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A review of factors associated with methadone maintenance treatment adherence and retention in Vietnam

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Abstract

Background: Starting in 2008, Vietnam's national MMT program expanded quickly, but it is struggling with increasing attrition rates and poor adherence among patients. Several studies have reported on MMT retention and adherence, but no overview has yet been published. The objective of this study is to fill that gap and to review factors associated with retention and adherence in MMT in Vietnam.

Methods: A systematic search was conducted using databases of literature - Pubmed, Cochrane, Scopus, Academic search premiere, and SoINDEX. Peer-reviewed empirical studies with full text in English discussing retention attrition and adherence regarding MMT in Vietnam were selected. The results were synthesized using qualitative methods.

Results: Adherence and retention rates varied among the 11 included studies. In general, patients in mountainous provinces had lower adherence and retention rates than those in big cities.

Retention rates decreased with the studies' follow-up period and had a downward trend over time. Factors associated with adherence and retention can be classified into three groups: individual,

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CRediT authorship contribution statement

Thuong Nong, MBA: Study conception, project implementation, data collection & analysis, interpretation of data, initial draft, and substantial revisions. **Dominic Hodgkin, PhD:** Overview of methods, interpretation of data, and substantial revisions. **Nguyen Thu Trang, PhD:** Study conception, project implementation, interpretation of data, and substantial revisions. **Steven J. Shoptaw, PhD:** Study conception, project implementation, interpretation of data, and substantial revisions. **Michael J. Li, MPH., PhD:** Study conception, project implementation, interpretation of data, and substantial revisions. **Hoang Thi Hai Van, MD., PhD:** Study conception, project implementation, data collection & analysis, interpretation of data, and substantial revisions. **Le Minh Giang, MD., PhD:** Study conception, project implementation, interpretation of data, and substantial revisions.

Declaration of Competing Interest

The authors report no conflicts of interest.

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community, and institutional factors. Important individual factors are age, education, awareness of MMT and HIV, and co-occurring disorders and comorbidities. Stigma is the major community risk factor, and methadone daily dose, the distance between home and clinic, and clinic's service hours are the three most important institutional factors.

Conclusions: The literature reviewed identifies important factors associated with MMT adherence and retention in Vietnam. The findings suggest further research exploring both subjective and objective factors and more policies to remove social and structural barriers to enhance treatment outcomes.

Keywords

Retention; Adherence; Attrition; Methadone maintenance treatment; MMT

1. Background

Methadone is a medication approved by the U.S. Food and Drug Administration (FDA) to treat opioid use disorder (OUD), and treatment involving the long-term prescribing of methadone is referred to as methadone maintenance treatment (MMT) (SAMHSA, 2021). Because methadone is a slow-onset and long-acting full opioid agonist, patients benefit from reduced withdrawal symptoms and cravings when they take the medication daily and remain in the treatment program long-term (NIDA, 2021). Poor adherence and poor retention are the main causes of adverse treatment outcomes.

Vietnam is a tropical lower-middle income country with 97 million inhabitants, including an estimated 189,000 people who inject drugs (Edsall et al., 2021). The Vietnamese government implemented MMT in 2008 as a harm reduction strategy for HIV due to the role of injection drug use in HIV transmission and infection (FHI 360, 2014). With the success of the MMT program in reducing opioid use and HIV transmission, in 2012, the Vietnamese government rapidly scaled it up nationwide to provide treatment to 80,000 people, about 50 % of the estimated total people with OUD in Vietnam at the time. Starting in 2008 with just a few piloted MMT clinics in two provinces, by the end of 2019 Vietnam had 335 clinics serving 52,200 patients across the nation (Ministry of Health, 2020).

Currently, MMT is the main medication for opioid use disorder (MOUD) in Vietnam. Following the implementation of MMT, in 2017, Vietnam had a buprenorphine treatment pilot, in the mountainous area to support patients whose access to methadone treatment is limited by distance and related factors (Korthuis, 2020). By the end of 2019, the buprenorphine treatment pilot served 351 patients in 7 mountainous provinces (Ministry of Health, 2020). However, the government has not yet developed a clear plan to support the expansion of this treatment. The government currently prefers buprenorphine less than methadone due to its high cost.

Despite the rapid expansion, Vietnam is now facing challenges to maintain the treatment outcome metrics that it achieved at the initial stage of the MMT program, with an increase in attrition rates across multiple regions. The attrition rate in the first six months of treatment in Ho Chi Minh City, one of the first two pilot provinces, was 1.9 % in 2008 and 8.8 % in

2009, but had increased to 26.6 % by 2011 (PAC of Ho Chi Minh city, 2011). In Hai Phong, another pilot province, the attrition rate during the first 6 months of treatment was only 6 % in 2008 (Ministry of Health, 2012), but by 2017, a longitudinal study showed a higher attrition rate of 23 % during the first 2 years and 33 % during the first 3 years (Pham et al., 2017).

In addition, patients' adherence rate is now lower than when the MMT program was initiated. In a study observing patients of the pilot clinics in Hai Phong and Ho Chi Minh cities from 2009 to 2011, 27.6 % patients missed dose for 1–2 days after 24 months of treatment, the equivalent of more than 70 % patients having complete adherence (FHI 360, 2014). A cross-sectional study in Nam Dinh province from January to September in 2018 reported a complete adherence rate of 43.3 % during the time of research although this result may not be typical nationally (Le et al., 2020a). Concurrent use of illicit drugs is another concern impacting Vietnam's MMT program.

Alongside the opioid epidemic, methamphetamine use in MMT patients has become a major emerging factor that has complicated MMT efforts throughout Vietnam (Nong et al., 2022). Methamphetamine co-use has become common among MMT patients (Le et al., 2019), with the estimates of prevalence ranging from 24 % to 51 % (Michel et al., 2017; Feelemyer et al., 2018). Return to opioid use and injection drug use are among the negative MMT outcomes linked to methamphetamine co-use (Hoang et al., 2018; Le et al., 2022).

Currently, Vietnam has inconsistent laws pursuing two different approaches to substance use disorders (SUD). The health sector considers people who use drugs (PWUD) as patients and provides them with MMT treatment. However, the labor and public security sectors follow procedures to compel PWUD to attend compulsory treatment centers, because drug use violates the Administrative Sanction Law (The National Assembly of Vietnam, 2012). The compulsory treatment model is criticized by international organizations as ineffective and non-evidence-based (United Nations, 2012). In 2013, the prime minister approved the Drug Rehabilitation Renovation Plan to promote voluntary, community-based treatment and reduce the number of public drug detoxification centers (which were called compulsory treatment centers at the time) and the number of PWUD detained in these centers from 63 % to 6 % by 2020 (Hieu et al., 2021). However, as of April 2020, Vietnam still had 97 public drug detoxification centers with 34,982 residents. The privatization process of treatment facilities has been slow. There were only 16 private drug detoxification facilities countrywide. Additionally, only 13 provinces and cities implemented family and community-based detoxification and provided services to 1711 people as of April 2020 (Hieu et al., 2021). With the support of the United Nations Office on Drugs and Crime (UNODC), Vietnam launched the first program for prisoners in Hanoi in 2015. Although Vietnam's Ministry of Public Service estimated that around 30 % of prisoners used drugs in 2015 (Talking Drugs, n.d.), MMT in prisons has not been prioritized to extend to other provinces in Vietnam. As the compulsory treatment centers compete for the government's investment, the low retention rate of MMT patients puts the health sector in a more disadvantaged position to advocate for the MMT programs in Vietnam (Nong et al., 2022).

Currently, many countries in Asia still utilize compulsory treatment for people who use drugs (UNAIDS, 2022; Lunze et al., 2018). Nine of these countries (China, Lao PDR, the Philippines, Malaysia, Myanmar, Thailand, Indonesia, Cambodia, and Vietnam) have committed to transitioning from compulsory treatment centers towards community-based voluntary treatment in health centers (Lunze et al., 2018). The introduction and increase of MMT are a part of the countries' effort to shift from punitive practice (compulsory treatment) to voluntary evidence-based treatment. Seven of the nine countries (except for Lao PDR and the Philippines) are providing MMT at different scales. The United Nations Office on Drugs and Crime and the Joint United Nations Program on HIV/AIDS (UNAIDS) issued a report on evidence-based treatment examples in East and Southeast Asia which highlighted the national scale-up of methadone treatment of Vietnam as one of the few best practices supporting the transition to voluntary community-based alternatives (UNODC and UNAIDS, 2022). Moreover, Vietnam was also one of the three countries, together with Indonesia and Malaysia pioneering MMT in closed settings in East and Southeast Asia (Ministry of Health, Viet Nam, 2018). Despite the political commitment to end compulsory treatment, the recent report by UNAIDS and UNODC also revealed that the number of compulsory treatment centers and people detained in these centers in seven countries in East and Southeast Asia (Cambodia, China, Laos, Malaysia, Philippines, Thailand, and Vietnam) has increased annually in most of these countries between 2012 and 2018. Methamphetamine use was significantly related to admission to compulsory treatment in the countries reporting data (Cambodia, China, Indonesia, Malaysia, Philippines, Thailand). In 2018, the prevalence of admission to compulsory facilities due to methamphetamine use was 51–97 % in Cambodia, Indonesia, Malaysia, the Philippines, and Thailand. UNODC and UNAIDS continue to call on East and Southeast Asia countries to reallocate funding from compulsory treatment modalities toward voluntary treatment and implement and scale up voluntary community-based treatment and services including opioid agonist therapy (UNODC and UNAIDS, 2022).

There are several studies on MMT treatment in Vietnam but there is no overview of adherence and retention. To fill this gap, we conduct a review of associated factors for MMT patients' treatment adherence and retention in Vietnam. Adherence and retention are distinct but related concepts. For purposes of this review, we refer to adherence as the degree of a patient's uptake of a treatment regime and medication compliance, while retention is the continued participation and/or attendance in their treatment, which is necessary for adherence (Holtzman et al., 2015). The study's findings will directly benefit Vietnamese policymakers and MMT clinic management by increasing their knowledge of factors that influence patients' adherence and retention and suggesting policies to improve treatment outcomes. Moreover, as Vietnam's MMT program is advanced in the region, other neighbors of Vietnam can also learn from the findings. More importantly, given the common political trend from compulsory to voluntary treatment, the study may encourage the governments of both Vietnam and neighboring countries to increase investment and support for MMT.

2. Method

2.1. Search strategy and selection process

A scoping review was conducted to review literature related to MMT treatment in Vietnam from January 2008 (the year the MMT pilots started) to November 2021 (the time of the search). Literature was searched using the following databases: Pubmed, Cochrane, Scopus, Academic search premiere, and SoINDEX. The search terms used for the database search were “opioid OR opiate AND substitution OR maintenance AND treatment OR therapy OR medication-assisted OR methadone OR opiate substitution treatment AND vietnam OR viet nam”, “methadone Vietnam or viet nam”, and “opioid OR opiate AND substitution OR maintenance AND treatment OR therapy OR medication-assisted OR methadone AND vietnam OR viet AND nam”. The total number of studies found from the database after removing duplicated results was 411. Of 411 articles, 72 studies were identified after the abstract screening, and 57 studies were assessed for full-text review, with 11 studies meeting inclusion criteria. 46 studies were excluded during the full-text review either because they did not directly discuss MMT adherence and retention ($n = 43$), or because they were not peer reviewed empirical papers ($n = 3$). The three excluded studies are a dissertation ($n = 1$), a meta-analysis ($n = 1$), and a literature review ($n = 1$). Lead author Thuong Nong searched articles on the databases, screened the abstracts, and reviewed the full text with the assistance of two research assistants from Hanoi Medical University. Fig. 1 illustrates the selection process.

2.2. Selection criteria

Eligibility criteria for inclusion of studies were: published in English and peer-reviewed empirical study (including qualitative and quantitative) that reported study settings, study population, research design, sample size, and factors associated with MMT adherence and retention. The systematic review excluded studies that were literature reviews, meta-analyses, dissertations, conference abstracts, and those without the abstract or full text in English (Peters et al., 2020).

2.3. Data abstraction and analysis

Among the 11 studies that met inclusion criteria, study designs included the following: cross-sectional studies ($n = 6$), retrospective study ($n = 1$), longitudinal study ($n = 1$) and qualitative studies ($n = 3$). 9 studies were conducted in MMT clinics, one study in both public and private MMT clinics, and one in HIV testing sites. The sample size varied from 17 to 2638. Study participants were MMT patients, people living with HIV (PLHA) who were also MMT patients, health care workers, people who inject drugs (PWID) who were also living with HIV, and family members. A spreadsheet was created to collect information on the authors' names, study site, study population, study design, study setting, and associated factors discussed in each article (Table 1).

Adapting the social ecological model (SEM) framework in the study of Bronfenbrenner, we categorized the protective and risk factors into three levels: individual, community and institutional levels (Bronfenbrenner, 1979). In this review, interpersonal relationship in the SEM framework is included in community-level factors and public policy is captured in

institutional factors. Under each factor category, findings in the selected studies were coded and presented in subthemes (Section 3.2). Findings about each factor's association with adherence or retention will be reported separately.

3. Results

3.1. Adherence and retention rate

The included studies measured the adherence rate based on the number of self-reported doses according to Vietnam MOH's criteria or the visual analog scale (VAS) or both. The MOH had guidance to assess adherence to MMT with three questions on 1) the number of daily doses missed in the last 3 days; 2) the number of doses missed during the last weekend; and 3) the number of doses missed in the last 3 months. Patients were considered to have achieved optimal adherence if they reported "none" to all three questions. The VAS method assessed the adherence in the past 7 days using a 100-point visual analog scale (VAS) scoring from 0 (non-adherence) to 100 (perfect adherence).

Of 11 included studies, there were 4 studies focusing on retention, 5 on adherence and 2 on both topics. Adherence and retention rates varied among the included studies. Generally, patients in mountainous or rural provinces had lower adherence rates than those in large metropolitan areas (Nguyen et al., 2017; Le et al., 2020b). The adherence rate in the mountainous and rural settings was 34.4 % and 43.3 % respectively (Nguyen et al., 2017; Le et al., 2020a) compared with a range of 61.8–80.9 % and 82.3 % in the big cities (Tran et al., 2018; Le et al., 2020b). Retention rates decreased with the studies' follow-up period and had a downward trend over time. One study reported a retention rate of 92 % in 2008 and 90 % in 2009, and 83.4 % in 2011 (PAC of Ho Chi Minh city, 2011). However, a longitudinal study in 2017 showed that the retention rate was 77 % during the first 2 years and 67 % during the first 3 years of client follow-up in Hai Phong city (Pham et al., 2017). The same trend was also found in another longitudinal study in Thai Nguyen. The retention rate dropped annually to 71.7 % after 4 follow-up years (Dao et al., 2018).

3.2. Factors associated with adherence and retention

Studies were investigated in terms of both protective and risk factors for MMT patients' adherence and retention. The analysis results are captured in Table 1, Table 2, and Fig. 2.

3.2.1. Individual factors—Individual factors included patients' sociodemographic characteristics, substance use before and during treatment, economic status, awareness of HIV and MMT, co-occurring disorders and comorbidities, and the length of treatment time.

3.2.1.1. Sociodemographic characteristics: Sociodemographic characteristics were found to have a strong association with patients' adherence and retention. Age was one important factor influencing patients' adherence to treatment. Patients of older age were reported to have better adherence ($n = 4$) (Tran et al., 2018; Pham et al., 2017; Le et al., 2020a; Nguyen et al., 2017). The study by Pham et al. on 1055 MMT patients in Hai Phong city showed that patients aged 51–69 had no treatment attrition and only accounted for 11.3 % of the total dose missing cases between 27 and 36 months of treatment, while the attrition

rate and missing dose rates in the younger groups were higher (up to 60.7 % and 50.9 %, respectively). Comparable patterns have been shown among patients in mountainous areas (i.e., Tuyen Quang province). Patients aged 50 and older in Tuyen Quang also had better adherence than younger ones (Nguyen et al., 2017).

Interestingly, higher education was found to be associated with lower treatment adherence in both cities and mountainous areas (n = 3) (Nguyen et al., 2017; Le et al., 2020a; Tran et al., 2018). It can be interpreted that patients with higher education might have more employment and social network opportunities, which may conflict with the medication schedule. Patient job types and income also affected their treatment adherence in various ways. Patients who worked as farmers, had low-income jobs, had mobile jobs, and had financial issues were observed to have low adherence. (Nguyen et al., 2017). Low income reduced the ability to pay for co-payment fees for MMT and transportation to MMT clinics, which hindered retention, and in turn, treatment adherence (Kiriazova et al., 2020; Pham et al., 2017).

Unmarried patients had better adherence than their married peers (n = 2) (Pham et al., 2017; Le et al., 2020b). In another similar finding, married patients who disclosed their health issues to their spouses and partners were more likely to miss their doses (Tran et al., 2018).

3.2.1.2. Clinical characteristics.: Patients' substance use before and during treatment was also included in several studies' analysis of adherence factors. Patients who had long years of drug use had better treatment adherence (n = 2) (Tran et al., 2018; Le et al., 2020b). However, concurrent use of substances (heroin and alcohol) during treatment reduced patients' adherence (n = 4) (Kiriazova et al., 2020; Le et al., 2020b; Pham et al., 2017). The pattern of use of substances also impacted patients' adherence differently. Injection patients had a lower adherence rate than non-injection ones. One study reported that smoking motivated patients' treatment. Tobacco, as a substitute, could help patients relieve the withdrawal symptoms and had benefits to support patient's adherence for the short-term (Nguyen et al., 2017). However, such tobacco use might put patients at a higher risk of morbidities and poor health status.

Lack of awareness of MMT and HIV was one of the reasons for patients' poor adherence and retention (n = 4) (Nguyen et al., 2017; Kiriazova et al., 2020). Patients were reportedly unmotivated to maintain their daily treatment because they had a negative opinion about methadone, considering it as a "free street drug" (Kiriazova et al., 2020) or a harmful drug; Their inadequate knowledge of HIV risk and MMT treatment benefits also reduced their motivation to adhere to the treatment (Nguyen et al., 2017). MMT patients who were living with HIV skipped their doses or stopped their treatment due to fear of the interaction between antiretroviral therapy (ART) and methadone (Kiriazova et al., 2020; Nguyen et al., 2017). This finding highlights the need for drug and health education for patients.

There was a high prevalence of co-occurring disorders and comorbidities among Vietnamese MMT patients, and these conditions' impact on MMT treatment was reported differently among the studies (n = 4). In a mountainous area, nonadherence was found to be higher among MMT patients who had pain and discomfort (Nguyen et al., 2017). However, in large metropolitan areas, patients who had pain and discomfort or other comorbidities had

better adherence than non-cooccurring/comorbidity patients ($n = 3$) (Mughal et al., 2021; Le et al., 2020b; Tran et al., 2018). HIV serostatus was reported as either negatively (Tran et al., 2018) or positively associated (Le et al., 2020b). One study also found that self-care and antiretroviral therapy (ART) supported MMT adherence (Tran et al., 2018). This could explain why HIV serostatus may affect patients' health outcomes and interrupt MMT. However, ART enables patients to receive more information and referrals to different healthcare services from counselors, which may in turn improve their health outcomes and MMT adherence. Also, mental health disorders were consistently found to be associated with poor adherence ($n = 2$) (Mughal et al., 2021; Nguyen et al., 2017).

Time in treatment had negative relationship with patient's drop-out. One study reported that the risk of drop-out was 36 % and 53 % among patients in their first year in MMT and the second year of the treatment respectively. The risk of drop-out then decreased to 34.5 %, 6.8 %, and 1.9 % from the third year to the fifth year (Dao et al., 2018).

3.2.2. Community factors

3.2.2.1. Family and peers.: As a significant factor, the family's role was discussed in five studies. The study by Le et al. (2020a) found that 77.7 % of surveyed MMT patients considered family as an important source of support for their treatment. Family support had a positive relationship with patients' adherence ($n = 2$); it served as a strong motivation for patients to pursue their treatment and supported patients' treatment cost, provided transportation to clinics, or reminded patients of daily clinic visits (Nguyen et al., 2017). However, two studies reported that family could be a risk factor, with family pressure contributing to patients' unwillingness to seek and adhere to the treatment (Nguyen et al., 2017). The patient also wanted to quit the treatment in order to perform their family responsibilities or to protect their family from the community stigma caused by their MMT participation (Nguyen et al., 2017).

Besides family, peer influence affected adherence and retention. MMT patients considered self-help groups as the main adherence support (Nguyen et al., 2017). Peers had an important role in helping patients access and maintain their treatment (Nguyen et al., 2017). Patients who disclosed their health issues to their friends missed fewer methadone doses than those who disclosed their health issues to their partners and spouses (Tran et al., 2018). However, having contact with peers who were actively using drugs was associated with a higher rate of suboptimal adherence ($n = 2$) (Le et al., 2020b; Nguyen et al., 2017).

3.2.2.2. Community stigma.: Community stigma had a significant negative impact on patients' MMT treatment. Three studies reported that community stigma against people who injected drugs and who were on MMT was a reason for patients' poor engagement in their treatment (Nguyen et al., 2017; Kiriazova et al., 2020). Stigma was measured based on patient's report in these studies. According to the patients in one study, stigma and social devaluation of people who use drugs were common in the community. People in the community did not understand the difference between people who are actively using drugs and MMT patients. Therefore, joining a MMT program meant that they confirmed themselves as "drug users" (Kiriazova et al., 2020) and exposed them to community stigma.

3.2.3. Institutional factors

3.2.3.1. Clinic characteristics.: Clinics' prescription of a higher dose of methadone is associated with a higher rate of adherence ($n = 3$) (Le et al., 2020b; Pham et al., 2017; Nguyen et al., 2017). Patients with a daily dose of more than 60 mg were less likely to miss their doses than those with lower methadone doses. A daily dose of more than 120 mg contributes significantly to decreasing attrition (Pham et al., 2017). One study found high rates of concurrent use of heroin and missing doses among patients during the induction stage. The authors concluded that the initial dose (20 mg) specified by the Ministry of Health's guideline was too low (Nguyen et al., 2017).

Distance from home to the clinic was a factor investigated in several studies ($n = 4$). Patients' non-adherence was correlated with the distance between their homes and the clinics (Nguyen et al., 2017; Johns et al., 2018; Kiriazova et al., 2020). Having to spend more than 30 min going to MMT clinics, or having mobility problems, was associated with a higher attrition rate (Pham et al., 2017; Johns et al., 2018).

Together with the distance between home and clinic, the clinic's service hours were a significant factor. Patients missed their doses or stopped treatment because the clinic's service hours conflicted with their work ($n = 5$) (Nguyen et al., 2017; Johns et al., 2018; Kiriazova et al., 2020; Pham et al., 2017; Tran et al., 2018).

Clinic staff was perceived as an important source to support patients' treatment (Le et al., 2020a), and three studies examined the role of clinic staff. Staff counseling and the attitude of health workers were reported to be critical for patient adherence and retention ($n = 2$) (Dao et al., 2018; Le et al., 2020a). Poor adherence and retention were linked with patients' dissatisfaction with clinic staff, with poor therapeutic relationships between patients and clinic staff, or staff had misconceptions toward the treatment purpose and procedures.

3.2.3.2. Other variables.: Some studies reported on other variables, including the treatment model, referral to treatment for comorbidities, involvement of police, and co-payment for MMT. Firstly, a higher rate of adherence was observed among patients enrolling with MMT clinics providing only MMT and general care services than those with MMT clinics with full services (MMT, HCT, ART, and general care). Tran et al. assumed that the potential interaction of ART and methadone would be the reason for poor adherence among MMT patients who have HIV (Tran et al., 2018). This assumption would be also related to MMT patients who have HCV. In addition, having the same demographic and substance use characteristics, patients of private MMT clinics had better adherence than public MMT clinics (Le et al., 2020a). Currently, public MMT clinics account for more than 90% of the total clinics in Vietnam. In the study of Le et al., both private and public MMT clinics had the same provision of services. However, private MMT clinics were less crowded than their public peers, implying a relationship between the client-to-staff ratio and patient adherence. Next, MMT clinics' referral to treatment services for comorbidities enhanced patients' adherence (Mughal et al., 2021; Pham et al., 2017). Also, one study reported that patients wanted to stay in treatment to avoid the observation of police on drug use in the community and legal issues related to their drug use (Nguyen et al., 2017). Moreover, one study found that the level of co-payment (\$15 per month) was related to 14 % of total

treatment attrition in Hai Phong (Pham et al., 2017) but another study examining the effects of user fees in seven other provinces found no relationship between co-payment and attrition (Johns et al., 2018). Co-payment might not be a barrier for Vietnamese patients to continue their treatment because the level of their cost contribution was much less than their spending on heroin before joining the treatment (Johns et al., 2018). Additionally, MMT patients may be able to afford the contribution because, as part of the Vietnamese family culture, they are often retained and financially supported by their families.

4. Discussion and conclusion

The findings of this review are generally consistent with international literature describing factors linked to outcomes using MMT for OUD. While the study's limitation and some inconsistent findings among the selected studies implied some specific topics for future research, the review's results provide several suggestions for Vietnam's drug-related policies and programs.

4.1. Statement of principal findings

The review provides key findings regarding the factors associated with adherence and retention of MMT in Vietnam. Important individual factors are age, education, awareness of MMT and HIV, and co-occurring disorders and comorbidities. Stigma is the major community risk factor, and methadone daily dose, the distance between home and clinic, and clinic's service hours are the three most important institutional factors.

4.2. Discussion of specific findings

The protective role of older age that was identified in this review confirms earlier work. The review found that in Vietnam, increasing age is associated with increased retention and adherence, which agrees with findings of prior research from other countries (Ruadze and Todadze, 2016; Sarasvita et al., 2012; Strike et al., 2005; Viera et al., 2020). Patients of older age and those who had a long period of drug use have better adherence and retention, possibly because they experienced enough negative and social consequences of drug use, resulting in a greater willingness to accept long-term treatment (Magura et al., 1998; Sarasvita et al., 2012). In Vietnam, patients with low incomes and financial issues have poorer adherence and retention, and this finding is consistent with studies of other countries (Chen et al., 2020). In addition, patients' concurrent use of illicit drugs is a risk factor for adherence and retention (Peles et al., 2008; Gryczynski et al., 2014; Perreault et al., 2008). Family and peers are also important positive factors in other countries (Abrantes et al., 2021; Jalali et al., 2018). Other studies also show that a lack of knowledge of MMT is prevalent among MMT patients (Schwartz et al., 2008; Zaller et al., 2009; Peterson et al., 2010). Patients' perception of MMT benefits is important to motivate them during the treatment (Kayman et al., 2011; Sarasvita et al., 2012). Stigma is a common barrier to treatment adherence and retention in many countries (Smith et al., 2020; Deng et al., 2020). Moreover, misperception of methadone also leads to stigma against MMT patients among their friends, family, community, and service providers. Some Vietnamese MMT patients mistakenly consider methadone as another harmful drug. They reported their fear of addiction to methadone and its harmful effects. Because of this misperception, MMT

patients are not differentiated from PWUD, a group that is stigmatized in the community. The review found that a higher level of education was associated with non-adherence among Vietnamese MMT patients. This finding is in line with the result of a systematic international review by Farmani et al., which reported that literacy level did not have a positive correlation with patient's maintenance in treatment. In fact, patients with higher education were found to have a higher degree of return to use than those who were illiterate (Farmani et al., 2018).

Most of the institutional factors found in the reviewed studies are consistent with the studies of other countries. In Vietnam, there is an association between higher doses of methadone and better adherence. Studies in other countries also examined methadone dose as an important factor and found an association between high doses of methadone and patient retention. Newman (2009) found that a daily dose of more than 80 mg would help most patients with OUD to suppress withdrawal symptoms and block the euphoric effects related to heroin. A lower dose of methadone may not achieve the blockage effect (Newman, 2009), which means that those patients will either experience withdrawal or will supplement using other opioids. Rather than argue over the need for uniformly higher doses, however, the more patient-centered framework is to identify the "right dose" for each patient, i.e., the dose at which withdrawal symptoms are blocked and supplementation of opioids is stopped. In addition, prior research also found that treatment location, service time, distance, staff's performance, and convenience to get service have important influences on adherence and retention (Lin et al., 2015; Zhang et al., 2019), as was found in this review.

The co-use of methamphetamine and other drugs among MMT patients shows detrimental effects on treatment outcomes. Drug use still violates the Administrative Sanction Law, and people who use drugs, including MMT patients who use illicit drugs during treatment, are sent to detention centers. MMT clinics currently have limited influence and ability to help patients when the detention system is involved, when patients experience other social adversity, or when opioid use is coupled with other drugs like methamphetamine.

4.3. Strengths and challenges

This review is the first to synthesize all the factors associated with adherence and retention in MMT in Vietnam. However, this review has some challenges. First, the review is only restricted to English literature without examining grey literature such as unpublished reports by the government and non-profit organizations and thus might miss important studies in Vietnamese and other languages. Moreover, the number of included studies was small compared to the total number of studies on MMT in Vietnam (11 out of 411 studies), and some of the former did not give direct findings or present a correlation. The study samples were small compared to the total number of Vietnamese MMT patients. Therefore, the review's generalizability may be limited. Moreover, all the Vietnam studies measured adherence based on patient self-reports, which could affect findings if self-reports are biased.

4.4. Areas for future research

Some inconsistent findings among the studies reviewed suggest that further research is needed to find out if the differences are due to patients' characteristics or to study methods. ARV treatment was reported as a protective factor, but HIV serostatus was reported to be either a risk factor or a protective factor in different studies. Therefore, to examine HIV serostatus as a factor, it is important to know whether participants with HIV are on ARV treatment. Moreover, married patients were reported to have poorer adherence and retention. Unmarried patients often live with their families and receive financial and emotional support from family and relatives. Therefore, compared with unmarried patients who live with their extended family, married patients may have more financial pressure and need to work. Therefore, studies on marriage factors need to clarify the comparison group (unmarried patients) whether they are living with parents or living alone. In addition, there are interactions among sociodemographic characteristics and between them with other factors. For example, patients with lower income have more self-stigma and stigma from the community and experience more anxiety and depression. Patients' low education is also associated with low income and unemployment, poor self-care, and health issues. Therefore, these relevant variables should be included in future studies to examine thoroughly all the social determinants of health that influence an individual's adherence and retention in MMT.

The inconsistent findings on co-payment also imply the need to investigate further on this factor. Co-payments are recognized as a major access barrier to needed health care (WHO, 2018). This barrier may be greater for people who use drugs, as most of them are low-income people. Studies in other countries showed that copay levels had a significant negative effect on outpatient and inpatient treatment for drug disorders (Stein et al., 2000; Lo Sasso and Lyons, 2002, 2004). MMT patients may be affected by co-payment more because they expect to have free treatment to compensate for their inconvenience and travel time to visit clinics every day. Since the last study on the copayment of MMT in Vietnam was 5 years ago, there should be new and regular surveys on patient satisfaction and willingness to pay user fees among MMT patients, especially for those living in rural areas, homeless people, or patients with comorbidities.

Several factors are missing in the included studies. Most of the studies showed a high prevalence of alcohol and tobacco use (more than 80 %) among MMT patients. However, there is only one study reporting the relationship between tobacco use and MMT adherence, and none of these studies reported alcohol use. Moreover, as mentioned earlier, the proportion of MMT patients using methamphetamine is increasing and has reached 50 % in some clinics. Studies on how methamphetamine use impacts patients' adherence and retention to MMT are needed. In addition, MMT is run in three different types of settings in Vietnam. The majority of MMT clinics are in the community and operated by the Ministry of Health; some are in prisons and run by the Ministry of Public Security; and others are in the community and run by the Ministry of Labor, Invalids, and Social Affairs. Evaluation research comparing patients' adherence and retention among these settings may be helpful to optimize these outcomes. In addition, existing literature only compared the difference in treatment outcomes and characteristics at the patient level between private and public but did not analyze the difference in the service and characteristics of the two types of providers.

An analysis of what makes the private clinics achieve better adherence and retention rate is important because MMT public clinics account for more than 95 % of the total clinics in Vietnam. Also, lack of health insurance is a barrier for MMT patients to access other treatment services. While self-care and access to other treatments were found to be positive factors, there should be a study to compare patients with and without health insurance to understand better the role of health insurance with the treatment effectiveness. Next, the current law requires MMT patients to be sent to compulsory treatment centers if they have two positive drug tests. Many studies reported “arrest” as a reason for attrition. It would be helpful to analyze what was the main reason for the arrest and how the law impacts the patient’s treatment access, adherence, and retention. Moreover, none of the selected studies discussed the impact of the lockdown during the COVID-19 pandemic on the MMT program. It is necessary to have more research assessing the influence of the lockdown and Vietnam’s temporary take-home program for MMT patients to respond to the lockdown in the south and the pilot take-home program in 21 MMT clinics implemented in the north during the pandemic on patients’ access and adherence. Additionally, MMT patients, as people with chronic diseases, can have uptake, engagement, and periodic lapses in treatment uptake. Patients may disengage or discontinue their treatment and return to it later. Therefore, new research evaluating these on a continuum rather than as binary outcomes are needed.

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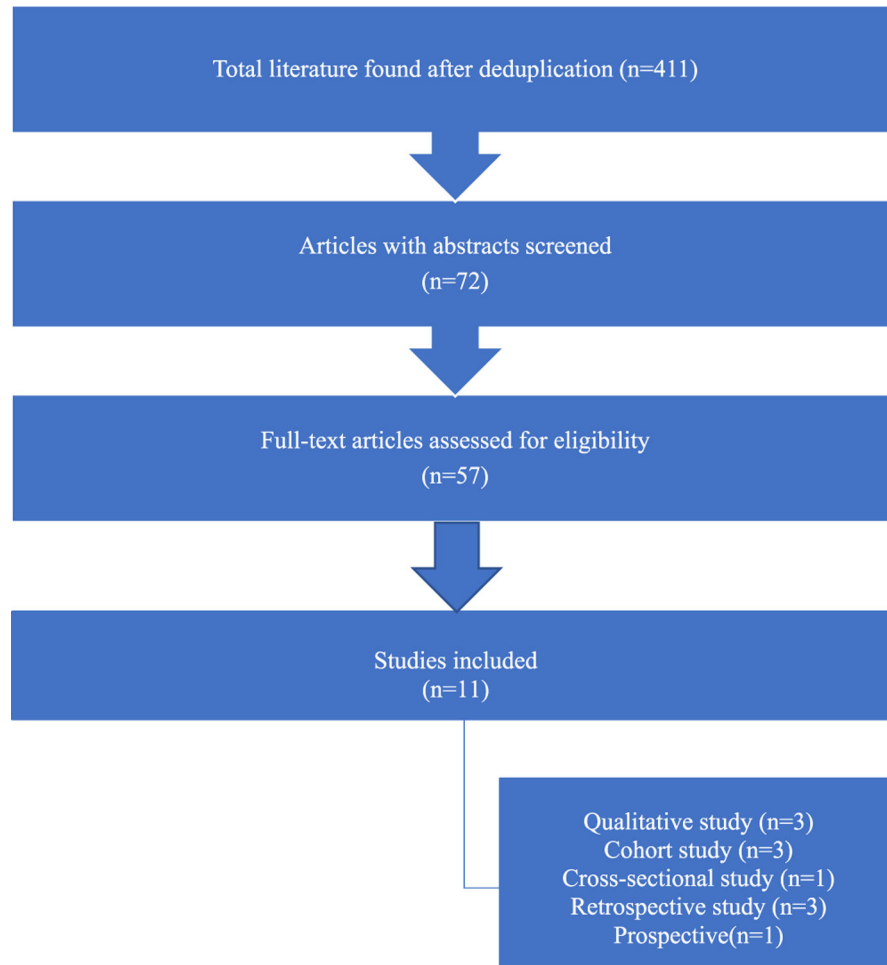


Fig. 1.
Study selection process.

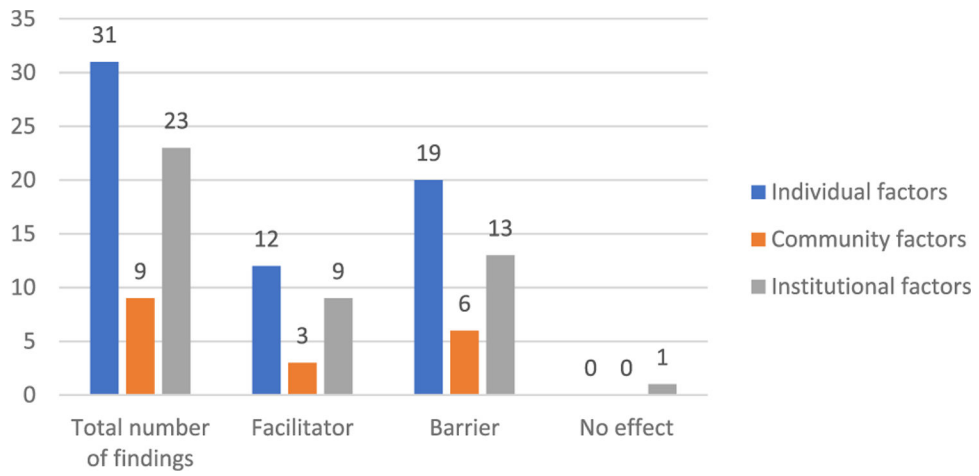


Fig. 2. Associated factors of MMT retention and adherence by factor levels.

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Table 1

Summary of included studies.

Author	Study setting	Site (province)	Study time	Study population	Sample size	Study design	Individual factors	Community factors	Institutional factors
Kiriazova et al. (2020)	HIV testing sites	Thai Nguyen	2015–2016	Healthcare providers, PWID living with HIV	62 (in three countries)	qualitative study	Substance use; negative perception of MMT; fear of interaction	stigma	service schedule; conflict between work and a daily visit to clinic; co-payment; transportation cost
Le et al. (2020b)	MMT clinics	Ho Chi Minh City	2018	MMT patients	450	cross-sectional study	Education level; marital status; time of substance use; concurrent substance use; comorbidity;		Methadone dose; ARV treatment; treatment service satisfaction
Johns et al. (2018)	MMT clinics	Binh Thuan, Dien Bien, Ha Noi, Ho Chi Minh City, Lai Chau, Long An, Thanh Hoa	2015–2016	MMT patients	1050	cohort	HIV serostatus; marital status, job		distance between home and clinic; service hours
	MMT clinics	Hai Phong	2016–2017	MMT patients and people who use drugs	58	qualitative study	perception of MMT;	family	Relationship with clinic staff;
Pham et al. (2017)	MMT clinics	Hai Phong	2011–2012	MMT patients	1055	longitudinal study	HIV serostatus; marital status; age; substance use; mental health issue; HCV		methadone dose; service schedule
Le et al. (2020a)	MMT clinics	Nam Dinh	2019	MMT patients	395	cross-sectional	age, education, marital status, income; smoking; drinking; illicit drug use (pattern)	peer support; family support	MMT model; distance between home and clinic; health worker's support
Dao et al. (2018)	MMT clinics	Thai Nguyen	2011–2015	MMT patients	2638	retrospective study			counseling; MMT treatment time
Nguyen et al. (2017)	MMT clinics	Tuyen Quang		MMT patients	241	cross-sectional study	age; education level, type of job, income; smoking; cooccurring disorders; comorbidities; duration of treatment		
Tran et al. (2018)	MMT clinics	Hanoi	2013	MMT patients	510	cross sectional study	HIV serostatus, age, education, pain/discomfort, poor self-care, disclosure of health issues to spouses/partners	Treatment model (solo vs integrated services)	
Mughal et al. (2021)	MMT clinics	Hanoi	Not stated	MMT patients who are living with HIV	400	cross sectional study	HIV serostatus, common mental health disorders		
Nguyen et al. (2017)	MMT clinics	Can Tho	2010–2015	MMT patients, health workers,	24	qualitative interview	mobile job, financial issues; awareness of HIV and MMT	stigma; peer influence;	low dose of methadone; waiting time; distance

Author	Study setting	Site (province)	Study time	Study population	Sample size	Study design	Individual factors	Community factors	Institutional factors
				and family member				family support and pressure	between home and clinic, conflict between work and daily visit to clinic; police; intersection support

Table 2

Summary of factors associated with adherence or retention.

Factors	Total number of findings on each factor	Facilitator (supporting factor)	Barrier	No effect
Individual factors	31	12	19	0
Sociodemographic characteristics	11	4	7	0
Age	4	4	0	0
Higher education	3	0	3	0
Low income	2	0	2	0
Marital status (married)	2	0	2	0
Substance use	7	2	5	0
Years of drug use before MMT treatment	2	2	0	0
Concurrent use	4	0	4	0
Pattern of use (injection)	1	0	1	0
Lack of awareness of MMT and HIV	4	0	4	0
Co-occurring disorders and comorbidities	8	5	3	0
HIV serostatus	1	1	0	0
Pain and discomfort	4	3	1	0
ART treatment	1	1	0	0
Mental health disorders	2	0	2	0
Time in treatment	1	1	0	0
Community factors	9	3	6	0
Family	3	2	1	0
Peer	3	1	2	0
Community stigma	3	0	3	0
Institutional factors	22	9	12	1
Higher methadone daily dose	3	3	0	0
Distance from home to the clinic	4	0	4	0
Clinic's service hours	5	0	5	0
Performance of clinic staff	3	1	2	0
Other variables	7	5	1	1
Clinic setting	2	2	0	0
MMT and general care service	1	1	0	0
Private clinic	1	1	0	0
Referral to comorbidities treatment	2	2	0	0
Police involvement	1	1	0	0
Co-payment required	2	0	1	1