7%) subjects showed severe anxiety (score 30–63), for a total of 30.5% subjects had varying degrees of anxiety.

Comparison between anxiety group and non-anxiety group

Subjects were divided into two groups according to BAI score: anxiety group (score 10–63) and non-anxiety group (score 0–9)^{20,21}. 54 subjects (30.5%) were divided into anxiety group and 123 subjects (69.5%) were divided into non-anxiety group. The characteristics of the anxiety group and non-anxiety group were compared.

The comparison results of various characteristics between anxiety group and non-anxiety group are shown in Table 2. There was no statistical difference in gender, age, marital status, living situation, drinking status, smoking status, cumulative duration of heroin use and cumulative duration of treatment between anxiety group and non-anxiety group. Meanwhile, those suffered from anxiety were currently treated at lower doses (19.2 ± 2.6 mg) compared to those did not suffer from anxiety (22.9 ± 2.6 mg) ($p < 0.05$). The proportion of those had ever interrupted treatment in anxiety group (55.6%) is higher than that in non-anxiety group (34.1%) ($p < 0.01$).

Correlation between different factors and BAI score

In order to explore the influence of different factors on anxiety, this study analyzes the correlation between different factors and BAI score.

Bivariate correlation analysis (Table 3) showed that the BAI score was negatively correlated with age, smoking status, QOL-DA score and PSQI score, while it was positively correlated with other factors (such as cumulative duration of heroin use, cumulative duration of MMT, MMT interruption, etc.). Among all the factors, the correlation between MMT interruption, QOL-DA score, PSQI score and BAI score were statistically significant ($p < 0.05$), and the correlation coefficients are 0.17, -0.80 and 0.50 respectively. From the above results, it can be concluded that the lower QOL-DA score that subjects got, the higher BAI score they got. In other word, the worse life quality the subjects had, the more severe anxiety they suffered from. Similarly, the higher PSQI score that subjects got, the higher BAI score they got, which means that subjects who have the worse sleep quality suffered from the more serious anxiety. To further explore the impact of life quality and sleep quality on anxiety in MMT users, the score of the four scales (physiology score, psychology score, society score and symptoms score) of QOL-DA, PSQI score and BAI score were put into multiple linear regression model. The result (Table 4) showed that the BAI score was significantly positively correlated with PSQI score ($B = 0.23$), and was significantly negatively correlated with physiology score ($B = -0.13$), psychology score ($B = -0.56$) and symptoms score ($B = -0.29$). Society score ($B = -0.04$) also had a positive correlation with BAI score, but t-test result showed that p-value > 0.05 . This result is consistent with the results of correlation analysis. It is worth noting that psychology score had the greatest influence on BAI score, and its regression coefficient is -0.56.

Discussion

In present study, we found that the prevalence of anxiety among MMT users was 30.5%. We also found that the dosage of methadone in anxiety group was lower than that in non-anxiety group. Compared with the non-anxiety group, the anxiety group had a higher methadone treatment interruption rate. We also found that good life quality and good sleep quality have positive effects on reducing the risk of anxiety.

We found that 30.5% MMT patients suffer from anxiety. The prevalence rate was lower than that shown by previous study conducted in Australia (67.7%)¹¹, but it was similar to that of another two studies conducted in China (23.0% and 33.6% respectively)^{12,13}. The discrepancy may due to the cumulative duration of methadone treatment of participants in studies. In a Chinese study¹², it was found that the longer the maintenance treatment lasted, the lower the prevalence of anxiety disorders among participants. The methadone treatment time for Australian participants is merely 1 week to 6 months, which is shorter than that in our study. Therefore, it is possible that the duration of methadone maintenance treatment may be a crucial factor affecting the prevalence of anxiety among MMT users. Most of the subjects in this study were accepted in the MMT program more than 12 months and were in stable stage, so the duration of treatment hadn't showed the obvious influence on anxiety. The influence of the MMT treatment duration on anxiety remains to be further explored.

The methadone therapeutic dose in anxiety group was lower than that in non-anxiety group. This indicates that low therapeutic dose increases the risk of anxiety symptoms. That was consistent with the result of a previous survey conducted in China¹⁰. Higher dose of methadone could reduce heroin craving, inhibit heroin's euphoric effect, prevent withdrawal symptoms and stabilize the behavior of drug addicts. Moreover, the higher dose of methadone is also related to the MMT retention rate increase and the improvement in treatment effectiveness²⁵⁻²⁸. Several studies had suggested that MMT users with mental problems or disorders might need higher therapeutic dose of methadone to get better treatment benefits^{25,26}.

The overall life quality of the subjects in anxiety group was worse than that of the subjects in non-anxiety group. This result was in line with a previous study which showed that psychiatric problems were associated with lower quality of life²⁹. The results of correlation analysis also showed that the improvement of life quality has a positive effect on reducing the risk of anxiety. This result is consistent with the results of previous studies suggesting that there is a certain correlation between quality of life and emotional problems of MMT users³⁰⁻³³. The evaluation of life quality in this study was composed of four dimensions: physical condition, psychological state, social function and withdrawal symptoms. This makes the evaluation more comprehensive. Similar to the results of previous studies, MMT users' good physical condition, good psychological state, sufficient social support and less withdrawal symptoms had positive effects on reducing the risk of anxiety^{29,31,33}. Good physical condition and less withdrawal symptoms mean that MMT users will bear less burden caused by physical problems, while good psychological state and good social function mean that MMT users will bear less psychological burden. Therefore, as suggested by previous studies, improving MMT users' quality of life by improving

their physical condition, psychological state, social function and reducing their withdrawal symptoms is an effective way to reduce the risk of anxiety^{29,31,34}.

The sleep quality of the subjects in anxiety group was worse than that of the subject in non-anxiety group. Moreover, correlation analysis results showed that poor sleep quality was positively correlated with anxiety severity, which is consistent with previous studies^{31,33,35-39}. Good sleep provides MMT users with opportunities to get adequate physical and mental rehabilitation. A previous study showed that sleep (especially NREM) can calm the anxious brain and restore the prefrontal cortex's ability to regulate emotions which preventing anxiety from worsening¹⁹. It suggests that improving the sleep quality of MMT users has a positive significance for reducing the risk of anxiety in MMT users.

In order to comprehensively evaluate the impact of life quality and sleep quality on anxiety of MMT users, we put the score of four dimensions of QOL-DA, PSQI score and BAI score into a multiple linear regression model for further analysis. Multiple linear regression model showed that the psychological dimension of QOL-DA had the greatest influence on BAI score. In other words, the factors related to the psychological state of MMT users would affect the life quality of MMT users and thus increase the risk of anxiety. Therefore, psychological intervention seems to be the key breakthrough. However, the majority of methadone treatment clinics and treatment centers in China only provide methadone medication and medication-related counseling for MMT users, and a fraction of treatment centers had social workers in order to assist doctors. Psychological counseling and psychotherapy services are seldom parts of methadone maintenance treatment services in China^{34,40}. The unmet mental health needs among MMT patients is a key factor affecting anxiety. Therefore, improving the current situation of limited psychological service resources in China and providing psychological intervention services (including psychological counseling, psychotherapy, social-family support) for MMT patients are conducive to reducing the risk of anxiety disorder. This is also advocated by relevant research^{34,41}.

Limitation

This study is a cross-section study, without dynamic observation of the influencing factors. In addition, this study only divided the anxiety group and non-anxiety group among MMT users for comparison, did not set a blank control group.

Conclusions

The prevalence of anxiety was common in MMT patients. Interruption of treatment, quality of life and sleep quality are key factors affecting anxiety condition of MMT patients. These are the key points need to be concerned to improve the quality of MMT services.

Abbreviations

MMT☒Methadone Maintenance Treatment

BAI Beck Anxiety Inventory

QOL-DA Quality of Life-Drug Addiction

PSQI Pittsburgh Sleep Quality Index

AIDS: Acquired Immune Deficiency Syndrome

HIV: Human Immunodeficiency Virus

Declarations

Ethics approval and consent to participate

IRB, Guangzhou Huiai Hospital approved this study.

Consent for publication

All participants signed informed consent.

Availability of data and materials

In order to protect the confidentiality and anonymity of participants, the data (transcripts) will not be shared.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

PC conceived and designed the study. PC, ZZ, JZ, SX, XF gathered the data. PC analyzed the data and wrote initial draft of paper. NF revised paper. All authors read and approved the final manuscript.

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Tables

Table 1
Characteristics of MMT users

	MMT users (N = 177)
Gender(males/females)	155(87.6%)/22(12.4%)
Age	51.8 ± 5.7
Years of education	
≤ 9	131(74.0%)
10–12	44(24.9%)
≥ 13	2(1.1%)
Marital status(single/married)	98(55.4%)/79(44.6%)
Living situation (alone/with partners)	57(32.2%)/120(67.8%)
Drinking status (yes/no)	58(32.8%)/119(67.2%)
Smoking status(yes/no)	174(98.3%)/3(1.7%)
Cumulative duration of heroin use(month)	261.4 ± 82.6
Cumulative duration of MMT(month)	100.9 ± 60.7
Current methadone therapeutic dose(mg)	37.3 ± 22.1
MMT Interruption (yes/no)	72(40.7%)/105(59.3%)
BAI score	7.1 ± 8.2
QOL-DA total score	163.5 ± 21.4
Physiology Score	33.3 ± 6.5
Psychology Score	39.6 ± 6.8
Society Score	39.2 ± 6.9
Symptoms Score	48.3 ± 7.2
PSQI total score	6.0 ± 4.0
Data are the amount of cases (percentage). Data about age, cumulative duration of heroin use, cumulative duration of MMT, current methadone dose, QOL-DA score and PSQI score are the mean ± standard deviation.	

Table 2
The comparison between anxiety group and non-anxiety group

	Anxiety group (n = 54)	Non-anxiety group (n = 123)	p-value
Gender(males/females)	45(83.3%)/9(16.7%)	110(89.4%)/13(10.6%)	0.26
Age	51.0 ± 5.1	52.2 ± 5.9	0.20
Years of education			
≤ 9	40(74.1%)	91(74.0%)	0.63
10–12	14(25.9%)	30(24.4%)	
≥ 13	-	2(1.6%)	
Marital status(single/married)	30(55.6%)/24(44.4%)	68(55.3%)/55(44.7%)	0.97
Living situation (alone/with partners)	21(38.9%)/33(61.1%)	36(29.3%)/87(70.7%)	0.23
Drinking status (yes/no)	16(29.6%)/38(70.4%)	42(34.1%)/81(65.9%)	0.56
Smoking status(yes/no)	54(100.0%)/-	120(97.6%)/3(2.7%)	0.25
Cumulative duration of heroin use(month)	253.9 ± 76.3	264.7 ± 85.3	0.43
Cumulative duration of MMT(month)	113.4 ± 53.1	95.4 ± 63.4	0.07
Current methadone therapeutic dose(mg)	19.2 ± 2.6	22.9 ± 2.6	0.03*
MMT Interruption (yes/no)	30(55.6%)/24(44.4%)	42(34.1%)/81(65.9%)	0.008**
QOL-DA total score	143.13 ± 22.3	172.46 ± 13.52	<0.01**
PSQI total score	8.74 ± 4.17	4.84 ± 3.38	<0.01**
Data are the amount of cases (percentage). Data about age, cumulative duration of heroin use, cumulative duration of MMT, current methadone dose, QOL-DA score and PSQI score are the mean ± standard deviation.			
T-test (for data with normal distribution), Chi-square test and Fisher's exact test were used to detect the differences of variables between two durations of anxiety: no anxiety and anxiety			
* p<0.05			
**p<0.01			

Table 3
The correlation between different factors and BAI score

	BAI Score
Gender	0.12
Age &	-0.11
Years of education	0.02
Marital status	0.01
Living situation	0.09
Drinking status	0.03
Smoking status	-0.16
Cumulative duration of heroin use(month)&	0.01
Cumulative duration of MMT(month) &	0.06
Current methadone therapeutic dose &	0.08
Change of methadone therapeutic dose	0.04
MMT Interruption	0.17*
QOL-DA Score&	-0.80**
Physiology Score &	-0.69**
Psychology Score &	-0.79**
Society Score &	-0.60**
Symptoms Score &	-0.72**
PSQI Score&	0.50**
Values listed in the table were R ² for Spearman correlation. Physiology, psychology, society and symptoms are four scales of QOL-DA.	
& R ² for Pearson correlation	
* p<0.05	
**p<0.01	

Table 4
Multiple linear regression analysis

	B	Std. Error	95%CI	t	p-value
Physiology Score	-0.13	0.13	-0.40, 0.13	-0.98	0.03*
Psychology Score	-0.56	0.16	-0.86, -0.25	-3.57	<0.01**
Society Score	-0.04	0.08	-0.20, 0.11	-0.56	0.57
Symptoms Score	-0.29	0.12	-0.52, -0.05	-2.43	0.02*
PSQI Score	0.23	0.10	0.03, 0.44	2.22	0.03*
* p \leq 0.05					
**p \leq 0.01					

Figures

The percentage of different levels of anxiety

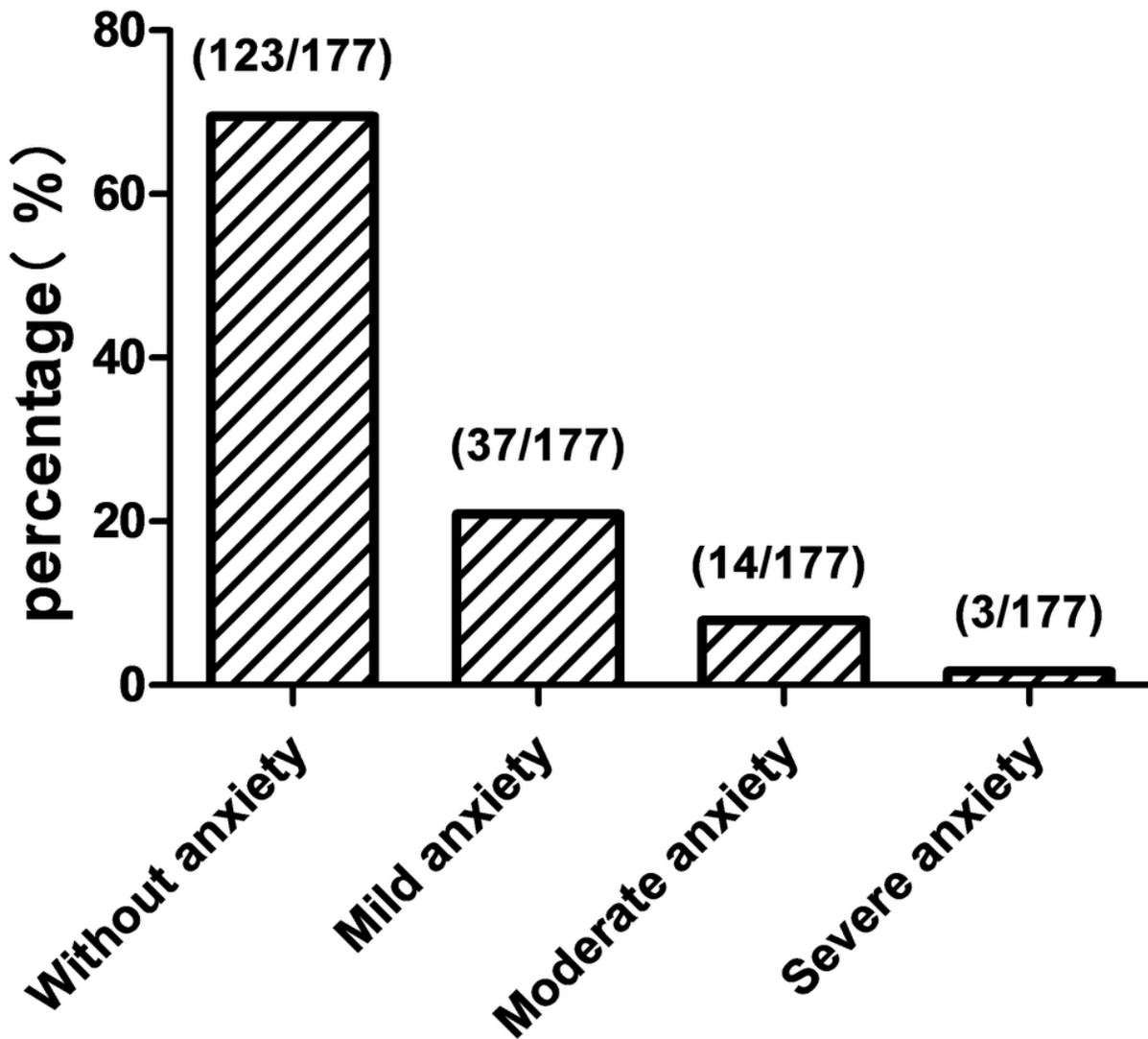


Figure 1

MMT users' evaluation by BAI. The percentages of subjects clarified by the cutoffs on BAI.