

Alcohol Drinking in Chinese Methadone-maintained Clients: A Self-medication for Depression and Anxiety?

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Objectives: Unhealthy alcohol use is associated with negative health outcomes in clients attending methadone maintenance therapy (MMT) programs. However, debates exist regarding the methadone dose of drinkers, and little is known about the health outcomes of drinkers with other types of alcohol use. This study examined the drinking pattern and its association with methadone dose, and depressive and anxiety symptoms in Chinese clients undergoing MMT.

Methods: A secondary data analysis was conducted with data from a large-scale cross-sectional survey of 549 clients of 3 MMT clinics in Wuhan, China. Depression, anxiety, and alcohol dependence were measured with Zung Self-rating Depression Scale, Zung Self-rating Anxiety Scale, and Alcohol Dependence Scale, respectively. Drinking pattern was assessed using 3 indicators: weekly amount of alcohol consumed, weekly frequency of alcohol consumed, and severity of alcohol dependence.

Results: The prevalence of current drinking, hazardous drinking, regular drinking, and alcohol abuse/dependence was 29.0%, 10.4%,

14.2%, and 8.7%, respectively. In adjustment analyses, relative to nondrinkers, drinkers had significantly lower weight-based methadone dose ($\beta = -0.136$, $P = 0.008$); hazardous drinkers, irregular drinkers, and drinkers without alcohol abuse/dependence had less severe depression ($\beta = -3.67$, $P = 0.004$; $\beta = -2.37$, $P = 0.034$; $\beta = -3.20$, $P = 0.001$) and anxiety ($\beta = -4.90$, $P < 0.001$; $\beta = -3.24$, $P = 0.006$; $\beta = -4.52$, $P < 0.001$), but drinkers with alcohol abuse/dependence had more severe depression ($\beta = 5.55$, $P < 0.001$) and anxiety ($\beta = 4.31$, $P = 0.005$).

Conclusion: In Chinese MMT clinics, drinkers may use alcohol to compensate for inadequate MMT and self-medicate negative emotions. Compared with nondrinkers, the severities of depression and anxiety were lower among drinkers without alcohol abuse/dependence, but higher among those with alcohol abuse/dependence.

Key Words: alcohol use, anxiety, depression, methadone maintenance treatment, self-medication

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Alcohol consumption is a common clinical phenomenon in clients of methadone maintenance therapy (MMT) clinics across countries (Ottomanelli, 1999; Soyka, 2015; Nolan et al., 2016). Empirical studies have shown that approximately one-third of the methadone-maintained clients have some forms of alcohol use disorders according to study-defined criteria, including excessive drinking, hazardous drinking, heavy alcohol use, risky alcohol use, and alcohol abuse/dependence (el-Bassel et al., 1993; Rittmannsberger et al., 2000; Nyamathi et al., 2009; Rengade et al., 2009; Ryder et al., 2009; Chen et al., 2011). Unhealthy alcohol use has been reported to be a significant risk factor for non-adherence to MMT, increased risk of death due to overdose, difficulties in integrating into normal social life, criminal activities, relapse to illicit drugs, and physical and mental morbidity (el-Bassel et al., 1993; Ottomanelli, 1999; Rengade et al., 2009; Kreek et al., 2010; Soyka, 2015; Nolan et al., 2016). Despite extensive international studies in this area, however, the underlying causes of alcohol drinking in patients undergoing MMT remain under debate. For example, it remains unclear that whether drinking is a result of MMT and whether alcohol-drinking clients request higher doses of methadone (Ottomanelli, 1999; Srivastava et al., 2008; Soyka, 2015).

China has the world's largest single MMT program, which has been available in nearly all provinces of China until

now and is currently providing services to over 160 thousand persons with opioid (mainly heroin) use disorders (Sullivan et al., 2015; Zhong et al., 2018). Although China's MMT program has substantially reduced heroin use, criminal behaviors, and heroin-related morbidity and mortality, it still has many challenges with poor adherence to MMT being a major one (Zhou and Zhuang, 2014; Sun et al., 2015). Due to the lack of training in addiction treatment and inappropriate concern for possible fatal overdose, Chinese service providers in MMT clinics (most of them are general practitioners and nurses) often prescribe a lower dosage of methadone compared with that in western countries (Lin and Detels, 2011). For example, survey data from several major Chinese cities indicate that the average doses of methadone in MMT clinics of Guangdong province and Ningbo municipality are as low as 46.1 and 37.0 mg/d, and high-dose methadone (≥ 60 mg/d) patients only account for 41.5% and 34.9% of the clients in MMT clinics of Chengdu and Guiyang municipalities, respectively (Chen et al., 2010; Xie et al., 2011; Fan et al., 2015; Leng et al., 2017). Because of the low rates of high-dose methadone across MMT clinics, the low dosage of methadone has been recognized as a strong risk factor for increased mortality and the early dropout from MMT in China (Bao et al., 2009; Liao et al., 2013; Zhou and Zhuang, 2014; Shen et al., 2016; Zhou et al., 2017). Further, there is also evidence that HIV-infected and HIV/hepatitis C virus-coinfected patients under opiate replacement treatment require higher methadone dose and HIV-positive MMT patients receiving lower doses of methadone are less likely to adhere to antiretroviral therapy (Lappalainen et al., 2015; Roncero et al., 2017).

In the general population, alcohol can serve a variety of functions, including ameliorating physical discomfort and negative emotions, and enhancing positive mood or well being (Kuntsche et al., 2005; Sayette, 2017). In the case of MMT clients, because these patients are still suffering from many health problems such as physical pain, depression, and anxiety (Yin et al., 2015; Yang et al., 2017), we speculate that MMT clients would be more likely to drink alcohol to self-medicate their negative emotions. This hypothesis is particularly suitable for Chinese clients receiving a low-dose MMT, due to the higher risk of uncontrolled negative emotions resulted from inadequate MMT.

Most previous studies found no significant difference in methadone doses between patients with and without unhealthy alcohol use (Rengade et al., 2009; Ryder et al., 2009; Chen et al., 2011). Nevertheless, there have been some preliminary findings showing a borderline trend towards higher methadone doses or greater increase in methadone doses in clients without than with alcohol use ($P = 0.085$ and $P = 0.05$) (Bickel and Amass, 1993; el-Bassel et al., 1993). A recently published study with a large sample of 2121 MMT participants in southwest China has reported that a low methadone dose (31–60 mg/d) was a significant predictor of heavier drinking (Duan et al., 2017). Because the majority of earlier studies employed relatively small samples of MMT clients (< 200), they may have limited statistical power to detect the significant methadone dosage difference between drinkers and nondrinkers. Importantly, there is evidence that

body weight is an important determinant of methadone dose (Mouly et al., 2015), but none of the existing studies control for weight when comparing methadone dosage between alcohol-using and nonalcohol-using patients (Bickel and Amass, 1993; el-Bassel et al., 1993; Rengade et al., 2009; Ryder et al., 2009; Chen et al., 2011), possibly resulting in false-negative results.

Alcohol use can be defined as a spectrum, including nondrinking, light drinking, moderate drinking, heavy drinking, abuse, and dependence (Reid et al., 1999; Rittmannsberger et al., 2000). Although significantly more depressive and anxiety symptoms in patients with than without unhealthy alcohol use and more depressive symptoms in heavy than moderate drinkers in MMT settings have been reported by 2 prior studies (el-Bassel et al., 1993; Nyamathi et al., 2012), little is known about the relationship between depression and anxiety, and other drinking types such as moderate drinking (relative to nondrinking). Findings from general population-based studies have shown that the association between depression and other psychological symptoms and drinking varied by the type of alcohol use (Graham et al., 2007; Coulson et al., 2014; Martinez et al., 2015; Salonsalmi et al., 2017). For example, Coulson et al. reported a U-shaped relationship between alcohol consumption and depression: significantly higher risk of depression in both nondrinkers and those consuming ≥ 3 standard drinks/d as compared with those consuming ≤ 2 standard drinks/d (Coulson et al., 2014). We therefore presume that the severity of depressive and anxiety symptoms of MMT clients would also vary depending on the drinking pattern.

The phenomena of drinking in MMT clients received little research attention in China. As far as we know, only one study by Duan et al. examined the characteristics of alcohol drinking of Chinese MMT clients (Duan et al., 2017). This study demonstrated a 16.6% prevalence of hazardous drinking, and several sociodemographic and clinical correlates of hazardous drinking, but did not provide data on the relationship between drinking pattern and mental health outcomes. To deepen our understanding on the alcohol use of MMT patients, the present study was set out to determine the drinking pattern and its association with methadone dose, and depressive and anxiety symptoms in Chinese clients undergoing MMT.

METHODS

Data Source and Sample

Between June, 2009 and July, 2010, we conducted a large-scale cross-sectional survey in 3 MMT clinics in Wuhan—a large metropolis with over 10 million people in central-southern China (Xu et al., 2017; Yang et al., 2017; Zhong et al., 2018). This study was a secondary data analysis based on data from it. By using cluster sampling, the study finally obtained a sample of 603 patients who were 20 years old or older, were undergoing MMT at the 3 clinics, and met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria for a life-time heroin dependence. The study collected a variety of variables and health outcomes, including sociodemographics, clinical characteristics,

self-destructive behaviors, sexual life satisfaction, and poor mental health indicators. Data were collected by self-report questionnaires, supplemented by a medical record review and face-to-face interview (when necessary). The current analysis focused on a subsample of 549 patients who had undergone MMT for at least 6 months, because the methadone dose has generally been stabilized after this treatment duration. Details of this study can be found elsewhere (Xu et al., 2017; Yang et al., 2017; Zhong et al., 2018).

Before the survey, the study protocol was approved by the Ethical Review Board of Wuhan Mental Health Center. All subjects voluntarily participated in the study and provided written informed consent.

Measures

Depression and Anxiety

We used the validated Chinese Zung Self-rating Depression Scale (SDS) and Zung Self-rating Anxiety Scale (SAS) to evaluate depressive and anxiety symptoms, respectively (Wang et al., 1999). Both scales have 20 items, and all items are rated on a 4-point scale (1 = a little of the time to 4 = most of the time). Total scores of the 2 scales vary between 20 and 80, with higher total scores denoting more severe depressive and anxiety symptoms.

Weight-based Methadone Dose

Daily methadone dose and body weight at the time of the survey were obtained from medical records. Weight-based methadone dose (WMD) was calculated by dividing the prescribed methadone dose by the body weight (mg/kg/d).

Alcohol Use

Patients were asked: “Did you drink at least once per month over the past six months?” Those who drank monthly in the past 6 months (current drinkers) were further asked to report types of alcoholic beverage (beer, wine, and white spirit), weekly frequency of drinking (<1, 1–2, 3–4, and ≥ 5 days), and quantity of alcohol drunk (expressed as the number of cans [250–350 mL] or bottles [330–600 mL] of beers, and the number of Chinese “*Liang*” [50 mL] for wines and white spirit) on a typical day of the last month.

Weekly amount of alcohol consumption in grams of pure alcohol was calculated based on types of alcoholic beverage, quantity of alcohol drunk, and weekly frequency of drinking, with the standard ethanol content being 4% for beer, 12% for wine, 38% for weak white spirits, and 53% for strong white spirits (Millwood et al., 2013). Hazardous drinking referred to a weekly amount of alcohol consumed that exceeded 196 g for men and 98 g for women, according to the threshold values recommended by the US National Institute on Alcohol Abuse and Alcoholism (Reid et al., 1999). Alcohol consumption at levels lower than threshold values for hazardous drinking was defined as moderate drinking.

Frequency of drinking was divided into 2 categories: irregular (≤ 4 days per week) and regular (≥ 5 days per week) (Lim et al., 2007).

Severity of alcohol dependence was assessed with the validated Chinese Alcohol Dependence Scale (ADS) (Skinner

and Allen, 1982; Zhang, 2005). ADS is a 25-item self-rating scale, with 6 items being scored on a 2-point scale (0 and 1), 16 on a 3-point scale (0, 1, and 2), and 3 on a 4-point scale (0, 1, 2, and 3). The total ADS score ranges between 0 and 47, with a higher score representing the greater severity of dependence. A score of 9 or higher was used to indicate a current diagnosis of alcohol abuse/dependence (Zhang, 2005).

It should be noted that quite a few MMT entrants were referred patients from compulsory detoxification centers, and they were not allowed to drink alcohol in the compulsory detoxification settings before MMT. Therefore, the commonly used timeframe for defining alcohol use, “12-month” (Xu et al., 2014), was not feasible for some patients who received MMT for less than 1 year. After the pilot study, we decided to use the 6-month timeframe to define alcohol use. Due to the same reason, the 12-month timeframe of ADS was replaced with 6 months in our study.

Covariates

Sociodemographic variables collected in this study included sex, age, education, marital status, employment status, and self-rated financial status (poor, fair, and good).

Clinical factors were main route of past heroin use, length of heroin use, duration of MMT, and antisocial personality disorders (APDs). To ascertain the presence of a lifetime diagnosis of APD, patients were administered the APD module of the Chinese Mini-International Neuropsychiatric Interview (MINI) (Si et al., 2009) by our trained investigators.

Statistical Analysis

Sociodemographic and clinical characteristics of patients with and without current drinking were described and compared by *t* test or chi-square test, as appropriate. Multivariable linear regression analysis that entered SDS/SAS total score as the outcome variable, sociodemographic and clinical factors as control variables, and drinking pattern as the only predictor (current drinking status, amount of alcohol consumed, frequency of drinking, and severity of alcohol dependence; nondrinking as the reference category for all comparisons), was used to analyze the independent association of drinking with depressive/anxiety symptoms. The independent relationship between current drinking and WMD was examined in the same manner. All analyses were performed with SPSS, version 16.0. The statistical significance level was set at $P < 0.05$ (2-sided).

RESULTS

The mean age of the 549 clients was 38.2 years (standard deviation [SD] 6.9, range 22–59), and 372 (67.8%) were males. The average durations of past heroin use and MMT were 10.0 years (SD: 4.0) and 25.2 months (SD: 10.4), respectively. The average methadone dose and WMD were 70.4 mg/d (SD 29.2) and 1.2 mg/kg/d (SD 0.5), respectively. In all, 210 (38.3%) patients were diagnosed with APD.

In all, 159 patients (29.0%) reported current drinking. Numbers of moderate, hazardous, irregular, and regular drinkers were 102 (18.6%), 57 (10.4%), 81 (14.8%), and 78 (14.2%), respectively. A total of 48 current drinkers (8.7%) were screened as having alcohol abuse/dependence

TABLE 1. Sociodemographic and Clinical Characteristics of Methadone-maintained Clients With and Without Current Drinking

Characteristics	Nondrinkers (n = 390)	Drinkers (n = 159)	Statistics	
	n (%)	n (%)	χ^2	P
Male sex	234 (60.0)	138 (86.8)	37.114	<0.001
Marital status of “married”	171 (43.8)	99 (63.2)	15.421	<0.001
Employed	192 (49.2)	97 (61.0)	5.841	0.016
Self-rated financial status: good	83 (21.3)	52 (32.7)	14.52	0.001
A history of heroin injection	329 (84.6)	132 (83.0)	0.154	0.695
Antisocial personality disorder	129 (33.1)	81 (50.9)	15.265	<0.001
	Mean ± SD	Mean ± SD	t	P
Age (yrs)	37.7 ± 6.5	39.4 ± 7.8	2.602	0.010
Education years	9.5 ± 2.7	9.3 ± 2.3	1.058	0.291
Duration of past heroin use (yrs)	9.6 ± 4.0	10.8 ± 3.8	3.005	0.003
Duration of MMT (mos)	24.7 ± 10.3	26.5 ± 10.4	1.842	0.066
Methadone dose (mg/d)	71.9 ± 29.6	66.6 ± 28.1	1.931	0.054
Weight-based methadone dose (mg/kg/d)	1.2 ± 0.5	1.0 ± 0.5	4.251	<0.001
Zung Self-rating Depression Scale	38.7 ± 8.2	38.3 ± 9.1	0.908	0.364
Zung Self-rating Anxiety Scale	45.8 ± 9.8	43.3 ± 9.2	3.211	0.001

according to ADS. The median amount of alcohol consumption per week was 94.7 g, ranging from 5 to 1184.

Table 1 shows characteristics of nondrinkers and drinkers. Compared with nondrinkers, drinkers were more likely to be men, older, married, and employed, and rate their financial status as “good,” have a longer duration of past heroin use, and suffer from APD ($P \leq 0.016$). There was a marginally significant trend for the lower methadone dose in drinkers than nondrinkers ($P = 0.054$); interestingly, when weight was considered, a significantly lower WMD in drinkers than nondrinkers was detected ($P < 0.001$). In this univariate analysis, drinkers and nondrinkers differed significantly in terms of anxiety ($P = 0.001$), but not depression ($P = 0.364$).

Table 2 displays the results of comparisons between subgroups according to the drinking pattern. Compared with nondrinkers, hazardous drinkers, regular drinkers, and drinkers without and with alcohol abuse/dependence, all had significantly lower WMDs; hazardous drinkers and drinkers without alcohol abuse/dependence had significantly less severe depressive symptoms, but drinkers with alcohol abuse/dependence had significantly more severe depressive symptoms; hazardous drinkers, irregular drinkers, regular drinkers, and drinkers without alcohol abuse/dependence all had significantly less severe anxiety symptoms, but drinkers with alcohol abuse/dependence had significantly more severe anxiety symptoms ($P < 0.05$).

After adjusting for sociodemographic and clinical covariates, relative to nondrinking, current drinking was still significantly associated with less severe anxiety symptoms (unstandardized coefficient [β] = -2.104 , $P = 0.012$) and lower WMD ($\beta = -0.126$, $P = 0.008$); hazardous drinking, irregular drinking, and drinking without alcohol abuse/dependence were all significantly associated with less severe depressive ($\beta = -3.665$, $P = 0.004$; $\beta = -2.365$, $P = 0.034$; $\beta = -3.197$, $P = 0.001$) and anxiety ($\beta = -4.897$, $P < 0.001$; $\beta = -3.243$, $P = 0.006$; $\beta = -4.517$, $P < 0.001$) symptoms,

but drinking with alcohol abuse/dependence was significantly associated with more severe depressive ($\beta = 5.546$, $P < 0.001$) and anxiety ($\beta = 4.305$, $P = 0.005$) symptoms (Table 3).

DISCUSSION

To the best of our knowledge, this is the first large-scale study examining the drinking pattern and its association with methadone dose, and depressive and anxiety symptoms in Chinese MMT clients. The main findings of this study were as follows:

1. Nearly one-third of the Chinese MMT patients drank alcohol, and the rates of hazardous drinking, regular drinking, and alcohol abuse/dependence were 10.4%, 14.2%, and 8.7%, respectively
2. By using WMD, we were able to find the significantly lower methadone doses in drinkers than nondrinkers. Results of multiple analyses according to drinking pattern further showed that, compared with nondrinkers, the significantly lower WMDs was seen in hazardous drinkers, irregular drinkers, and drinkers without and with alcohol abuse/dependence, and marginally significantly lower WMDs were also observed in moderate and regular drinkers ($P = 0.093$ and $P = 0.090$).
3. Very interestingly, corresponding to the significantly lower WMDs in hazardous drinkers, irregular drinkers, and drinkers without and with alcohol abuse/dependence, we found the significant negative associations of depressive and anxiety symptoms with hazardous drinking, irregular drinking, and drinking without alcohol abuse/dependence, despite an unexpected positive association between depressive and anxiety symptoms and alcohol abuse/dependence.

Existing research focused on pathological drinking but seldom studied the spectrum of alcohol use in MMT patients (Ottomanelli, 1999; Soyka, 2015; Nolan et al., 2016). These

TABLE 2. Comparisons Between Drinkers With Different Types of Alcohol Use and Nondrinkers in Chinese Methadone Maintenance Treatment Clinics

Indicators	Amount of Alcohol Consumption			Frequency of Alcohol Consumption			Severity of Alcohol Dependence		Results of Multiple Comparisons*
	① Nondrinkers (n = 390)	② Moderate Drinkers (n = 102)	③ Hazardous Drinkers (n = 57)	④ Irregular Drinkers (n = 81)	⑤ Regular Drinkers (n = 78)	⑥ Without Alcohol Abuse/Dependence (n = 111)	⑦ With Alcohol Abuse/Dependence (n = 48)		
Weight-based methadone dose (mg/d/kg)	1.2 ± 0.5	1.1 ± 0.6	1.0 ± 0.3	1.1 ± 0.6	1.0 ± 0.4	1.1 ± 0.4	1.0 ± 0.6	③ < ①; ⑤ < ①; ⑦ < ①, ⑥ < ①	
Depressive symptoms	38.7 ± 8.2	39.3 ± 10.1	35.7 ± 6.1	38.8 ± 10.6	37.3 ± 6.9	35.4 ± 6.5	44.6 ± 11.0	③ < ②, ③ < ①; ⑦ > ①, ⑦ > ⑥, ⑥ < ①	
Anxiety symptoms	45.8 ± 9.8	43.9 ± 10.4	40.6 ± 5.8	42.7 ± 10.1	42.9 ± 8.2	40.3 ± 7.6	48.8 ± 10.1	③ < ②, ③ < ①; ④ < ①, ⑤ < ①; ⑦ > ①, ⑦ > ⑥, ⑥ < ①	

*Fisher least significant difference (LSD) test, *P* < 0.05.

studies defined unhealthy alcohol use with a variety of ways, and their rate estimates varied widely: those with a cut-off value on the Alcohol Use Disorder Test or Michigan Alcohol Screening Test reported a prevalence of 20.9% to 35% (el-Bassel et al., 1993; Rengade et al., 2009; Ryder et al., 2009; Chen et al., 2011) and those with a threshold value on the amount or frequency of alcohol consumption reported a prevalence of 49.5% to 52% (Rittmannsberger et al., 2000; Nyamathi et al., 2009). Compared with these prevalence estimates, our study reported a lower prevalence of unhealthy alcohol use, in terms of all types of pathological drinking: hazardous drinking, regular drinking, and alcohol abuse/dependence. A similarly lower prevalence of hazardous drinking (16.6%) was also reported in the aforementioned Chinese study with a sample of MMT patients from southwest China (Duan et al., 2017). Hence, it seems that the Chinese MMT clients have lower prevalence of unhealthy alcohol use than western clients. This difference may be related to China's unique drug treatment policy (Yang et al., 2014), as we mentioned above, before MMT, many patients were treated in compulsory detoxification centers where they had little chance to drink; it is possible that many of them would no longer drink after entering MMT program. However, due to heterogeneity in the definition of alcohol use, timeframe for the assessment of drinking pattern, threshold values for excessive drinking, and instrument for the screening of alcohol abuse/dependence across studies, it is potentially problematic to directly compare our rates with those of previous studies.

There is convincing evidence that a low-to-moderate dose of methadone can suppress but not eliminate psychiatric symptoms, therefore a high-dose methadone is recommended for MMT clients; otherwise patients would seek other drugs such as alcohol to compensate for the inadequate MMT (Donny et al., 2002, Faggiano et al., 2003). Accordingly, the lower methadone dose in drinkers than nondrinkers was found in our study. Further, it seems that drinking alcohol works in reducing the negative emotions of MMT patients who were receiving a low dose of methadone, as partly evident by the overall negative association between current drinking and anxiety symptoms.

Psychopharmacological studies have found that both inhibitory and excitatory neurotransmitters can be affected by alcohol use. For example, it can cause the release of γ -aminobutyric acid (GABA), which acts primarily at the GABA_A receptors and generates sedative effects, resulting in the relief of anxiety (Olsen and Liang, 2017). Alcohol consumption also can stimulate the release of dopamine and β -endorphins, and increase serotonin activity, which generates euphoric and antidepressive effects, leading to the mitigation of depression (Faingold et al., 1998). Both mechanisms can explain the negative associations of depressive and anxiety symptoms with hazardous drinking, irregular drinking, and drinking without alcohol abuse/dependence.

The positive association of depressive and anxiety symptoms with drinking with alcohol abuse/dependence suggests that alcohol drinking may exacerbate the negative emotions of MMT patients who had been alcohol abused/dependent. Hence, drinking seems like a failed

TABLE 3. Independent Association Between Drinking Pattern and Weight-based Methadone Dose, and Depressive and Anxiety Symptoms, Controlling for Sociodemographic and Clinical Variables

Drinking Pattern	Weight-based Methadone Dose (mg/kg/d)		Depressive Symptoms		Anxiety Symptoms	
	Unstandardized Coefficients	P	Unstandardized Coefficients	P	Unstandardized Coefficients	P
Nondrinking (reference group)	1		1		1	
Drinking	-0.128	0.008	-0.739	0.396	-2.104	0.022
Moderate drinking	-0.096	0.093	0.746	0.448	-0.685	0.502
Hazardous drinking	-0.185	0.015	-3.665	0.004	-4.897	<0.001
Irregular drinking	-0.151	0.025	-2.365	0.034	-3.243	0.006
Regular drinking	-0.106	0.09	0.809	0.46	-1.023	0.376
Drinking without alcohol abuse/dependence	-0.110	0.049	-3.197	0.001	-4.517	<0.001
Drinking with alcohol abuse/dependence	-0.167	0.041	5.546	<0.001	4.305	0.005

attempt to self-medicate in MMT patients with alcohol abuse/dependence; this phenomenon is consistent with the elevated risk of comorbid depression and anxiety in patients with alcohol dependence (Gallagher et al., 2018). We consider that these patients also have the motivation to use alcohol to temporarily relieve or mask their negative feelings, but, because of the impaired emotion regulation associated with alcohol dependence (Petit et al., 2015), these patients exhibited higher level of depression and anxiety.

Much evidence has shown that the health consequence of alcohol drinking is influenced by its quantity and frequency, but the alcohol exposure–outcome relationship is not as simple as a linear relationship (Zakhari and Li, 2007; Coulson et al., 2014; Koloverou et al., 2015). In this study, we found that the beneficial effects of drinking on depressive and anxiety symptoms of MMT patients were limited to certain types of alcohol consumption. Unlike the commonly reported better mental health in moderate drinkers than nondrinkers or excessive drinkers (El-Guebaly, 2007), significantly less severe depressive and anxiety symptoms were found in hazardous drinkers in this study. Due to cross-tolerance induced by polydrug use, patients’ tolerance to alcohol would be higher than the general population. In this case, threshold values for defining excessive drinking of MMT patients would be higher than those of the general population; in other words, hazardous drinkers according to the threshold value of the general population in our study were not real hazardous drinkers (may be moderate drinkers of MMT patients). In addition, the effect of alcohol on methadone metabolism might depend on the frequency of alcohol intake, because experimental research has found the peak blood methadone concentration increases after short-term alcohol intake, but decreases after long-term alcohol intake (Nolan et al., 2016). Considering that irregular drinkers are more likely to drink alcohol intermittently, a way similar to short-term drinking, significantly less depressive and anxiety symptoms were presented in irregular drinkers.

Finally, although significant associations between some types of drinking and lower risk of depression and anxiety were found in this study, we do not intend to convey the impression or information that drinking is good for the mental health of MMT clients in certain situations. A prospective study has found that drinking to alleviate mood symptoms is a significant risk factor for the later development of alcohol

dependence (Crum et al., 2013). Because the interaction between alcohol and methadone would complicate MMT, even result in fatal overdose, treating physicians in MMT clinics should advise their patients not to drink alcohol or stop drinking. Based on our clinical experiences in MMT, Chinese healthcare providers in MMT clinics seldom assess patients’ alcohol drinking habit. So a potential clinical implication of findings from the present study is that Chinese healthcare providers should be aware of the potential influence of drinking on the efficacy of MMT and take alcohol drinking pattern into consideration when determining or adjusting the methadone dose of a patient.

This study has several limitations. First, data of this study were collected cross-sectionally, not prospectively, so it may be questionable to regard drinking as a result of inadequate MMT and as a treatment for negative emotions. For example, patients may be prescribed lower doses of methadone due to their less severe depressive and anxiety symptoms. However, the elevated levels of depressive and anxiety symptoms and decreased WMDs in drinkers with alcohol abuse/dependence do not support this possibility. Therefore, the possibility of drinking as a self-medication for inadequate MMT is high. Second, our assessments on drinking pattern do not include never drinking and former drinking. It remains unclear whether the lower risk of depression and anxiety in certain types of drinkers versus non-drinkers would still exist after excluding abstainers from non-drinkers. Third, polydrug use is common among MMT patients, but we did not collect data on concomitant use of benzodiazepines and other addictive drugs. Therefore, the possible confounding effects of co-use of addictive drugs on associations between drinking and methadone dose and negative emotions could not be excluded. Cautions are needed when interpreting our results. Fourth, due to limited research funding, we did not collect data on blood methadone concentration and blood alcohol concentration, which are exact measures of current methadone dose and amount of alcohol consumed, respectively. Finally, because this was a self-report questionnaire survey and patients are generally not allowed to drink when they are receiving MMT, MMT patients may have the tendency to respond drinking pattern questions in a way that is socially acceptable: the so-called “social desirability bias”. As a result of this, frequency and amount of alcohol consumed by MMT patients may be underreported in our study.

CONCLUSIONS

In summary, nearly 1 out of every 3 Chinese MMT patients drink alcohol, and approximately 1 out of every 10 suffer from unhealthy alcohol use, indicating that alcohol use is a common issue in Chinese MMT clinics and therefore deserves clinical attention. The significantly lower WMDs in drinkers than nondrinkers and the significant association of depressive and anxiety symptoms with drinking pattern suggest that, in Chinese MMT clinics, drinkers may use alcohol to compensate for inadequate MMT and self-medicate negative emotions. However, the associations between negative emotions and alcohol use vary by drinking patterns; in particular, compared with nondrinking, drinking without alcohol abuse/dependence is significantly associated with less severe depressive and anxiety symptoms, whereas drinking with alcohol abuse/dependence is significantly associated with more severe depressive and anxiety symptoms. Further large-scale prospective studies are warranted to confirm the effects of alcohol drinking on depression and anxiety of MMT patients.

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