ORIGINAL ARTICLES

The effectiveness of buprenorphine treatment for people with opioid use disorder in Vietnam

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ABSTRACT

Objectives: This study assesses the effectiveness of BMT using two outcomes: opioid use and treatment discontinuation over a 12-month period among people with opioid use disorder (OUD) in Vietnam.

Methods: We conducted a retrospective cohort study in Lai Chau, Dien Bien, and Son La provinces during 2019–2020. Information from 505 participants was included. The study assessed treatment effectiveness using two outcomes: opioid use and treatment discontinuation. Mixed-effects logistic and Cox regression models were used to identify risk factors for these outcomes.

Results: About 60% of participants in BMT and 34% in MMT reached recommended dosages. Receiving BMT or MMT was not related to opioid use during treatment (aOR=1.01, 95% CI: 0.83 – 1.23). Retention rate for MMT and BMT were 62.2% and 48.1% respectively. BMT increased the hazard of treatment discontinuation compared to MMT (aHR=1.88, 95% CI: 1.28-2.77, p-value 0.001).

Conclusion: BMT and MMT were both effective in reducing opioid use reducing opioid use among people with OUD in Vietnam. However, BMT was less capable of retaining participants in care, highlighting the need to address retention challenges in future OUD treatment strategies.

Keywords: *Buprenorphine treatment, opioid use disorder, treatment discontinuation, retention, effectiveness.*

INTRODUCTION

Opioid use disorder (OUD) is a widespread public health issue. It is estimated that 61.3 million people had used opioids in 2020, among them, 35.77 million resided in Asia (1). Maintainence treatment for OUD, notably with the full agonist methadone and the partial agonist buprenorphine, has been shown to be effective in reducing opioid use, lowering HIV transmission risks related to drug use, and decreasing criminal activity (2). Despite its proven effectiveness, access to OUD treatment remains limited in addressing the global opioid epidemic (2, 3).

Methadone has been approved for OUD maintenance treatment since 1974 and it is currently the most widely available medication for this treatment (2, 4). However, its daily supervised dosing requirement and logistical barriers pose significant challenges to accessibility (5). In constrast, buprenorphine, licensed for OUD maintenance treatment since 2000, offers a safer alternative to methadone with fewer drug interactions, making it suitable for patients with comorbidities (6). Its flexible dosing schedule and ability to be dispensed in office-based clinics or pharmacies address barriers like daily supervised dosing, expanding access to OUD treatment (7).

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In Vietnam, methadone maintenance treatment (MMT) has been implemented since 2008 as part of an HIV harm reduction strategy, but it faces challenges in increasing the number of patients and improve treatment adherence among their patients (8). Based on this rationale, BMT had been piloted for two years (2019–2020) in three mountainous provinces in Northern Vietnam (Lai Chau, Dien Bien, Son La). However, after the pilot, BMT was not scaled up for national implementation. This article assesses the opioid use outcomes and treatment discontinuation of BMT at 12 months, with the goal of providing evidence on the effectiveness of BMT as an alternative to MMT in remote areas. In this study, effectiveness is defined as reductions in opioid use and improved treatment retention compared to MMT, which are commonly used primary outcomes in evaluating medications for opioid use disorder (MOUD) (9).

METHODS

Study design: A retrospective cohort study. Data for this study were derived from a pilot implementation of BMT conducted As part of the pilot, BMT was integrated into existing MMT clinics, with trained providers delivering care at district-based main clinics and commune-level dispensing sites to enhance accessibility and resource efficiency.

Study site and time: The study was conducted in Lai Chau, Dien Bien, and Son La from 2019 to 2020.

Study subjects: A retrospective cohort study was conducted to collect data of participants who had started either 1) BMT between April 2019 and April 2020 or 2) MMT between January 2019 and January 2020, with MMT serving as the comparison group. We recruited MMT participants three months before the start of BMT to prevent provider-induced bias that might favour the new treatment (BMT).

Sample size and sampling methods: A convenient sampling method was applied. All patients who started MMT between 1/2019 and 1/2020 or BMT between 4/2019 and 4/2020 were invited to participate in the study by clinic staffs. All participants provided informed consent to join the study. Ultimately, 505 patients were enrolled (222 in the MMT group and 283 in the BMT group).

Study variables and qualitative research topics

Primary outcomes: 1) Opioid use (It was defined as a positive urine drug screen with morphine (9) and 2) treatment discontinuation (Participants who had not taken medication for at least 30 consecutive days were considered to have discontinued treatment (10)).

Covariates: 1) Demographic characteristics, 2) drug use history and 3) opioid treatment from medical records.

Processing and analyzing data

We used Chi-square, Mann-Whitney tests, depicted the prevalence, a mixed-effect analysis, the mixed-effects logistic regression model, random effects. To fit the final models for mixed effects regression, we first based on prior knowledge to select covariates. Thus, we adjusted for potential confounders such as age, gender, and educational attainment in the final model regardless of its p-values in univariable models. We also included the exploratory variables of interest for this study including MOUD type (MMT vs. BMT) and type of clinic (main clinic vs. dispensing site). Ultimately, we also considered covariates that had p-values from univariable models less than 0.1.

To explore treatment discontinuation, we used time-to-event analysis, with the time starting from treatment initiation and ending at discontinuation, or when 12 months had passed or the study ended. A Kaplan-Meier

curve illustrated probabilities of treatment discontinuation in MMT and BMT groups. We built a Cox regression model to explore risk factors of treatment discontinuation. We tested the proportional-hazards assumption using Schoenfeld residuals test for covariates that were included in the Cox final model including age, sex, education, MOUD type, type of clinic, concurrent methamphetamine use, received counselling. The assumption was met for all those covariates (p-values of proportional hazards test > 0.05). All analysis was performed in STATA/MP 14.0.

Research ethics: The study was approved by the Institutional Review Board of Hanoi Medical University (IRB) under approval number #32/HMUIRB on 23 August 2019.

RESULTS

Participant Characteristics

Table 1 presented the characteristics of 505 participants (283 under BMT and 222 under MMT). Compared with MMT participants, more BMT participants were female (10.9% vs. 5.4%, p-value 0.027), had never been to school or were illiterate (29.9% vs. 15.6%, p-value <0.001).

Regarding drug use, participants who received BMT had a longer history of heroin use (7.0 vs 6.0 [years], p-value 0.038) but were more likely not to use opioids in the last 3 months (78.4% vs. 63.1%, p-value <0.001). Significantly more BMT participants had concurrent methamphetamine use (26.9% vs. 2.3%, p-value <0.001).

Regarding OUD treatment, more BMT participants received a high medication dose (59.4% vs. 33.8%, p-value <0.001). They were also more likely to receive treatment at a dispensing site (47.3% vs. 29.3%, p-value <0.001). More BMT participants received less than one counselling session per month (23.0% vs. 13.5%, p-value <0.001). Participants in the two groups were similar in other variables.

Table 1. Demographic characteristics and OUD treatment (n=505)

	Total (n=505)	Buprenorphine (n = 283)	Methadone (n = 222)	p-value
Sex at birth				
Male	462 (91.5)	252 (89.1)	210 (94.6)	0.027
Female	43 (8.5)	31 (10.9)	12 (5.4)	
Educational level				
Never been to school/Illiterate	118 (23.6)*	84 (29.9)	34 (15.6)	<0.001
Middle school and below	236 (47.3)	114 (40.6)	122 (56.0)	
High school and above	145 (29.1)	83 (29.5)	62 (28.4)	
Dose (MMT cut-off of 60 mg/day, BUP cut-off of 16 mg/day)				
Low	303 (60.0)	115 (40.6)	147 (66.2)	<0.001
High	202 (40.0)	168 (59.4)	75 (33.8)	
Years of heroin regular use (Median, IQR)	6.0 (8.0)	7.0 (8.0)	6.0 (7.0)	0.038
Opioid use within the last 3 months of presentation				
No	362 (71.7)	222 (78.4)	140 (63.1)	<0.001
Yes	143 (28.3)	61 (21.5)	82 (36.9)	

	Total (n=505)	Buprenorphine (n = 283)	Methadone (n = 222)	p-value
Concurrent methamphetamine use				
No	424 (84.0)	207 (73.1)	217 (97.7)	<0.001
Yes	81 (16.0)	76 (26.9)	5 (2.3)	
Type of clinic				
Main clinics	306 (60.6)	149 (52.6)	157 (70.7)	<0.001
Dispensing sites	199 (39.4)	134 (47.3)	65 (29.3)	
Counselling sessions received (Median, IQR)	7 (7)	7 (7)	9 (7)	0.127
None	39 (7.7)	12 (4.2)	27 (12.2)	<0.001
Less than once per month	95 (18.8)	65 (23.0)	30 (13.5)	
Monthly	371 (73.5)	206 (72.8)	165 (74.3)	

**Predominant ethnic in Vietnam; IQR: Interquartile Range*

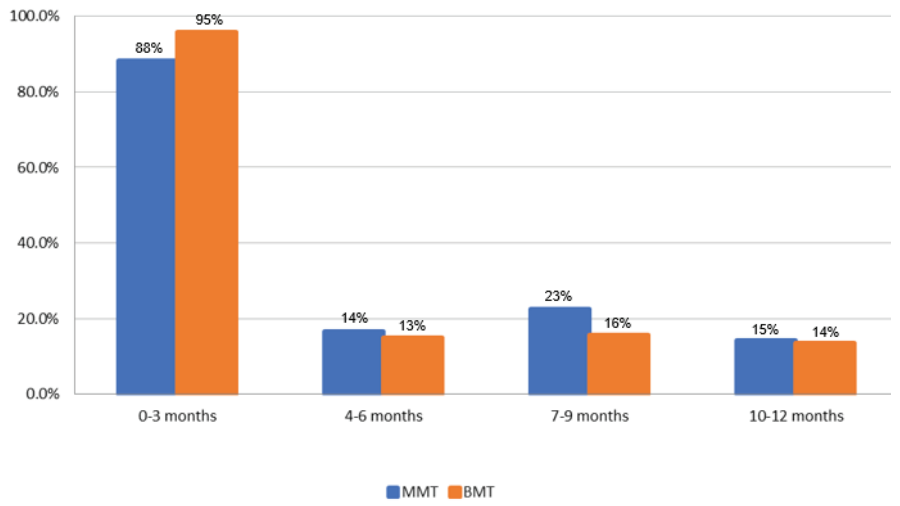

Figure 1. Urine tests positive with morphine over time (n=505)*

** Statistical comparisons between MMT and BMT showed significant differences at 0-3 months ($p < 0.001$), but no significant differences at 4-6 months ($p = 0.168$), 7-9 months ($p = 0.240$), or 10-12 months ($p = 0.772$).*

Opioid Use During Treatment

Opioid use decreased significantly in both BMT and MMT groups overtime (from 95.8% to 13.5% and from 88.3% to 14.3%, respectively) (Figure 1). Opioid use was more common among BMT participants in the first three months of treatment (95.8% vs. 88.3%, p-value 0.001) but we found no significant differences in the following months.

The multivariable mixed-effects logistic regression model (Table 2) shows that age (AOR=0.98, 95% CI: 0.97-0.99, p<0.001), having a high school or above education level compared to having never been to school (AOR=0.73, 95% CI: 0.54 – 0.99, p=0.046) and concurrent methamphetamine use (AOR=1.72, 95% CI: 1.35-2.19, p <0.001) were significant predictors for opioid use among BMT participants throughout the 12 months of treatment.

Table 2. Results from mixed-effects logistic regression model on opioid use during the 12 months after BMT or MMT initiation (n=505)

	Crude Odds Ratio (95% CI)	p-value	Adjusted Odds Ratio (95% CI)	p-value
Age	0.98 (0.97 – 0.99)	<0.001	0.98 (0.97 – 0.99)	<0.001
Education				
Never been to school/Illiterate	1		1	
Middle school and below	0.98 (0.79 – 1.22)	0.860	0.88 (0.67 – 1.16)	0.375
High school and above	0.84 (0.66 – 1.06)	0.142	0.73 (0.54 – 0.99)	0.046
Concurrent methamphetamine use				
No	1		1	
Yes	1.68 (1.37 – 2.07)	<0.001	1.72 (1.35 – 2.19)	<0.001

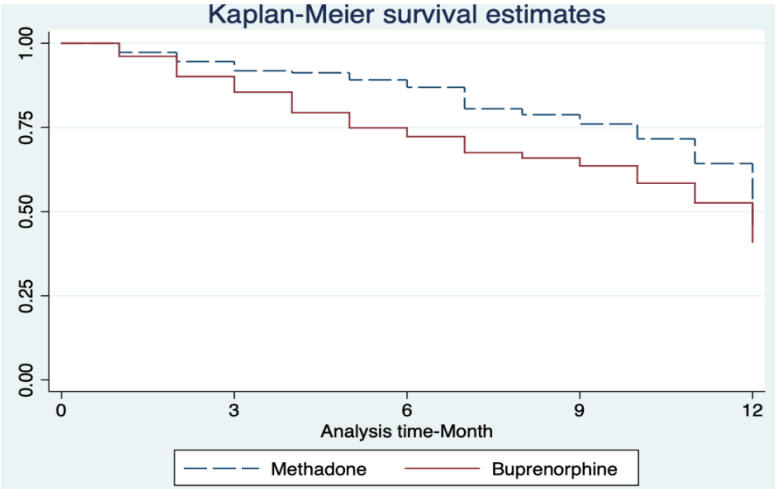

Figure 2. Kaplan-Meier survival curves for time to treatment discontinuation, stratified by methadone and buprenorphine groups. (logrank test: p = 0.0035)

Treatment Discontinuation

Figure 2 presents the Kaplan-Meier survival curves for the length of time until treatment discontinuation in the two treatment groups. The overall retention rate after 12 months of MMT participants was higher than that of BMT participants (62.2% vs. 48.1%, log-rank test p=0.0035, detailed data shown in table 3).

Table 3. Survival rates for MMT and BMT participants over 12 months

Month Interval	MMT	BMT
	Survival (95% CI)	Survival (95% CI)
1 - 2	0.973 (0.940 - 0.988)	0.961 (0.931 - 0.978)
2 - 3	0.943 (0.902 - 0.967)	0.901 (0.860 - 0.930)
3 - 4	0.914 (0.865 - 0.946)	0.854 (0.807 - 0.890)

Month Interval	MMT	BMT
	Survival (95% CI)	Survival (95% CI)
4 - 5	0.908 (0.857 - 0.941)	0.792 (0.740 - 0.835)
5 - 6	0.887 (0.829 - 0.925)	0.744 (0.688 - 0.792)
6 -7	0.864 (0.801 - 0.907)	0.717 (0.659 - 0.767)
7 - 8	0.798 (0.723 - 0.854)	0.658 (0.594 - 0.716)
8 - 9	0.778 (0.702 - 0.839)	0.640 (0.572 - 0.700)
9 - 10	0.749 (0.667 - 0.815)	0.613 (0.538 - 0.680)
10 - 11	0.701 (0.609 - 0.775)	0.552 (0.456 - 0.638)
11 - 12	0.622 (0.516 - 0.711)	0.481 (0.355 - 0.596)

In the multivariable Cox regression model (Table 4), BMT participants were more likely than MMT participants to discontinue treatment (aHR=1.88, 95% CI: 1.28-2.77, p-value 0.001). Younger individuals (aHR=0.96, 95% CI: 0.95-0.98, p-value 0.001), and those who had higher education level compared to having never been to school (Secondary school and above: aHR=2.46, 95% CI: 1.21 – 4.99, p = 0.013; High school and above: aHR=2.56, 95% CI: 1.21 – 5.43, p = 0.014) were more likely to discontinue treatment.

Table 4. Results from a Cox regression model on treatment discontinuation

	Crude Hazard Ratio (95% CI)	p-value	Adjusted Hazard Ratio (95% CI)	p-value
MOUD type				
Methadone	1		1	
Buprenorphine	1.63 (1.16 – 2.30)	0.005	1.88 (1.28 – 2.77)	0.001
Age	0.96 (0.95 – 0.99)	0.001	0.96 (0.95 – 0.98)	<0.001
Education				
Never been to school/Illiterate	1		1	
Secondary school and below	2.17 (1.24 – 3.80)	0.006	2.46 (1.21 – 4.99)	0.013
High school and above	2.41 (1.36 – 4.26)	0.003	2.56 (1.21 – 5.43)	0.014

DISCUSSION

This study compared the effectiveness BMT and MMT in a resource-limited setting, focusing on opioid use reduction and treatment discontinuation. While BMT and MMT demonstrated comparable efficacy on opioid use reduction, differences were observed in treatment discontinuation.

Concurring with previous studies, we found that both buprenorphine and methadone were effective at reducing opioid use among participants (11, 12). Among 303 patients enrolled between July 2005 and December 2007, retention in buprenorphine/naloxone treatment was 74%, 67%, 59% and 49% during Quarters 1,2 3, and 4, respectively. Past 30 day illicit opioid use decreased from

84% of patients at baseline to 42% in retained patients over the year. Patients were 52% less likely to use illicit opioids for each quarter in treatment (OR = .66; 95% CI 0.61–0.72. In both groups, opioid use decreased by more than four times after just three months of treatment. Although buprenorphine participants had higher initial opioid use, these findings suggest both treatments achieve similar outcomes, supporting buprenorphine as a viable alternative. The results emphasize the importance of early engagement and retention in MOUD treatment, and highlight the potential for expanding access to both medications in settings like Vietnam.

Participants with a urine test positive with methamphetamine at any time during the study period had higher odds of opioid use. This link between methamphetamine use and opioid relapse has been established in previous studies, both in Vietnam and other countries (13) but methamphetamine and alcohol use are growing rapidly and, as in other countries, polysubstance use is widespread. The objective of this study was to understand the interplay between heroin, methamphetamine, and alcohol use among people with opioid use disorder (OUD. Given the increasing methamphetamine use among people with OUD under maintenance treatment in Vietnam (14, 15) and to identify risk factors associated with higher severity of methamphetamine use. We used survey data and medical record abstractions from 428 people with opioid use disorder who also use methamphetamine while partaking in methadone treatment in five clinics in Hanoi, Vietnam. We used multinomial logistic regression to assess other risk factors and problems associated with high methamphetamine use severity. Those who reported injecting heroin in the past 3 months (AOR = 4.05, 95% CI [1.30, 12.55], p = 0.02, methamphetamine use interventions that are integrated into maintenance treatment programs for OUD would ensure the effectiveness of both opioid and methamphetamine use treatments.

Our finding that BMT participants were more likely to discontinue treatment than MMT participants is similar to what prior work showed (2, 16). In our study, the overall retention rate after 12 months was 62.2% for MMT and 48.1% for BMT, aligning with or exceeding those reported in other global studies (17). The difference in treatment discontinuation between the two medications in our study may be influenced by various factors. One possible explanation for this difference, as noted by Oesterle et al. (2019), is that methadone's greater dosing flexibility may contribute to a higher degree of chemical dependency, which, in turn, might encourage greater retention in treatment (2). These factors may contribute to buprenorphine's higher treatment discontinuation compared to methadone, and further research is needed to explore this issue.

Study limitations: The cohort study used retrospective data from medical records. Data from different clinics were inconsistent. To address this, we used mixed-effects models, which can handle unbalanced or incomplete data over time. Additionally, we only assessed BMT outcomes at 12-month follow-up. Our focus on the 12-month outcome may not capture these longer-term trends, potentially overestimating the difference in treatment discontinuation between BMT and MMT in the longer term.

CONCLUSION

Buprenorphine and methadone were both effective in reducing opioid use, but participants receiving BMT are at higher risk of dropouts. Additionally, methamphetamine use was associated with increased opioid use during treatment. While this pilot study was conducted in 2019–2020 and BMT has not been scaled up in Vietnam since, the findings

provide valuable insights into retention challenges and co-occurring substance use in OUD treatment that may inform future initiatives or research in similar settings.

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